Abstract Book

Society of Surgical Oncology
72nd Annual Cancer Symposium

San Diego, California
March 27 - 30, 2019

Electronic supplement to
Annals of Surgical Oncology
An Oncology Journal for Surgeons

72nd ANNUAL
Cancer
SYMPOSIUM

Society of Surgical Oncology

March 27-30, 2019 • San Diego, California

Annals of Surgical Oncology
An Oncology Journal for Surgeons

The Official Journal of the Society of Surgical Oncology

Abstract Book

Society of Surgical Oncology
72nd Annual Cancer Symposium
San Diego, California
March 27 – 30, 2019

CONTENTS

Volume 26, Supplement 1, February 2019

This supplement was not sponsored by outside commercial interests.

Session Titles and Abstract Contents

ABSTRACTS

Accepted for
PLENARY and PARALLEL SESSIONS

72nd Annual Cancer Symposium
Society of Surgical Oncology
March 27–30, 2019
San Diego, CA

Ann Surg Oncol (2019) 26:S5–S224
https://doi.org/10.1245/s10434-019-07174-5

1

Local-Regional Recurrence (LRR) Data from the American College of Surgeons Oncology Group (ACOSOG) Z1041 (Alliance): A Randomized Neoadjuvant Trial of Sequential Versus Concurrent Anthracycline with Trastuzumab and Paclitaxel Plus Trastuzumab in HER2-Positive (HER2+) Breast Cancer (BC) K. Hunt,[1]* V. Suman,[2] F. Meric-Bernstam,[1] M. Leitch,[3] M.J. Ellis,[4] J.C. Boughey,[2] G. Unzeitig,[5] M. Royce,[6] A. Buzdar.[1] *1. Breast Surgical Oncology, MD Anderson Cancer Center, Houston, TX; 2. Mayo Clinic, Rochester, MN; 3. UT Southwestern, Dallas, TX; 4. Baylor College of Medicine, Houston, TX; 5. Doctors Hospital of Laredo, Laredo, TX; 6. University of New Mexico School of Medicine, Albuquerque, NM.*

Introduction: The ACOSOG Z1041 trial addressed the timing of trastuzumab with neoadjuvant chemotherapy (NAC) in patients (pts) with HER2+ BC. We previously reported that concurrent or sequential anthracycline and trastuzumab produced similar pathologic complete response in the breast (pCRb), disease-free (DFS) and overall survival (OS) rates. We now report LRR and survival rates based on achievement of pCR in the breast and nodes (pCRb+n). Methods: Operable HER2+ BC pts were randomized to FEC→PT (Arm 1) or PT→FECT (Arm 2) where treatment was 5-FU (F), epirubicin (E) and cyclophosphamide (C) x 4 cycles; paclitaxel (P) and trastuzumab (T) weekly x 12. Eligibility included tumor >2 cm or positive lymph nodes. Stratified log rank test (SLR) was used to assess DFS and OS (from start of NAC) between regimens. Cumulative incidence function for data with competing risks was used to estimate LRR rate among pts who had surgery. Results: From Sept 15, 2007 to Dec 15, 2011, 282 pts (arm 1, n=140; arm 2 n=142) were enrolled. The analysis cohort excludes 2 pts randomized to arm 1 who withdrew consent prior to treatment. With a median follow-up of 5.1 years (yr) after registration, there were 47 disease events and 20 deaths (see table). DFS and OS did not differ by treatment arm (SLR p= 0.933 and 0.734, respectively) or estrogen receptor (ER) status (SLR p= 0.195 and 0.440, respectively). DFS and OS were higher in pts with pCRb+n at surgery compared with pts who had residual disease at surgery (log rank p< 0.001 and p=0.0212, respectively). Estimated 4 yr cumulative incidence of LRR is 2.9%. Conclusions: Concurrent anthracycline with trastuzumab offers no additional benefit in terms of achieving pCR in pts with HER2+ BC. Estimated 4 yr cumulative incidence of LRR after surgery is 2.9%. Achieving pCR is associated with improved DFS and OS.

Disease Events in ACOSOG Z1041

Post registration outcomes	FEC → P+T Arm 1 (n=138)	P+T → FEC+T Arm 2 (n=142)
local recurrence	5	3
regional recurrence	0	2
distant disease	13	16
second primary cancer	2	3
distant disease with second primary	0	1
Deaths		
due to this cancer	5	7
other	1	2
unknown	2	3

2

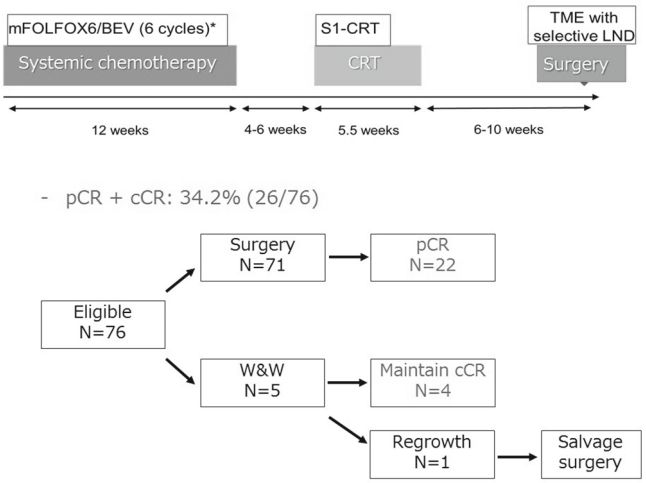
Immune Enrichment Only Improves Outcomes in Pancreatic Cancer with Activated Stroma R. Torphy,[1]* X. Peng,[2] R.A. Moffitt,[3] J. Yeh.[2] *1. University of Colorado, Aurora, CO; 2. University of North Carolina, Chapel Hill, NC; 3. Stony Brook University, Stony Brook, NY.*

Non-negative matrix factor deconvolution previously identified four molecular subtypes of pancreatic cancer (PC) including tumor- (classical vs basal) and stroma-specific (normal vs activated) subtypes. While immunotherapies have had limited success in treating PC, further work is needed to identify new treatment strategies or subtypes that may be more responsive. We evaluated the significance of a computationally defined immune score and its association with outcome. We developed an algorithm, DECODER, to perform an unbiased deconvolution of bulk tumor RNA expression from 145 patients in The Cancer Genome Atlas dataset. DECODER was used to score immune enrichment and to classify tumors as immune high vs low. Immune enrichment was compared across tumor and stroma subtypes. A multivariable model was used to evaluate the association of immune enrichment and overall survival (OS). Intra-tumoral lymphoid structures were quantified on matched hematoxylin and eosin stained tissue to evaluate the correlation with immune enrichment scores. The histologic presence of lymphoid structures correlated with DECODER immune scores with 81.1% of tumors containing lymphoid structures being classified as immune high (p<0.01). There was no difference in immune scores between classical and basal tumor subtypes. Tumors with a normal stroma subtype were more often scored immune high than tumors with activated stroma (69.5% vs 32.9%, p<0.001). On multivariable analysis controlling for tumor and stroma subtype, N stage, T stage, grade, and margins, a high immune score was independently associated with a prolonged OS in patients with activated stroma (HR 0.32, p=0.04), but not in patients with normal stroma (HR 1.07, p=0.87). Molecular quantification of immune enrichment in PC successfully identifies tumors with increased immune infiltrate. Stroma, but not tumor subtype, is associated with immune enrichment with normal stroma being associated with increased immune enrichment. However, immune enrichment is only prognostic in tumors of patients with activated stroma. Future work is needed to characterize if specific cell populations are differentially enriched and its biological significance.

3

Phase II Trial of Neoadjuvant Chemotherapy, Chemoradiotherapy and Laparoscopic Surgery with Selective Lateral Node Dissection for Poor-Risk Rectal Cancer T. Konishi,[1]* E. Shinozaki,[3] K. Murofushi,[2] S. Taguchi,[2] T. Nagasaki,[1] T. Yamaguchi,[1] T. Akiyoshi,[1] Y. Fujimoto,[1] S. Nagayama,[1] Y. Fukunaga,[1] K. Yamaguchi,[3] M. Ueno.[1] *1. Dept of Gastroenterological Surgery, Cancer Institute Hospital, Tokyo, Japan; 2. Dept of Radiation Oncology, Cancer Institute Hospital, Tokyo, Japan; 3. Dept of Medical Oncology, Cancer Institute Hospital, Tokyo, Japan.*

Background: Although neoadjuvant chemoradiotherapy (CRT) reduces local recurrence in rectal cancer, it does not improve survival. Induction chemotherapy has been explored as a novel option to improve oncological outcomes in poor-risk locally advanced rectal cancer (LARC). The present study is designed to evaluate the safety and efficacy of induction FOLFOX with bevacizumab followed by S1-based CRT in MRI-defined poor-risk LARC. Methods: This study was conducted as a prospective phase II trial at a single high-volume cancer center in Japan. Eligible patients had low rectal adenocarcinoma with MRI-defined poor-risk features, including CRM<1mm, T4b, positive lateral node, mesorectal N2 disease and/or requiring APR. Patients received 6 course of mFOLFOX with bevacizumab followed by S1-based CRT (50.4Gy). Surgery was conducted through a laparoscopic approach. Lateral node dissection was selectively added only when the patients had enlarged lateral nodes. Results: A total of 76 patients were eligible for the study. Seventy-three patients completed 6 courses of chemotherapy and 75 completed planned radiation dose. Two cases had GI perforation during neoadjuvant therapy. Seventy-one patients underwent surgery and 22 had pCR. Five patients underwent nonoperative management after cCR and one had local regrowth. Clinical and/or pathological CR rate was 34.2%. All surgical procedures were successfully performed thorough a laparoscopic approach without conversion, including combined resection of adjacent structures (n=18) and lateral node dissection (n=50). Among those underwent surgery, mesorectal ypN+ was found in 14 patients (20%) and lateral ypN+ in 9 patients (13%). Clavien-Dindo grade 3-4 complications occurred in 15 patients (21%). There was no mortality. Conclusions: The present regimen achieved a high CR rate with favorable compliance and tolerable postoperative complications in poor-risk LARC. Multicenter study is warranted to evaluate this regimen.



Phase II trial of induction FOLFOX with bevacizumab followed by S1-based chemoradiotherapy for MRI-defined poor-risk rectal cancer achieved 34.2% complete response.

4

Interim Analysis of a Randomized, Open-Label Phase II Study of Talimogene Laherparepvec Neoadjuvant Treatment Plus Surgery versus Surgery for Resectable Stage IIIB-IVM1a Melanoma

R. Andtbacka,[1] R. Dummer,[2] D.E. Gyorki,[3] A.C. Berger,[4] L. Demidov,[5] E. Chan,[6] S.A. Treichel,[6] M.B. Faries,[7] M.I. Ross.[8]* *1. University of Utah Huntsman Cancer Institute, Salt Lake City, UT; 2. University Hospital of Zurich, Zurich, Switzerland; 3. Olivia Newton-John Cancer Centre, Austin Health, Melbourne, VIC, Australia; 4. Thomas Jefferson University Hospitals, Philadelphia, PA; 5. N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation; 6. Amgen Inc., Thousand Oaks, CA; 7. John Wayne Cancer Institute, Santa Monica, CA; 8. University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: There is no approved neoadjuvant treatment (neo) for resectable stage IIIB-IVM1a melanoma (MEL). Talimogene laherparepvec (T-VEC), a HSV-1-based oncolytic virus, may reduce risk of visceral and bone metastases in unresectable Stage IIIB-IVM1a MEL (Andtbacka SSO 2015). This randomized study evaluated neo T-VEC in high risk resectable MEL (NCT02211131). Methods: Patients (pts) with resectable stage IIIB/C/IVM1a MEL, ≥ 1 injectable cutaneous, subcutaneous, or nodal lesions ≥10 mm, and no systemic tx 3 mos prior were randomized 1:1 to 6 doses/12 wks of T-VEC followed by surgery (surg) (Arm 1) vs upfront surg (Arm 2). T-VEC was given at standard dosing until surg, no injectable tumors, or intolerance. This interim analysis was planned for when the 75th pt in Arm 1 completed the safety follow-up visit (30+ days post surg). Results: 150 pts were randomized (76 Arm 1, 74 Arm 2). Of all pts, ≥ 94% had no prior radio/systemic tx, 91% had prior surg and 84% had no plans for adjuvant tx. 75% in Arm 1 and 93% in Arm 2 had surg as planned. Of the 19 pts who did not have surg in Arm 1, 11 had progressive disease. In Arm 2, 17 pts recurred within 14 wks post-surg. For pts who had surg in Arm 1, the pathological complete response (pCR) rates was 21%. Negative margin resection (R0) rates were 56.1% for Arm 1 and 40.6% for Arm 2 (80% CI: 3-28% for the difference). For all randomized pts, pCR rate in Arm 1 was 15.8%; R0 rates were 42.1% (Arm 1) vs 37.8% (Arm 2). Overall response (OR) rate (CR+PR) in Arm 1 was 14.7% (80% CI: 9-22%). In the safety set (73 pts in Arm 1, 69 pts in Arm 2), tx-emergent AEs were 93% in Arm 1 (1 grade 4 pain, no grade 5) and 45% in Arm 2 (all ≤ grade 3). In Arm 1, preop AE was 89.5% (most common: pyrexia 35%) and intra/postop AE was 29.8% (most common: seroma 5.3%). In Arm 2, intra/postop AE rate was 45% (most common: pain 7.2%). Conclusions: 12 wks of neo T-VEC produced a pCR rate in stage IIIB-IVM1a MEL higher than observed by ORs and may account for the higher R0 margin in Arm 1. No unexpected toxicities were noted. Analysis of recurrence-free survival is ongoing.

5

Changing Trends in Industry Funding for Surgical Oncologists

J.A. Santamaria-Barria,[1]* S. Stern,[2] A.M. Khader,[1] M. Garland-Kledzik,[1] A.J. Scholar,[1] T.D. Fischer,[1] A. Bilchik.[1] *1. Department of Surgical Oncology, John Wayne Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA; 2. Department of Biostatistics, John Wayne Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA.*

Background With reductions in public research funding, alternate sources of funding have become an essential component of clinical research by surgical oncologists (SOs). Aim To examine current trends in industry funding of SOs. Methods Surgeon members of the Society of Surgical Oncology were identified at www.surgonc.org, and then matched with board certification status and years in practice at www.absurgery.org. Departmental and hospital data were evaluated, and industry payments from 2013 to 2017 were matched with the Open Payment Database at https://openpaymentsdata.cms.gov. Results Of the 1,670 SOs identified, 922 (55%) had academic positions: 588 (64%) male and 334 (36%) female, with median years in practice of 17 and 12, respectively. Between 2013 and 2017, industry funding included $46,596,706 in research payments to 162 SOs (17.5%): $40,774,716 (87%) for research related to drugs and clinical trials, compared to $5,194,199 (11%) for surgical devices (P=0.018). Funding correlated with academic leadership and years in practice (P=0.0001 and P=0.0037). Massachusetts ($9,060,976), Texas ($7,656,228), and New York ($4,210,864) received the most funding, whereas Utah ($438,047/SO), Washington ($339,916/SO), and Oregon ($275,934/SO) received the highest average payments per SO. The majority of funding was from Novartis ($16,045,608), Amgen ($6,810,832), and Merck ($3,758,299), for an oncolytic vaccine (talimogene laherparepvec; $5,939,007), a BRAF inhibitor (dabrafenib; $5,727,309), and a KIT inhibitor (imatinib; $4,323,586). Male SOs received funding more frequently than females (120/588, 20% vs. 42/334, 12.6%; P=0.0027). Males also received significantly more in general payments (travel/lodging, food/beverage, consulting/speaker fees): $48,830 vs. $11,867 per male and female SO, respectively (P=0.0001). Conclusion The majority of industry research payments to SOs are related to novel pharmaceutical rather than device clinical trials, which highlights the expanding influence SOs play in systemic therapies. Industry payments are influenced by location, gender, and academic leadership. Further studies are needed to assess the impact of industry support on peer-reviewed funding and academic advancement.

6

Tumor Penetrating Polymeric Nanoparticle Improves Response in a Drug Resistant Pancreatic Cancer PDX Model

M. Jajja,* L. Zhu, D. Wang, C. Staley, B. El-Rayes, D.A. Kooby, L. Yang. *Winship Cancer Institute, Emory University, Atlanta, GA.*

Introduction: Pancreatic cancer has poor response to chemotherapy with desmoplastic stroma identified as a delivery barrier. To overcome this, we developed a nanoparticle (NP) drug delivery system using an engineered ligand of receptor binding region of urokinase plasminogen activator (ATF) and the catalytic domain of metalloprotease (MMP14) carrying SN38 (CPT-11 analog). Hyaluronic acid (HA), a naturally occurring protein was chosen as the backbone to produce a biocompatible NP. HA can also bind to CD44, highly expressed in epithelial cancers. Dual uPAR, CD44 targeting allows for targeted delivery and facilitates receptor mediated endocytosis of NP-drug complex. MMP14 activity degrades extracellular matrix to deplete the stromal barrier. Methods: HA modified with 5β-cholanic acid can self-assemble into a 200nm sized NP. SN38 was encapsulated inside and recombinant ATFmmp14 was conjugated to surface to form the complete particle (HANP) (Fig 1a). Cytotoxicity assays were conducted to determine IC_{50} in cell lines. Patient derived xenograft (PDX) model of a drug resistant pancreatic cancer was used for efficacy studies. Orthotopically implanted tumors were treated with HANP (10mg/kg SN38 dosage) weekly for 6 weeks via tail vein and overall survival compared to conventional chemotherapy. Results: HANP has stronger in-vitro cytotoxicity than conventional Irinotecan (>80x) and liposomal irinotecan (Onivyde) (>1100x) in a PDX derived cell line (Fig 1b). In-vivo efficacy study demonstrated a significant improvement in survival of PDX bearing mice with HANP (median survival 50 days), compared to FOLFIRINOX and Gemcitabine-Abraxane (median survival 37 days each). Replacement of Irinotecan with HANP in the FOLFIRINOX regimen led to a median survival >72 days

($p<0.001$) (Fig 1c). Short-term toxicity studies demonstrated a -2% weight change at 3 weeks with HANP compared to -2% for FOLFIRINOX and -4% for combination. Conclusions: HANP alone or in combination with FOLFIRINOX led to significantly improved survival in a pancreatic PDX model. Further studies are underway to evaluate preclinical PD/PK for eventual translation to a targeted therapy for advanced pancreatic cancer.

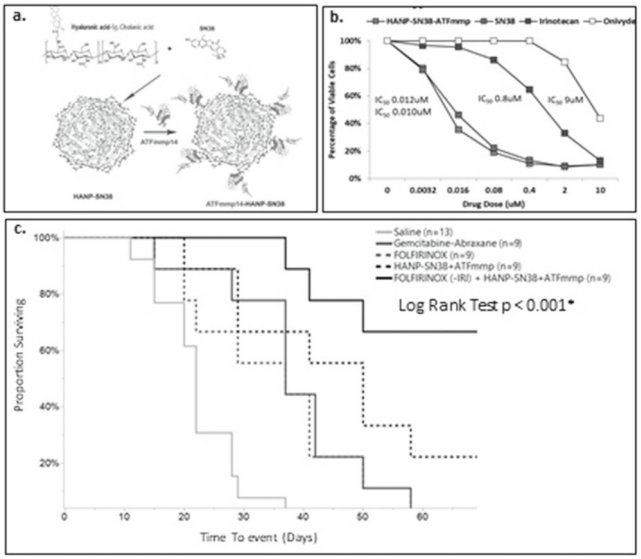


Figure 1. (a) Schematic of final HANP complex preparation. (b) Comparative IC_{50} of HANP with SN38 alone and commercially available irinotecan formulations. (c) Kaplan-Meir survival analysis.

8

Treatment Outcomes of Neoadjuvant Immunotherapy in Patients with Locally Advanced Melanoma K. Mahuron,* L. Levine, A. Daud, M. Alvarado. *University of California, San Francisco, San Francisco, CA.*

Introduction Patients with locally advanced melanoma have a high risk of recurrence (up to 50%), and the role of neoadjuvant immunotherapy is undefined. Immunotherapy is often limited due to adverse side effects, and we have previously demonstrated that therapy can be stratified with immune profiling of pretreatment biopsies. This study compares the outcomes of patients with locally advanced melanoma who received either neoadjuvant or adjuvant immune profile directed immunotherapy. Methods This is a prospective study of 21 patients diagnosed with Stage III or oligometastatic Stage IV melanoma intended for surgical resection. Pretreatment biopsies underwent immune profiling with flow cytometric analysis, and patients were stratified to anti-PD-1 monotherapy or PD-1/CTLA-4 blockade accordingly. Patients with documented follow up history were included in efficacy and safety analysis. Results Of the 21 patients included in our study, 13 received anti-PD-1 monotherapy and 8 received PD-1/CTLA-4 blockade. The majority of patients (80%) underwent surgical resection. Of the 12 surgical patients receiving neoadjuvant therapy, 7 (58%) achieved a complete pathologic response and 3 (25%) had progression. Of the 5 surgical patients receiving adjuvant therapy, 2 (40%) had progression. 4 patients were managed nonsurgically due to a complete response on imaging and remain recurrence free at a median follow-up of 31.8 months. Toxicity profiles were consistent with previous reports, and adverse effects were more frequent with CTLA blockade (87.5%) and required over half of these patients to transition to anti-PD-1 monotherapy. Conclusions Our study supports the role of neoadjuvant immunotherapy for locally advanced melanoma. While the adjuvant group in this study is small, the recurrence rate for the neoadjuvant group is lower than expected. Also, our study suggests that there may be a role for nonsurgical management in this patient population with careful selection, and immune profile treatment stratification decreases the use of anti-CTLA agents and their associated adverse effects. Our study merits further investigation with a larger cohort validation study.

9

Surgical Management of the Axilla in Clinically Node Positive Patients Receiving Neoadjuvant Chemotherapy S.M. Wong,* A. Weiss, E. Mittendorf, T.A. King, M. Golshan. *Dana-Farber/ Brigham and Women's Cancer Center, Boston, MA.*

Background: The feasibility of sentinel lymph node biopsy (SLNB) in clinically node positive patients converting to clinically node negative following neoadjuvant chemotherapy (NAC) has been evaluated in several large clinical trials. This study was undertaken to determine whether SLNB has been broadly adopted in clinical practice for patients receiving NAC. Methods: The National Cancer Database was used to identify women diagnosed with clinically node positive, stage II-III breast cancer who received NAC followed by surgery between 2012-2015. Temporal trends in axillary surgery were evaluated and multivariable logistic regression analyses were performed to determine factors associated with receipt of SLNB. Results: Of 12,965 women with clinically node positive disease at baseline, 2530 (19.5%) underwent SLNB, 2707 (20.9%) underwent SLNB followed by axillary lymph node dissection (ALND), and 7728 (59.6%) underwent upfront ALND after NAC. The use of SLNB increased from 31.8% in 2012 to 49% in 2015 ($p<0.001$). Using ypN0 status as a surrogate for patients converting to cN0 after NAC, among 5127 (39.5%) patients, use of SLNB for initial axillary staging increased from 38.2% to 58.4% over the study period ($p<0.001$), and was the only axillary procedure performed in 42.2% of patients in 2015. In women with low volume residual nodal disease including isolated tumor cells (ITCs) (n=214) and micrometastases (n=501), SLNB was the only axillary procedure performed in 36.9% and 23.6% of cases. In 7123 women with ypN1 disease, SLNB was the only axillary procedure performed in 13.0%. In adjusted analyses, factors significantly associated with attempt of SLNB included clinical N1 disease (vs cN2), age <45 years, treatment facility type, triple-negative and HER2-positive subtypes, and year of diagnosis. Conclusion: The use of SLNB in clinically node positive patients receiving NAC increased significantly between 2012 and 2015. SLNB alone was performed in over 10% of patients with ypN1disease, over 20% of patients with micrometastases, and 35% of patients with ITCs; the oncologic safety of omission of ALND in these patients requires further evaluation.

10

Is Axillary Clinical Exam Alone Sufficient to Select Node-Positive Patients Who Downstage After NAC for SLNB? A Comparison of the Accuracy of MRI versus Clinical Exam T. Moo,* M. Jochelson, E. Zabor, M. Stempel, M. Raiss, A. Tadros, M. El-Tamer, M. Morrow. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction The National Comprehensive Cancer Network (NCCN) endorses sentinel lymph node biopsy (SLNB) use in patients with clinically positive axillary nodes who become node negative after neoadjuvant chemotherapy (NAC). MRI is frequently used to assess treatment response post NAC. Patients eligible for SLNB based on a negative clinical exam (CE) may have abnormal lymph nodes (LNs) on MRI leading to further work-up or axillary dissection. We compare the accuracy of post-NAC MRI to CE alone in predicting pathologic status of sentinel lymph nodes (SLNs) in cN1-2 patients. Methods We identified patients with T0-4, cN1-2 breast cancer who underwent NAC and subsequent SLNB between 3/2014-7/2017. Patients were grouped based on whether a post-NAC MRI was done. MRIs were reviewed by a single reviewer for abnormal LNs and compared to SLN pathology. MRI accuracy in predicting SLN status was assessed and compared to CE alone. Results 342 patients met study criteria. All patients had a negative CE of the axilla post NAC. 57 did not have biopsy confirmation of positive LNs and were excluded; 285 were analyzed. Median age was 49 years; 94% of tumors were ductal histology; 37% were HER2+; 25% were triple negative. Post-NAC MRI was done in 68% (193/285). Patients undergoing lumpectomy vs mastectomy were more likely to have a post-NAC MRI (88% vs 54%, $p<0.001$); all other clinicopathologic parameters were comparable (Table). 32% (61/193) had abnormal LNs on MRI; among these, 56% (34/61) had a positive SLN on final pathology compared to 42% (55/132) of patients with no abnormal LNs on MRI and 52% (48/92) of patients who had CE alone ($p=0.12$). There was no significant association between MRI finding and SLN status among patients who had post-NAC MRI ($p=0.09$). Positive predictive value of MRI was 56%, negative predictive value was 58%, and overall accuracy in predicting SLN status was 58%. Conclusions Post-NAC MRI finding of abnormal axillary LNs is no more accurate than CE alone in predicting SLN pathologic status in patients with cN1-2 disease. In this setting, abnormal LNs on MRI should not preclude SLNB.

Clinicopathologic and treatment characteristics among patients undergoing post-NAC MRI vs clinical exam alone

Variable	Overall (n=285)	Clinical exam + MRI (n=193)	Clinical exam only (n=92)	p-value
Age, median (range)	49 (24-85)	50 (24-77)	49 (28-82)	0.78
Tumor type				0.17
IDC	267 (94%)	184 (95%)	83 (90%)	
ILC	8 (3%)	3 (2%)	5 (5%)	
Mixed/other	10 (3.5%)	6 (3%)	4 (5%)	
Histologic grade				0.42
1	1 (0.5%)	1 (0.5%)	0	
2	23 (8%)	13 (6.5%)	10 (11%)	
3	255 (89.5%)	177 (92%)	78 (85%)	
N/A	6 (2%)	2 (1%)	4 (4%)	
LVI				0.87
Yes	127 (45%)	84 (44%)	43 (47%)	
No	108 (38%)	75 (39%)	33 (36%)	
Suspicious	12 (4%)	8 (4%)	4 (4%)	
N/A	38 (13%)	26 (13%)	12 (13%)	
Clinical T				0.57
Tis/x	3 (1%)	1 (0.5%)	2 (2%)	
T1	46 (16%)	31 (16%)	15 (16%)	
T2	158 (56%)	111 (57.5%)	47 (51%)	
T3	63 (22%)	41 (21%)	22 (24%)	
T4	15 (5%)	9 (5%)	6 (7%)	
Clinical N				0.18
cN1	280 (98%)	188 (98%)	92 (100%)	
cN2	5 (2%)	5 (2%)	0	
Subtype				0.15
ER+/HER2-	109 (38%)	66 (34%)	43 (47%)	
ER+/HER2+	58 (20%)	44 (23%)	14 (15%)	
ER-/HER2+	47 (17%)	31 (16%)	16 (17%)	
ER-/HER2-	71 (25%)	52 (27%)	19 (21%)	
NAC type				0.56
ACT based	274 (96%)	186 (96%)	88 (96%)	
Other	11 (4%)	7 (4%)	4 (4%)	
Type of surgery				<0.001
Lumpectomy	117 (41%)	103 (53%)	14 (15%)	
Mastectomy	168 (59%)	90 (47%)	78 (85%)	
No. of SLNs removed (median, range)	4 (0,14)	4 (1,13)	4 (0,14)	0.36

NAC, neoadjuvant chemotherapy; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; N/A, not available; LVI, lymphovascular invasion; ER, estrogen receptor; ACT, doxorubicin plus cyclophosphamide followed by weekly paclitaxel; SLN, sentinel lymph node

11

Axillary Lymph Node Dissection in Node-Positive Breast Cancer: Are 10-Nodes Adequate and When is Enough, Enough?
L.H. Rosenberger,[1]* Y. Ren,[2] S.M. Thomas,[2] R.A. Greenup,[1] O.M. Fayanju,[1] E. Hwang,[1] J.K. Plichta.[1] *1. Surgery, Duke University Medical Center, Durham, NC; 2. Duke University Department of Biostatistics and Bioinformatics, Durham, NC.*

BACKGROUND National guidelines define adequacy of axillary lymph node dissection (ALND) as retrieval of ≥ 10 lymph nodes (LN). We aimed to identify the number of LNs needed to guide treatment decisions and the association of the number of LNs with overall survival (OS). METHODS Using the National Cancer Data Base (2010-2015), we identified patients ages 18-75, with node-positive breast cancer who were categorized by treatment sequence into: 1) neoadjuvant treatment (NAT) (cN1-3 or ypN1-3), and 2) upfront surgery (pN1-3). A multivariable Cox proportional hazards model with restricted cubic splines (RCS) was used to characterize the functional association of LN retrieval with OS. A Monte Carlo Markov Chain procedure was used to estimate the threshold values of LN retrieval associated with a marked change in OS. Patients were characterized as having "low", "moderate", and "high" LN retrieval based on these thresholds. RESULTS 135,539 patients were identified; 32,800 (24.2%) received NAT and 103,229 (75.8%) underwent upfront surgery. The low, moderate, and high retrieval thresholds were found to be 1-6, 7-21, and >21 LNs (upfront surgery), and 1-7, 8-22, and >22 LNs (NAT) (Figure 1). After adjustment, high vs. low (OR 1.83, p<0.001) LN groups were associated with a greater receipt of adjuvant chemotherapy after adjustment for positive LNs. A high vs. low LN retrieval was associated with reduced adjuvant radiation (OR 0.65, p<0.001) but was not with adjuvant endocrine therapy (p=0.40). After adjustment, high compared to low LN retrieval was also associated with improved OS (HR 0.78, p<0.001). ALND with retrieval of fewer than 6 (upfront surgery) or 7 (NAT) LNs was associated with inferior OS, while retrieval of 21 (upfront surgery) or 22 (NAT) LNs was associated with improved OS, after which point, survival did not improve with removal of additional nodes (Figure 1). DISCUSSION In node-positive breast cancer, the number of nodes retrieved is significantly associated with adjuvant treatment decisions. Removal of >20 LN confers no significant survival benefit in both upfront surgery and NAT patients.

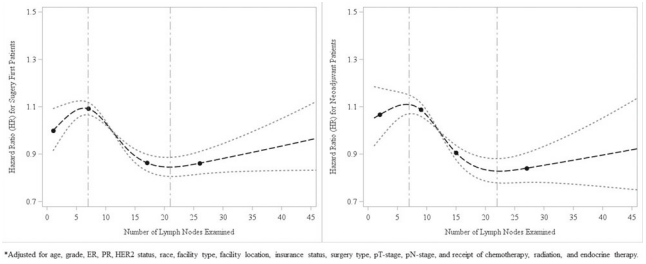


Figure 1. Association between Total Number of Lymph Nodes Retrieved and Survival, in Patients undergoing Upfront Surgery (A), or Neoadjuvant Treatment (B).

12

Axillary Lymph Node Ultrasound Following Neoadjuvant Chemotherapy in Biopsy-Proven Node-Positive Breast Cancer: Results from the SN FNAC Study D. Morency,[2]* S. Dumitra,[2] E. Parvez,[2] M. Basik,[1] J. Boileau.[1] *1. Jewish General Hospital, Montreal, QC, Canada; 2. McGill University, Montreal, QC, Canada.*

BACKGROUND: The Sentinel Node Following Neoadjuvant Chemotherapy(SN FNAC) study found that in biopsy-proven node-positive(N+) breast cancer, sentinel biopsy(SNB) can be done following NAC with a low false negative rate (FNR 8,4%). In ACOSOG Z1071, axillary ultrasound(AxUS) post-NAC helped identify patients with suspicious lymph nodes(LN) and lower the SNB FNR. Using US to detect residual positive LN after NAC can lead to unnecessary completion node dissection(CND) in patients that achieved an axillary pathological response(pCR). The aim of this study was to evaluate the role of AxUS post-NAC as a predictor of the axillary response. METHODS: The SN FNAC trial was a prospective, multicentric study of patients with biopsy-proven N+ breast cancer (T0-3, N1-2) who underwent SNB followed by CND. All patients underwent an US of the axilla at initial diagnosis and following NAC. RESULTS: From 2009 to 2012, 145 patients were enrolled in the study. The axillary pCR following NAC was 30.3%. We were able to obtain data on AxUS following NAC in 135 patients. Of the 57 axillary-positive US, 46 (80.7%) had positive LN at surgery compared to 40 (51.3%) of the 78 axillary-negative US patients(p<0.001). AxUS following NAC had a sensitivity of 53.3%, a specificity of 77.6%, a positive predictive value of 80.7%, a negative predictive value of 48.7% and an accuracy of 62.2%. When comparing patients with a positive and a negative AxUS, 52.6% vs 32.1% were pN1, 14.0% vs 15.4% were pN2 and 14% vs 3.8% were pN3(p=0.001). Patients with a positive AxUS had larger size SN metastases (7 vs 5 mm; p=0.011) and an increased number of total positive LN (median 3 vs 2). The addition of post-NAC AxUS would result in a numerically lower SNB FNR but not statistically significant (4% vs 8.4%; p=0.432). Using a suspicious post-NAC AxUS as an indication for CNB would have increased the number of CND in patients with axillary pCR by 20.8%. CONCLUSION: AxUS post-NAC can help detect remaining positive axillary LN and be used as an adjunct to SNB. However, SNB itself is sufficient to assess the axilla post NAC and the addition of AxUS might result in unnecessary CND.

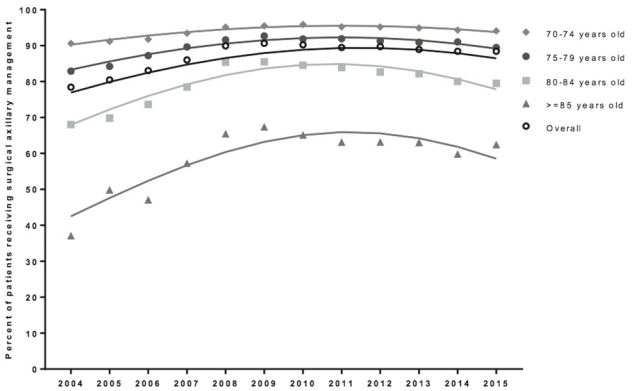
13

Trends in Surgical Axillary Management in Early Stage Breast Cancer in Elderly Women: Continued Overtreatment? R. Louie,* S. Downs-Canner, C. Gaber, P. Strassle, K.K. Gallagher, D.W. Ollila. *Surgery, University of North Carolina - Chapel Hill, Chapel Hill, NC.*

In the past two decades, three randomized trials in the US and Europe demonstrated that women >70 with early stage ER/PR+ breast cancer had equivalent disease-specific mortality regardless of axillary lymph node sampling and dissection. In 2016, the Society of Surgical Oncology published a campaign to encourage patients and providers to reconsider the role of axillary surgery in this population. The aim of this study is to identify factors contributing to the adoption of non-operative management of the axilla in these patients. We used the National Cancer Database to perform a retrospective analysis from 2004-2015 of women ≥70 years old with clinical T1/T2, ER+/PR+ invasive ductal carcinoma who underwent partial or total mastectomy, with or without surgical axillary management (SAM). We defined SAM as sentinel lymph node biopsy and/or axillary lymph node

dissection. Women who underwent chemotherapy were excluded. We used multivariable logistic regression to model the odds of SAM across region, care setting, and Charlson-Deyo scores, and analyzed temporal trends using Poisson regression. From 2004-2015, 87,342 of 99,940 women who met inclusion criteria (83%) underwent SAM. Overall, the percent of SAM increased from 78.4% to 88.4% between 2004-2015 (p<0.001). Increase in SAM was consistent across region (p=0.81) and care setting (p=0.09), but we saw a smaller rate of increase in older patients (p<0.001). Compared to women aged 70-74, women 75-79 (p=0.003), 80-84 (p<0.001), and ≥85 (p<0.001) were less likely to receive SAM. Omission of axillary surgery was more likely to occur in patients in New England (OR 0.33, p<0.001) and patients with a Charlson-Deyo score of 3 (p<0.001). SAM continues to be the preferred option of managing the axilla in elderly women with clinical T1/T2, ER/PR+ IDC despite the literature showing no survival benefit. While patients >80 were less likely to be treated by SAM, there was unexplained regional variation. Further analysis may identify factors to improve dissemination of current literature pertaining to SAM and better define patient selection based on more than age alone in early stage breast cancer in the elderly.

Figure 1: Observed and predicted percent of patients receiving surgical axillary management overall and by age group.



14

Completion Axillary Lymph Node Dissection Does Not Decrease Local-Regional Recurrence in Women with Micrometastasis Undergoing Mastectomy P. Jadeja,[1]* R. Ha,[2] K. Ruddy,[2] V. Nieto,[2] B. Taback.[2] *1. Breast Surgery, Summit Medical Group, Florham Park, NJ; 2. Columbia University Medical Center, New York, NY.*

Background: There is increasing debate on the role of completion axillary lymph node dissection (cALND) in women with subclinical axillary micrometastasis. The goal of this study is to evaluate axillary outcomes and local and regional recurrences in women with micrometastsis undergoing mastectomy. Methods: Single-institution, IRB approved, HIPAA compliant retrospective review of the electronic medical record identified clinically node-negative patients who underwent mastectomy as upfront treatment of breast cancer with a subsequent sentinel lymph node (SLN) micrometastasis. Patients who underwent completion axillary lymph node dissection (cALND) were compared to those who did had no further axillary surgery. Non sentinel node (NSN) metastasis, local recurrence (LR), and distant recurrences rates were documented. Two tailed p-value < 0.05 was defined as significant. Results: Among 660 clinically node-negative patients undergoing mastectomy as upfront treatment for breast cancer, 69 patients (10.5%) were identified with a subclinical SLN micrometastasis. Among 69 patients, 37 (53.6%) underwent cALND, of whom 4 (5.8%) underwent postoperative radiation, and 32 patients (46.4%) had no further axillary surgery or radiation. Among patients undergoing cALND, positive NSN metastasis were identified among 9 patients (24.3%). Among 69 patients, 4 (5.8%) of patients developed distant (n=2) or LR (n=2). All distant recurrences occurred among patients who underwent cALND. Therefore, there was no statistically significant difference among LRR or distant recurrences in the two groups (p=0.23). No axillary recurrences were identified over the median 9 year follow up period in either group. Conclusion: Local and regional recurrence after mastectomy are exceedingly low. Despite minimal utilization of postmastectomy radiation therapy, long-term follow-up in this patient cohort, demonstrates that axillary recurrences are exceedingly rare regardless of completion axillary lymph node dissection. This study provides first-time evidence to support recommending no further axillary surgery in mastectomy patients with SLN micrometastasis.

15

Trends in Utilization of Sentinel Node Biopsy and XRT in Women ≥ 70 J. Gunn,[1]* R. Lemini,[1] K.N. Partain,[1] T. Yeager,[1] K. Attwood,[2] S. McLaughlin,[1] S.P. Bagaria,[1] E.M. Gabriel.[1] *1. Mayo Clinic, Jacksonville, FL; 2. Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

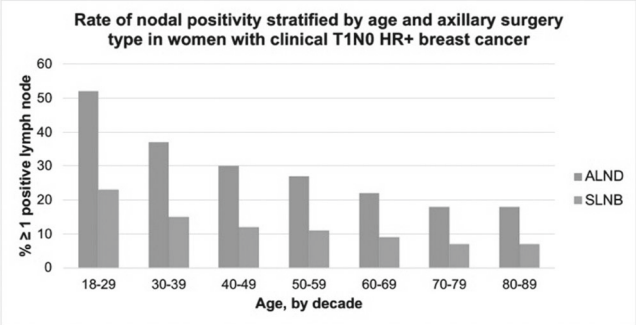
Background: The Choosing Wisely campaign released the recommendation for omission of axillary staging in women ≥70 years old with early stage (T1-T2) hormone receptor positive breast cancer and clinically negative nodes based on seminal data by Hughes et al published in 2004. We hypothesized that this omission of axillary staging and adjuvant radiation (XRT) has not been widely adapted since then with the secondary hypothesis that there is a disparity in adherence based on treating facility type. Methods: Using the National Cancer Data Base (NCDB), we selected malignant breast cancer patients ≥70 with ER+ tumors ≤2 cm with clinically negative lymph nodes and no evidence of metastasis who underwent surgical resection and had known XRT status from 2004-2015. The use of sentinel lymph node biopsy (SNB) and XRT status was also summarized by year of diagnosis to determine trends over time. Results: In total, 57,232/69,985 (81.8%) patients had SNB examined. Of the 12,753 patients in whom SNB was omitted, 1,472 (11.5%) were treated at community cancer centers, 6,296 (49.4%) at comprehensive community cancer programs and 4,985 (39.1%) at academic facilities (p-value <0.001). Interestingly, fewer patients had nodes examined in 2004-2006 (74.8%) compared to 2013-2015 (81.4%)(p-value <0.001)(Table 1). In total, 33,891 (48.4%) received XRT. There was a no significant trend over time with regards to patients receiving XRT. Conclusion: Following the release of the Hughes et al. paper in 2004, there has been no real change over time in axillary staging or in XRT treatment for early stage favorable breast tumors. However, there was a difference observed in omission of SNB based on facility type and setting. Further monitoring is needed to determine if these trends persist following the release of the Choosing Wisely recommendation.

16

Nodal-Positivity Decreases with Age in Women with Early Hormone Receptor-Positive Breast Cancer S. Downs-Canner,* P. Strassle, C. Gaber, R. Louie, K.K. Gallagher, D.W. Ollila. *University of North Carolina at Chapel Hill, Chapel Hill, NC.*

Introduction: Despite the Society of Surgical Oncology's Choosing Wisely campaign and randomized trials demonstrating safety of omitting axillary surgery in older women with early stage breast cancer, the rate of axillary surgery remains high. We compared nodal positivity in early-stage, hormone receptor positive (HR+) patients across age and histologic subtype, to provide context for clinicians deciding optimal management of the axilla. Methods: Adult women diagnosed with non-metastatic, clinical T1, N0 or Nx, HR+ and HER2 negative ductal, lobular, or special histologic subtype (tubular, mucinous, cribiform, and papillary with invasion) breast cancer between 2012 and 2015 treated by breast conservation in the National Cancer Database were included. Women were excluded if they had neoadjuvant radiation and/or chemotherapy or missing data on axillary evaluation. The association between age and lymph node (LN) positivity was compared using multivariable logistic regression. Results: 154,152 women met inclusion criteria. Among women ≥70 (n=51,917), 14% had no axillary evaluation, 17% underwent axillary lymph node dissection, and 69% underwent sentinel lymph node biopsy (SLNB). In patients 70 and older who had SLNB, 2% of those with a special histologic subtype cancer had ≥1 positive LN vs 8% with ductal or lobular histology (p<0.001). Lymph node positivity decreased by decade of age (p<0.0001). The percent of women treated by SLNB with ≥1 positive LN was 15% for ages 30-39, 12% for ages 40-49, 11% for ages 50-59, 9% for ages 60-69, and 7% for those in their 70s and 80s (Figure 1). Among those undergoing SLNB, compared to patients 50-59 years old, women aged 70-79 and 80-89 were significantly less likely to have ≥1 positive LN, after controlling for year of diagnosis, demographic, and socioeconomic variables (HR 0.64, 95% CI 0.60, 0.74 and HR 0.66, 95% CI 0.60, 0.74, respectively). Conclusion: Women ≥70 with clinical T1N0 HR+ breast cancer treated by breast

conservation and SLNB have very low rates of LN positivity, especially compared to younger patients. This data provides reassurance to clinicians choosing to omit axillary evaluation in this selected group.



17

Impact of Neoadjuvant Versus Adjuvant Chemotherapy on the Extent of Axillary Surgery for Clinically Node-Negative Breast Cancers of Triple-Negative and HER2 Over-Expressing Phenotypes

J.L. Thompson,* T.J. Koehler, A.T. Davis, G. Wright. *Spectrum Health/Michigan State University, Grand Rapids, MI.*

Background: Breast cancer patients with triple-negative or HER2 over-expressing phenotypes are recommended to receive chemotherapy for primary tumors greater than 1 cm regardless of nodal status. Neoadjuvant chemotherapy may eradicate subclinical nodal metastases and reduce the extent of axillary surgery performed. Methods: A query of the NCDB PUF was performed for new cases of female breast cancer from 2012-2015. Inclusion criteria were: clinical N0 status, receipt of chemotherapy, and receipt of axillary surgery. Exclusions were made for women with hormone-positive/HER2-negative tumors or distant metastatic disease. Subjects were divided in to groups based on receipt of neoadjuvant or adjuvant chemotherapy. The primary endpoint was the extent of axillary surgery defined as sentinel lymph node biopsy alone or axillary lymph node dissection (ALND). Subgroup analyses were performed based on tumor phenotype and surgery of the primary site. A multivariate logistic regression model to predict ALND included age, race, facility type, Charlson/Deyo score, grade, clinical T stage, lymphovascular invasion, and receptor status phenotype. Results: There were 60,771 women included. Neoadjuvant chemotherapy was received by 15,967 (23.9%). The rate of ALND was 30.1% and was higher in patients who received adjuvant chemotherapy (30.6% vs. 28.8%, p<0.001). The extent of axillary surgery was reduced most significantly among tumor phenotypes for patients with hormone-negative, HER2-positive disease (30.0% vs 25.8%, p<0.001). ALND rates were more substantially reduced for patients who received mastectomy (41.3% vs 36.1%, p<0.001) compared with those who received partial mastectomy (21.8% vs. 20.1%, p=0.002). Multivariate analysis showed that receipt of adjuvant chemotherapy was an independent predictor of axillary lymph node dissection (OR 1.26, 95% CI 1.19-1.33). Conclusion: Neoadjuvant chemotherapy reduces the extent of axillary surgery in clinically node-negative patients with non-luminal breast cancers. In the post-Z0011 era this is most significant for women who underwent mastectomy.

18

Breast Conserving Therapy Results in Improved Survival Compared with Mastectomy for Early-Stage Breast Cancer: A Propensity Score Matched Comparison Using the National Cancer Data Base

E.L. Burkheimer,* R.F. Natwick, T.J. Koehler, A.T. Davis, G. Wright. *Spectrum Health/Michigan State University, Grand Rapids, MI.*

Background: Current surgical treatment recommendations for early-stage breast cancer are largely based on the NSABP B-06 trial which found equivalent survival between mastectomy and lumpectomy. We sought to compare breast conserving therapy (BCT) with mastectomy for treatment of early stage breast cancer in a contemporary patient population. Methods: A query of the NCDB PUF was performed for female breast cancer patients diagnosed from 2004-2015. Patients with stage I or II disease were included. BCT was defined as receipt of lumpectomy plus radiation. Propensity scores were tabulated using age, race, Charlson/Deyo score, tumor site, laterality, histology, grade, tumor size, nodes positive, lymph-vascular invasion, ER, PR, and HER2/neu status, receipt of chemotherapy, and receipt of endocrine therapy. Patients who received BCT vs mastectomy were matched using a 1:1 nearest neighbor technique. The primary outcome measure was overall survival. Subgroup analysis was performed by stage. Results: After exclusions and matching, two equal groups of 101,118 patients remained. Median follow-up was 42 months. The population consisted of women whose mean age was 60±12 years. The majority had invasive ductal histology (77%) and node negative disease (84%). Receptor status included ER positive (83%), PR positive (73%), and HER2/neu positive (15%). Chemotherapy was received in 38% and endocrine therapy in 71%, respectively. Propensity score matching yielded equivalent groups across all target variables. The 5-year overall survival was superior for BCT when compared with mastectomy (92.9% vs 89.7%, p<0.001) (Fig. 1). This survival advantage persisted for both stage I (p<0.001) and stage II (p<0.001) disease on subgroup analysis. Conclusion: BCT results in superior overall survival compared with mastectomy for early-stage breast cancer using well-matched, contemporary data. Patients should be informed of these results to aid in treatment decision-making given the lack of evidence to support mastectomy.

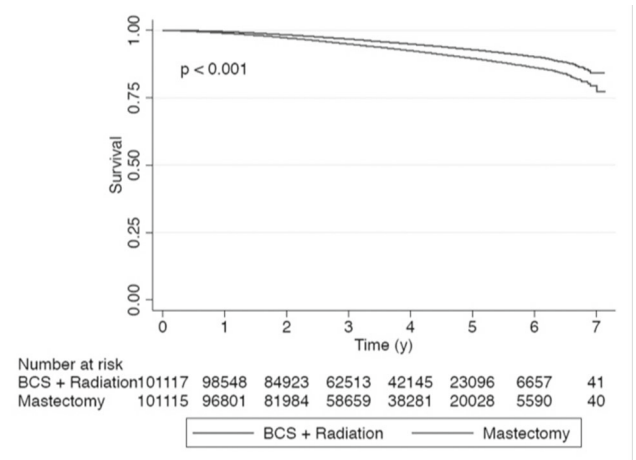


Fig 1. Overall survival for breast conserving therapy vs mastectomy for early-stage breast cancer.

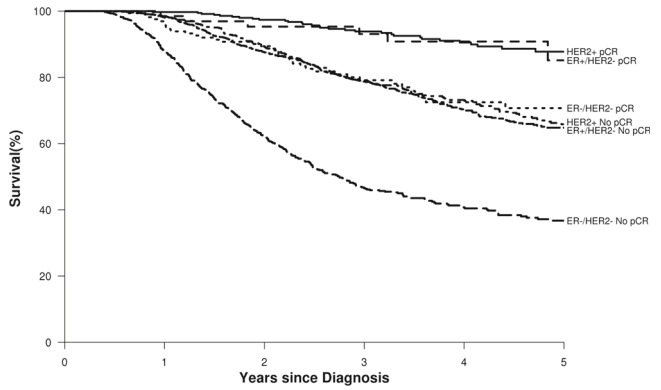
19

Biologic Subtype, Treatment Response and Outcomes in Inflammatory Breast Cancer: A NCDB Study

A.R. Kupstas,* T. Hoskin, C.N. Day, J.C. Boughey, T.J. Hieken. *Surgery, Mayo Clinic, Rochester, MN.*

Introduction Inflammatory breast cancer (IBC) is postulated to be a biologic entity distinct from other invasive breast cancers. However, both data and current clinical practice support the relevance of biologic subtype in determining treatment, response and outcomes. We aimed to validate this in a large current National Cancer Data Base (NCDB) patient cohort. Methods Non-metastatic IBC patients treated 2010-2015 with neoadjuvant systemic therapy and surgery were identified from NCDB. Approximated biologic subtype was categorized as ER+/HER2-, ER-/HER2- and HER2+. We defined total pathologic complete response (pCR) as ypT0/ypTis, ypN0. We used chi-square tests to compare response across subtypes and Kaplan-Meier analysis for overall survival (OS) with log-rank for univariate and Cox proportional hazards regression for multivariable analysis. Results We identified eligible 4068 IBC patients, median age 56 years. Approximated biologic subtype was 1575 (39%) ER+/HER2-, 1323 (33%) HER2+ and 1170 (29%) ER-/HER2-. Overall, 3351 patients (84%) were cN+ at presentation and 3254 (80%) received adjuvant radiation, without significant differences across subtypes. The proportion with total pCR varied significantly by subtype: ER+/HER2- (6%), HER2+ (39%), and ER-/HER2- (19%), p<0.001, as did the proportion with breast pCR (10%, 45%, 25%) and nodal pCR (17%, 57%, 33% for cN+ subset). Five-year OS varied significantly across subtypes (65% for ER+/HER2-, 74% HER2+ and 44% ER-/HER2-, p<0.001) and by total pCR within subtype (p < 0.01 for each, Figure). On multivariable analysis adjusting for age, cN status and receipt of adjuvant radiation, ER-/HER2- subtype

(HR 2.9, 95% CI: 2.5-3.4, p<0.001 vs HER2+) and absence of total pCR (HR 3.2, 95% CI: 2.5-4.1, p<0.001) predicted worse survival. Conclusions We found both IBC treatment response and survival varied with approximated biologic subtype as seen among other invasive breast cancers. These data support continued tailoring of systemic treatment to approximated biologic subtype, and highlight the markedly improved outcomes for HER2+ patients and the need for novel strategies to improve care for patients with ER-/HER2- IBC.



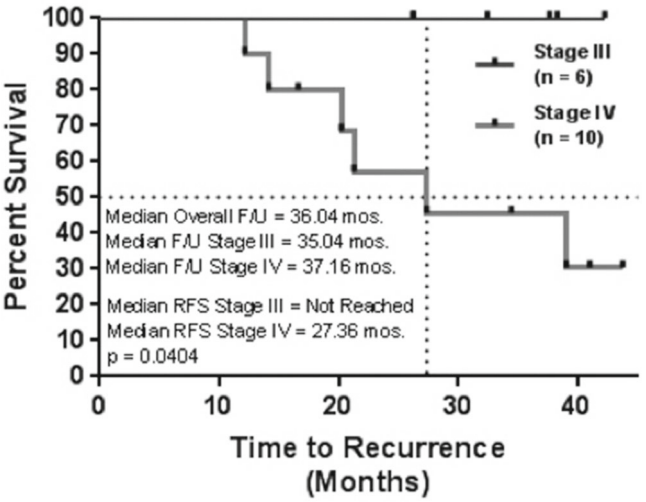
Overall Survival by pCR within Biologic Subtypes

20

HER-2 Dendritic Cell Vaccine to Prevent Recurrence for Patients with HER-2 Driven High-risk Invasive Breast Cancer: Results of a Pilot Study L.M. de la Cruz,[1]* J.S. Ankeny,[2] R.E. Roses,[1] C.S. Fisher,[3] S. Xu,[1] d. Weiner,[2] A. Beyer,[2] R. Mick,[1] B.J. Czerniecki.[2] *1. surgery, university of pennsylvania, Washington, DC; 2. Moffitt Cancer Center, Tampa, FL; 3. Indiana University, Indiannapolis, IN.*

BACKGROUND Type I polarized HER2 pulsed dendritic cell vaccines (HER2-DC1) can increase anti-HER2 CD4 Th1 response and clinically impact patients with early stage breast cancer (BC). We have shown that in patients with advanced breast cancer there is a substantial loss of anti-HER2 CD4 Th1. We aimed to assess the safety of HER2-DC1 in patients previously treated with HER2 therapy and determine if restoration anti-HER2 CD4 Th1 was achieved. METHODS After IRB approval, we prospectively enrolled women with BC, HER2 3+ or 2+ by IHC (regardless of FISH status) that were either Stage III-IV, ≥ N2, or recurrent HER2 metastatic BC with no evidence of disease (NED) after treatment. Immune responses were measured by ELISPOT or in vitro sensitization assay. Quantified response by response repertoire and cumulative response. Descriptive statistics were measured and Kaplan-Meier curve was performed. RESULTS Sixteen patients were enrolled with 100% completing vaccination. Six patients had Stage III and 10 had Stage IV disease and all were NED prior to enrolling with median follow up of 36.04 months. Total of 46 adverse events (AE) were reported, most common AE was grade I (n=28, 89.1%) with rare grade II and III AE (n=1, 4.3% each). The most common AE were fatigue, pain/bruising at site of injection, chills, and fevers. No subjects with Stage III BC had recurrent disease during follow up and in patients with Stage IV group, 6 (60%) had recurrence with a median recurrence free survival (RFS) of 27.36 months (Figure 1). All patients had depressed immune response prior to treatment and exhibited increase activity and response to the number of peptides after administration of HER2-DC as well as an overall increase in immune response in patients with some degree of variability. CONCLUSION Depressed Th1 responses are not immunologically "fixed" and could be restored with HER2-DC1. We showed HER2-DC1 was safe and may be more beneficial in preventing recurrence of patients prior to the development of active metastatic lesions. An additional study in high risk HER2 patients with residual disease following neoadjuvant therapy is in progress.

Figure 1. Recurrence Free Survival after DC-1 Vaccination



21

A 520-Gene NGS Panel Analysis of Mutations and Translocations in Matched Primary Breast Cancer and Metastases Confined to Sentinel Node N. Liao,[1]* G. Zhang,[1] Y. Wang,[1] B. Chen,[1] L. Guo,[1] L. Cao,[1] K. Li,[1] Z. Zhang,[2] T. Hou,[2] J. Liu.[2] *1. Department of Breast Cancer, Cancer Center, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China; 2. Burning Rock Biotech, Guangzhou, China.*

Background: We hypothesized that critical mutational events are required for a primary breast cancer to grow in the sentinel lymph node (SLN). This is the first study to compare matched primary breast cancer with metastases confined to the SLN with a 520 sequencing NGS panel. Methods: Targeted deep sequencing was performed using an NGS panel including 520 cancer-related genes, and spanning 1.6MB of human genome. The mutational profiles were compared between 17 matched primary breast tumors and a single SLN metastasis. Six of the 17 sentinel SLNs had no detected genomic alterations, possibly due to the insufficient tumor cellularity, because all of them were micro-metastasis (<2.0 mm; pN1mic). Results & Conclusion: Among the 11 samples with detectable genomic mutations, there were 244 genomic aberrations identified in 114 genes, including 76 single nucleotide variants (SNVs), 28 insertions or deletions (INDELs), and 139 copy-number amplifications (CNAs). Among these 11 samples, the genomic alterations in 6 of metastatic SLNs shared the mutation spectrum of the matched primary tumors. Importantly, in the other 5 patients, there were 17 novel genomic alterations occurring only in the SLN metastases, including the aberrant amplification of *CDKN1B, CDK4, HSP90AA1, DAXX, MEN1, NFKBIA, IL7R,* and *MYC*, as well as the non-synonymous mutations of *IGF2* (R135C), *TRRAP* (R204H), *BCORL1* (A1166fs), *SUFU* (E441D), *MPL*(E488*), and *NUP93* (Q280R). Also importantly, there were recurrent amplifications of CDK4, *CDKN1B* and *DAXX* in 2 individual SLN metastases, suggesting potential roles for these driver genes in the development of SLN metastasis. Conclusion: Of the 17 mutations found only in SLN metastases, only the CDK4 and MYC mutations have been reported as significant driver genes in breast cancer, while the other 15 genomic mutations are important candidates for further study. These findings highlight the importance of using a large NGS-based panel for elucidating the molecular mechanism involved in the development of sentinel node metastasis.

22

Genomic Concordance Between Primary Breast Cancer and Matched Axillary Lymph Node Metastasis M. Srour,* K. Carlson, B. Gao, F. Dadmanesh, Y. Qu, X. Cui, A.E. Giuliano. *Cedars-Sinai Medical Center, Los Angeles, CA.*

Introduction: Sentinel lymph node (SLN) biopsy guides breast cancer treatment and prognostication. To date, there have been few studies examining the genetics of SLN metastasis. The aim of this study is to characterize and compare gene expression patterns of primary breast cancers (PBC) and autologous matched SLN metastases. Methods: 11 patients with stage 2 ER/PR positive, HER2 negative breast cancer with macrometastasis to the SLN who did not have neoadjuvant therapy were selected. The tumor-specific area was isolated from breast and SLN paraffin embedded tissue sections. Gene expression of a panel of 2567 cancer-associated genes was analyzed with the HTG EdgeSeq system coupled with the Illumina Next Generation Sequencing (NGS) platform. Results were validated with whole RNA-Sequencing. Results: 22 samples (11 pairs) of PBC and matched SLN metastasis were analyzed for 2567 genes. Compared with the PBC, SLN metastasis had 139 statistically significant upregulated genes and 151 downregulated genes. SLN had at least a 5-fold change (FC) in upregulation in 16 genes and downregulation in 16 genes, compared to PBC [Figure 1]. Although SLN tumor cells showed increased expression of immunoregulatory genes such as cytokines, they also had a higher expression of SOCS1 (2.94 FC, p=0.001), the negative regulator of cytokine signaling, and IDO1 (2.40 FC, p=0.015), a key negative regulator of immune responses. Notably, there was upregulation of anti-apoptosis genes (BIRC3, BCL2A1) in the SLN. Conversely, downregulated genes were associated with extracellular matrix modeling and cell differentiation including KRT14 (-14.47 FC, p<0.001), COL17A1 (-12.02 FC, p<0.001), and FN1 (-5.2 FC, p<0.001). Interestingly, genes known to promote tumor development and progression (WNT2, FGF4, MMPs, SPARC, and LOX) were downregulated. Conclusion: In ER/PR positive, HER2 negative PBC, SLN metastasis has a distinct gene expression profile. Genes associated with anti-apoptosis and anti-immune response are upregulated, and genes associated with promoting tumor progression are downregulated.

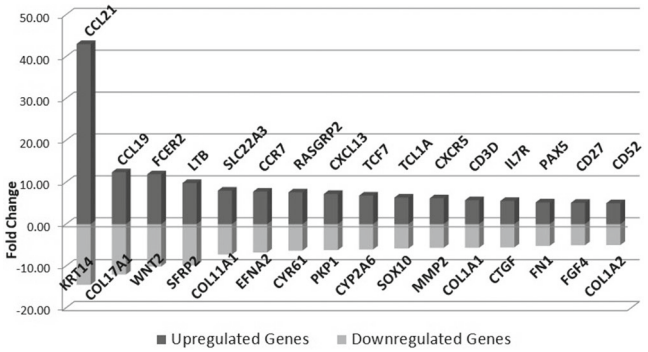


Figure 1. Upregulated and Downregulated Genes in Lymph Node Metastasis Compared with Primary Breast Cancer. 16 upregulated genes (top in dark grey) and 16 downregulated genes (bottom in light grey) showed at least a 5-fold change in gene expression.

23

Overexpression of MYC mRNA is More Clinically Relevant than MYC Amplification in Triple-Negative Breast Cancer E. Katsuta,* T. Takeshita, L. Yan, M. Opyrchal, K. Takabe. *Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Introduction: The use of clinical targeted DNA-sequencing to detect genomic alterations, including mutation and copy number alterations has become a routine in clinical practice for targeted therapy. However, the interpretation of the results in each gene remains understudied. MYC is one of the essential oncogenes and it plays a crucial role in regulation of the cell cycle and proliferation in various types of cancers including triple-negative breast cancer (TNBC). MYC amplification is often part of a clinical targeted DNA-sequencing panel under the assumption that reflects high expression of MYC gene. We hypothesized that MYC amplification is not a surrogate of its high gene expression, and the latter better associates with clinical outcome of TNBC. Methods: Clinical and genomic data, including mRNA and amplification, were obtained from The Cancer Genome Atlas (TCGA). Results: Among 1080 patients, 229 tumors (21.2%) showed MYC amplification in TCGA breast cancer cohort. 156 patients (15.5%) were classified as TNBC. In agreement with previous reports, there was greater proportion of TNBC subtypes in MYC amplified tumors (p<0.001), as well as in MYC mRNA high expression tumors (p<0.001). Thus, we focused on TNBCs. We found that MYC mRNA expression was not significantly elevated in MYC amplified TNBCs compared from non-amplified TNBCs (p=0.074). Interestingly, none of the clinicopathological demographics was associated with either MYC amplification or high expression. However, gene set enrichment analysis demonstrated that MYC target gene sets (v1; p<0.001, v2; p<0.001) as well as cell cycle related gene sets, including E2F targets (p=0.013) and G2/M check point (p=0.018) gene sets were significantly enriched in MYC high expressing TNBCs, whereas no gene set was enriched in MYC amplified TNBCs. In terms of survival, high expression of MYC was significantly associated with worse OS (p=0.026), whereas MYC amplification was not associated with OS (p=0.515) in TNBCs. Conclusion: MYC mRNA expression was not significantly high in MYC amplified TNBCs. MYC higher expressions, but not amplifications, associate with worse prognosis in TNBC.

24

Dynamic Neutrophil to Lymphocyte Ratio: A Novel Prognosis Measure for Triple Negative Breast Cancer D. Moldoveanu,* G. Best, V. Pravongviengkham, A.N. Meguerditchian, S. Dumitra, S. Meterissian. *General Surgery, McGill University, Montreal, QC, Canada.*

Background Recent successes of immunotherapy have highlighted the importance of host immunity in the development and progression of malignancies. The neutrophil to lymphocyte ratio (NLR) at diagnosis has been described as a readily-available measure of systemic inflammation and a prognostic factor for several malignancies, including triple-negative breast cancer (TNBC). This study assessed the value of the NLR as an independent prognostic marker in TNBC and explored the association between dynamic NLR changes and patient outcomes. Methods Clinical records of patients aged 18 to 80 with TNBC of all stages treated at our institution between January 2006 and December 2016 were reviewed. Patients diagnosed with inflammatory or autoimmune conditions were excluded. Clinical and demographic data were collected, including blood test results and treatments received. The primary and secondary study outcomes were overall survival (OS) and disease-free survival (DFS) respectively. Kaplan-Meier survival analysis and Cox models were calculated using the R statistical software. Results A total of 332 women with TNBC met the inclusion criteria with a median age of 59. A NLR of >2.84 at diagnosis was associated with decreased OS, a threshold within the range reported in the literature. Furthermore, a NLR >7.82 at any time during the patient's follow-up was a strong predictor of 5-year mortality (HR 7.8, p <0.001). This relationship remained significant in a multivariate Cox model including age and stage (HR=7.80, p<0.001). Among neoadjuvant chemotherapy recipients, a maximal NLR score below the 7.82 threshold was associated improved survival (HR=9.83, p=0.029). Patients who developed recurrence had higher NLR than their counterparts throughout the course of their follow-up. The NLR also significantly rose over the final 18 months of life (p<0.01). Conclusion The NLR is a significant prognostic marker in TNBC both at diagnosis and during the course of the disease. Moreover, dynamic changes in NLR are strong predictors of recurrence and timing of death. Further prospective validation is necessary for its implementation in routine clinical care.

25

The Tyrer-Cuzick Model Overpredicts Invasive Breast Cancer Risk in Women with LCIS M.G. Valero,[1]* E. Zabor,[1] A. Park,[1] E. Gilbert,[2] A. Newman,[1] T.A. King,[3] M. Pilewskie.[1] *1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Weill Cornell Medical College, New York, NY; 3. Department of Surgery, Brigham and Women's Hospital; Breast Oncology Program, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA.*

Background Risk assessment is paramount to personalized screening and risk-reduction strategies in women with high-risk breast lesions. The Tyrer-Cuzick model has been shown to overestimate risk in women with atypical hyperplasia, although its accuracy among women with lobular carcinoma in situ (LCIS) is unknown. Here we evaluate the accuracy of the Tyrer-Cuzick model for predicting invasive breast cancer (IBC) development among women with LCIS. Methods Women with LCIS participating in surveillance from

1987-2017 were identified from a prospectively maintained database. Chart review was performed to calculate a Tyrer-Cuzick score (version 7) near the time of LCIS diagnosis. Patients with prior or concurrent breast cancer, a BRCA mutation, receiving chemoprevention, or with pleomorphic LCIS were excluded. Invasive cancer-free probability was estimated using the Kaplan-Meier method. Performance of the Tyrer-Cuzick model in this patient population was assessed using a calibration plot and a concordance index (C-index) for right censored survival time data. Results 1192 women with a median follow-up of 6.2 years (interquartile range [IQR] 2.7-10.1) were included. Median age at LCIS diagnosis was 49 years (IQR 45-55); 87.9% of women were white, 37% were postmenopausal, 28% had a first-degree family member with breast cancer, and 13.3% had a second-degree family history. 182 patients developed an IBC; median age at diagnosis was 54 years (IQR 49-61). 5- and 10-year cumulative incidences of invasive cancer were 12% (95% confidence interval [CI] 10-14%) and 19% (95% CI 16-22%), respectively. The mean and median Tyrer-Cuzick 10-year risk scores were 20.9 and 20.1 (IQR 17.4-24.3), respectively. The calibration plot indicates that the Tyrer-Cuzick model is not well calibrated in this patient population (Figure). Discrimination measured by the C-index was 0.497. Conclusion The Tyrer-Cuzick model overpredicts IBC risk for women with LCIS. Individual risk estimates are not concordant between predicted risk and IBC development, suggesting that this model should not be used on breast cancer risk assessment in women with LCIS.

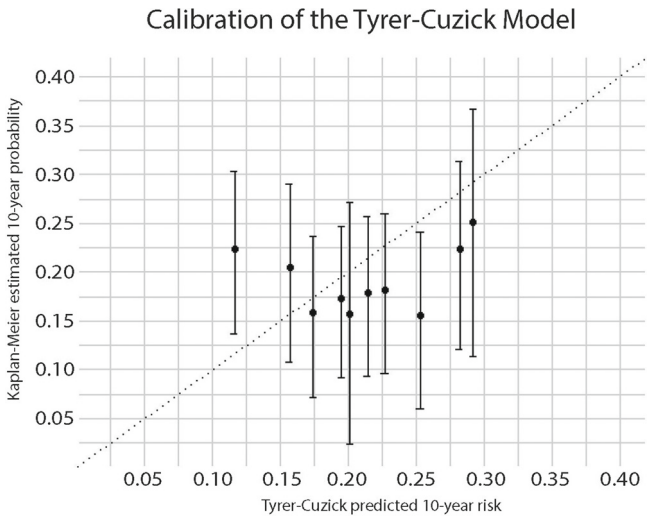
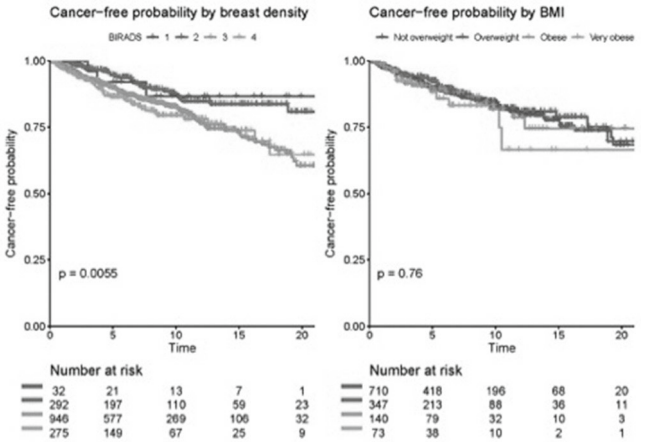


Figure. Calibration of predicted-to-observed 10-year cancer probability

26

Do BMI and Breast Density Impact Cancer Risk Among Women with LCIS? C. Minami,[1]* E. Zabor,[1] A. Park,[1] E. Gilbert,[2] A. Newman,[1] T.A. King,[3] M. Pilewskie.[1] *1. Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; 2. Weill Cornell Medical College, New York, NY; 3. Department of Surgery, Brigham and Women's Hospital; Breast Oncology Program, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA.*

Introduction Both body mass index (BMI) and breast density impact breast cancer (BC) risk. Whether obesity and density represent additive risk in women with lobular carcinoma in situ (LCIS), an already high-risk group, is unknown. Methods Patients diagnosed with LCIS from 1980-2017 were identified from a prospectively maintained database. BMI was categorized by World Health Organization classification. Density was captured as the mammographic BIRADS value at time near LCIS diagnosis. Other covariates included age at LCIS diagnosis, menopausal status, family history, chemoprevention, and prophylactic mastectomy. Cancer-free probability was estimated using the Kaplan-Meier method, and Cox regression models were used for univariable and multivariable analyses. Results 1589 patients were identified. Obese patients had less-dense breasts, were older, more likely to be postmenopausal, and less likely to have MRI screening. With a median follow-up of 7 years, 234 women developed BC (161 invasive, 82 ductal carcinoma in situ); 5 and 10-year cumulative incidences of BC were 10% and 17%, respectively. In univariable and multivariable analyses, BMI was not associated with a statistically significant increased BC risk, although in multivariable analysis, increasing BMI had non-significant positive effect sizes for association with hazard of cancer (overweight HR 1.02, obese HR 1.46, very obese HR 1.73, p>0.05). Increased breast density (BIRADS 1,2 vs 3,4) was significantly associated with increased BC risk (HR 2.67, 95% CI 1.63-4.38)(Figure). On multivariable analysis, use of chemoprevention was associated with a significantly decreased BC risk (HR 0.4, 95% CI 0.22-0.7), accounting for this variable's time-dependent nature. Exploratory analyses did not demonstrate significant interaction between BMI and breast density, or between BMI and menopausal status. There was no interaction between chemoprevention efficacy and BMI or density. Conclusions The increased risk of developing BC in patients with LCIS is not mutable by obesity, but increased breast density was shown to be an additional risk factor. Chemoprevention proved to be a durable protective factor against BC in this cohort irrespective of BMI or density.



Cancer-Free Probability by Breast Density and BMI
BMI, body mass index; BIRADS, Breast Imaging Reporting and Data System

27

Evaluation of Surgical Disparities Between African American and European American Women Treated for Breast Cancer within an Equal-Access Military Healthcare System L. Lovejoy,[2] M. Hueman,[1] C. Shriver,[1] R. Ellsworth.[1]* *1. Murtha Cancer Center, Bethesda, MD; 2. Windber Research Institute, Windber, PA.*

Background: Survival disparities in African American women (AAW) with invasive breast cancer may be attributable to access to medical care. Here, wee evaluated surgical disparities between AAW and European American women (EAW) treated within an equal-access military treatment facility (MTF). Methods: All AAW (N=233) and EAW (N=533) with early-stage invasive breast who had initial surgical diagnoses performed at Walter Reed National Military Medical Center (2001-2017) without neoadjuvant therapy were identified. Surgical delay was defined as the time between diagnostic biopsy and first breast operation. Differences in surgical interval and procedures were evaluated using Chi-square and Student t-tests with a P-value <0.05 defining significance. Results: Surgical delays of >60 days did not differ significantly between populations (7% AAW, 6% EAW) with an average surgical interval of 35.6 days in AAW and 33.6 days in EAW. Frequency of re-excision (31% AAW, 33% EAW), mastectomy (39% in AAW, 39% in EAW), prophylactic removal of the second breast (25% in AAW, 33% in EAW) and sentinel lymph node biopsy (AAW 87%, EAW 91%) did not differ significantly between populations. Within the subpopulation diagnosed between 2001 and 2013, the 5-year survival rate did not differ significantly (AAW 95%, EAW 97%). Discussion: In contrast to data from the general US population, treatment intervals and surgical procedures did not differ significantly between AAW and EAW treated within an equal-access MTF. These data demonstrate that when quality surgical breast care was available to all patients, disparities in survival were not detected between AAW and EAW. Our results stress the importance of equalizing access to breast care to reduce outcome disparities in the often underserved African American population. The opinions or assertions contained herein are the private ones of the author/speaker and are not to be construed as official or reflecting the views of the Department of Defense, the Uniformed Services University of the Health Sciences or any other agency of the U.S. Government.

28

The Unintended Beneficial Side-Effects of Non-Surgical Treatment on the Regional Recurrence Risk in Breast Cancer Patients

J.v. Steenhoven,[1]* A. Kuijer,[2] M. Roos,[1] K. Schreuder,[3] S. Elias,[4] P.v. Diest,[5] S. Siesling,[3] M. Smidt,[6] T.v. Dalen.[1] *1. Department of Surgery, Diakonessenhuis Utrecht, Utrecht, Netherlands; 2. Department of Surgery, St. Antonius Hospital, Nieuwegein, Netherlands; 3. Department of Research, Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands; 4. Department of Epidemiology, Julius Center for Health Sciences and Primary Care, Utrecht, Netherlands; 5. Department of Pathology, University Medical Center Utrecht, Utrecht, Netherlands; 6. Department of Surgery, University Medical Center Maastricht, Maastricht, Netherlands.*

Introduction: For patients who undergo breast conserving surgery (BCT) and have a tumour positive sentinel lymph node (SLN N+) the Z0011 study showed that a 27% chance of additional lymph node metastases translates into only 1.5% of patients developing regional metastases without further axillary treatment. Likewise, in SLN N0 patients, the 5-year RR rate of 0.5-1% is much lower than the reported 7% false negative rate of the SLNB procedure. In this study, we aimed to quantify the effect of non-surgical treatment modalities on the regional recurrence (RR) risk in a large cohort of SLN N0 breast cancer patients. Methods: Patients surgically treated for primary unilateral invasive breast cancer staged as SLNB N0 between 2005-2008 and with five years follow-up data regarding RR were available through the Netherlands Cancer Registry. Patients treated by axillary lymph node dissection, patients who underwent BCT and received no radiotherapy (RT) and patients who underwent mastectomy followed by RT were excluded. We compared the crude 5-year risk of developing RR using Kaplan-Meier statistics. Multivariable cox regression analysis was used to model the hazard of developing RR over five years in order to quantify the hypothesized effect of adjuvant systemic therapy and of RT on the breast. Results: A total of 14.064 patients underwent surgery for primary breast cancer and had a negative SLNB (pN0). For all patients, the crude risk of developing RR after 5-years was 1.2%. Cox regression analysis revealed a hazard ratio (HR) of 0.45 [95%CI 0.33-0.63], 0.33 [95% CI 0.19-0.58], 0.45 [95% CI 0.28-0.74] and 0.73 [95%CI 0.28-1.95] for patients treated by RT as routine part of BCT, endocrine therapy, chemotherapy and targeted therapy respectively. Histological grade, tumour size and young age were also associated with a higher RR risk (Table 1). Conclusion: Non-surgical treatment modalities not intending to treat the axilla independently reduce the risk of developing RR. The respective contributions of radiotherapy and systemic therapies accumulate into a more than tenfold lower risk of developing RR than the risk of additional lymph node metastases.

Cox regression proportional hazards of developing regional recurrence after a negative sentinel lymph node biopsy (n=14,064)

VARIABLE	HAZARD RATIO	95% CI	P value
BCT (vs. amputation)	0.45	0.33-0.63	<0.001
CT (vs. no CT)	0.33	0.19-0.58	<0.001
ET (vs. no ET)	0.45	0.28-0.74	0.002
TT (vs. no TT)	0.73	0.28-1.95	0.54
Tumoursize (vs. T1a-b)			
T1c	2.47	1.46-4.19	0.001
T2	4.22	2.31-7.74	<0.001
Age (vs. <35)			
35-50	0.72	0.25-2.07	0.55
50-70	0.42	0.15-1.22	0.11
>70	0.28	0.08-0.87	0.027
Grade (vs. grade I)			
II	2.93	1.76-4.91	<0.001
III	4.42	2.36-8.29	<0.001
Intrinsic subtypes (vs. HR+/HER2-)			
HR+/HER2+	1.28	0.70-2.34	0.43
HR-/HER2+	1.15	0.51-2.6	0.73
TN	1.35	0.75-2.43	0.32
Unknown	1.09	0.65-1.83	0.74
Lobulair (vs. ductal)	0.57	0.28-1.12	0.11
Multifocal (vs. unifocal)	1.47	0.94-2.30	0.091

BCT; breast conserving therapy, CT; chemotherapy, ET; endocrine therapy, TT; targeted therapy, HR; hormone receptor, HER2; human epidermal growth factor receptor 2, TN; triple negative breast cancer CI; confidence interval

29

The Prognostic Value of the AJCC 8th Edition Staging System for Patients Undergoing Neoadjuvant Chemotherapy for Breast Cancer

O. Kantor,[1]* J. Bao,[1] N. Jaskowiak,[1] K. Yao,[2] J. Tseng.[1] *1. Surgery, University of Chicago, Chicago, IL; 2. NorthShore University HealthSystem, Evanston, IL.*

Background: The AJCC 8th edition staging system for breast cancer has been validated in several groups of patients but has not been examined for its prognostic impact on patients undergoing neoadjuvant chemotherapy (NCT). Our objective was to determine the value of the AJCC 8th edition clinical staging system for this subset of breast cancer patients. Methods: The National Cancer Data Base was used to identify patients with invasive unilateral breast cancer from 2010-2015 who underwent NCT. Comparison of the 7th and 8th edition AJCC clinical classifications and Kaplan-Meier survival curves were used for analysis. Results: 76,178 patients underwent NCT for unilateral clinical stage I-III breast cancer from 2010-2015. Both 7th and 8th edition clinical staging could be assigned to 59,678 patients (75.4%). With the 7th edition clinical staging, 8.6% of patients were stage IA, 0.2% IB, 32.9% IIA, 29.3% IIB, 17.8% IIIA, 8.1% IIIB, and 3.3% IIIC. With the 8th edition clinical prognostic staging, 4.6% of patients were stage IA, 14.4% IB, 22.9% IIA, 24.1% IIB, 5.6% IIIA, 23.0% IIIB, and 5.4% IIIC. Overall, 37.5% of patients were downstaged and 27.8% were upstaged from the 7th to the 8th edition classification [Table 1]. Kaplan Meier curves comparing 7th and 8th edition staging differed in overall survival (OS) rates (mean follow up 41.5 months). 7th compared to 8th edition estimated 5yr OS were: 90.7% vs 91.9% for stage IA; 87.3% vs 92.3% for stage IB; 88.9% vs 88.8% for stage IIA; 83.9% vs 85.1% for stage IIB; 77.3% vs 83.5% for stage IIIA; 69.3% vs 75.1% for stage IIIB; and 64.5% vs 61.3% for stage IIIC. The 8th edition clinical prognostic staging was a better predictor of survival than the 7th edition (ROC 0.67 vs 0.62, p<0.01). Conclusions: There are significant differences in the clinical stage of patients undergoing NCT by the 7th vs 8th edition AJCC staging with 65% of patients having a shift in clinical stage. This is reflected in differences in 5yr OS rates between the two staging systems with the 8th edition having a better predictive value for survival. The 8th edition staging will help improve prognostic modeling in patients undergoing NCT.

Table 1. AJCC 7th edition clinical anatomic staging compared to 8th edition clinical prognostic staging groups.

	8th IA	8th IB	8th IIA	8th IIB	8th IIIA	8th IIIB	8th IIIC
7th IA	2670 (54.1%)	2130 (43.2%)	54 (1.1%)	65 (1.3%)	0 (0%)	14 (0.3%)	0 (0%)
7th IB	0 (0%)	41 (33.9%)	36 (29.8%)	36 (29.8%)	1 (0.8%)	6 (5.0%)	1 (0.8%)
7th IIA	0 (0%)	4856 (25.7%)	5557 (29.4%)	8244 (43.6%)	39 (0.2%)	178 (0.9%)	16 (0.1%)
7th IIB	0 (0%)	1261 (7.5%)	4605 (27.4%)	5085 (30.3%)	652 (3.9%)	5154 (30.7%)	52 (0.3%)
7th IIIA	0 (0%)	0 (0%)	2909 (28.5%)	414 (4.1%)	2261 (22.2%)	2023 (19.8%)	2595 (25.4%)
7th IIIB	0 (0%)	0 (0%)	0 (0%)	0 (0%)	214 (4.6%)	4138 (89.3%)	281 (6.1%)
7th IIIC	0 (0%)	0 (0%)	0 (0%)	0 (0%)	59 (3.1%)	1683 (89.6%)	136 (7.2%)

Green=downstaging, purple = upstaging

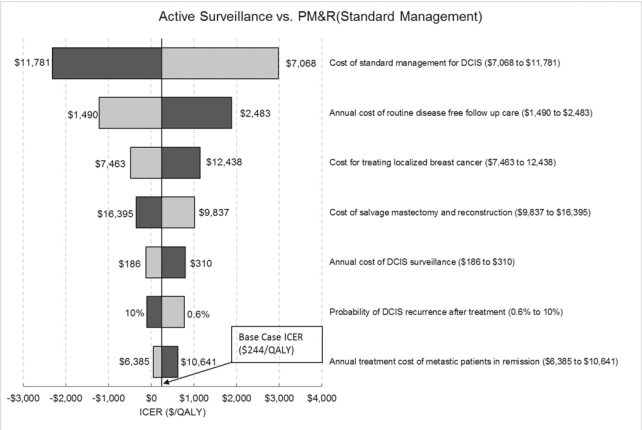
30

Cost-effectiveness Analysis of Active Surveillance Compared to Partial Mastectomy Plus Radiation for Ductal Carcinoma In Situ: Is Nonoperative Management a Viable Option?

S. Sun,[1]* R. Suk,[2] H. Kuerer,[1] S.B. Cantor,[1] B.M. Raber,[1] A.A. Deshmukh.[2] *1. The University of Texas MD Anderson Cancer Center, Houston, TX; 2. University of Texas Health School of Public Health, Houston, TX.*

Background: Since the advent of screening mammogram, the prevalence of ductal carcinoma in situ (DCIS) has increased 500-fold, suggesting that we are over-diagnosing and may be over-treating many women with low propensity for progression to invasive disease. Our objective was to assess the comparative cost-effectiveness of partial mastectomy and radiation (PM&R), the most common current standard practice, and active surveillance (AS) for women with DCIS. Methods: We constructed a state-transition age-representative micro-simulation model to simulate the clinical course of women with DCIS. We compared AS to PM&R in women with low/intermediate grade, hormone receptor-positive DCIS. Transition probabilities and utilities (quality of life scores) were extracted from published studies. Direct costs were based on Medicare reimbursement rates; other direct non-health related costs

(e.g. lost wages, travel costs) were also considered. The simulated individuals were followed until death. The optimal strategy over the lifetime was determined using incremental cost-effectiveness ratios (ICER) — estimated from a societal perspective. Future costs and QALYs were discounted at an annual rate of 3%. Results: AS was more effective (10.82 vs. 9.95 QALYs) and at a slightly higher cost ($16,683 vs. $16,468) when compared with PM&R, resulting in an ICER of $244 per QALY gained. Because this ratio is well below the commonly accepted willingness-to-pay threshold of $100,000 per QALY, AS resulted in cost-effective use of healthcare resources when compared with PM&R. Sensitivity analyses were performed on cost parameters using 25% range variation. This showed that the cost for PM&R for DCIS led to the widest variation in ICER, however AS remained cost effective (Figure 1). Conclusions: This study shows that for women with low/intermediate grade, hormone receptor-positive DCIS, AS was a cost-effective strategy when compared with the most common current standard practice. This conclusion supports several ongoing randomized controlled trials evaluating active surveillance as a potential viable treatment option for DCIS.



31

KRAS Mutation is Associated with Immunosuppressive Tumor Microenvironment in Mismatch-Repair Proficient Colorectal Cancer M. Marco,* S. Choi, C. Chen, J. Shia, R. Pelossof, J. Garcia-Aguilar. *colorectal service, Memorial Sloan Kettering Cancer Center, Wayne, NJ.*

Background: KRAS-mutant ($KRAS^{mut}$) colorectal cancers (CRC) are associated with worse prognosis and resistance to therapy. We have previously shown that $KRAS^{mut}$ CRC have different transcriptomic signature of stromal and immune-related genes compared to KRAS-wild type ($KRAS^{wt}$) tumors. Here, we validated the immune-related changes in the tumor microenvironment associated with the KRAS mutation in CRC. Methods: The expression of different immune markers were assessed using multiplex immunofluorescence (IF) technique. Sequential slides were cut from paraffin blocks. Each slide was stained with 4 IF antibodies. The stained slides were scanned, and quantification of immune cells was done using ImageJ software. DNA extracted from each tumor was profiled for 420 cancer genes using targeted exome-capture sequencing (MSK-IMPACT assay). DNA mismatch-repair (MMR)proteins' deficiency were tested by immunohistochemistry. Results: The study included 39 MMR-proficient CRCs of patients resected at our institute. AJCC stages I-III were not different between $KRAS^{mut}$(n=15) and $KRAS^{wt}$(n=25) tumors. M2-macrophages (CD68+CD163+ cells) and IL17-producing cells (IL17+ cells) were significantly higher in $KRAS^{mut}$ tumor cores (TC) compared to $KRAS^{wt}$ TC (p=0.002, and 2.9e-6, respectively; Fig.1). T-helper cells (CD3+CD4+cells) were significantly lower (p=3.9e-4) in $KRAS^{mut}$ TC compared to $KRAS^{wt}$ TC. Treg (CD3+CD4+FOXP3+cells) were significantly higher in $KRAS^{mut}$ invasive margins (IM) compared to $KRAS^{wt}$ IM (p=0.01). $KRAS^{mut}$ TC had significantly higher ratios of Treg/T-helper cells, and Treg/CD8+cytotoxic T cells (p=0.008, and 0.04, respectively) compared to $KRAS^{wt}$ TC. There was no difference in CD20+ B cells, CD56+ NK cells, and immune check-point ligands; PD1, PDL1, and CTLA4 between $KRAS^{mut}$ and $KRAS^{wt}$ TC or IM. Conclusions: KRAS oncogene is associated with more pro-tumorigenic (M2 macrophages, IL17 and Treg) and less anti-tumorigenic (CD4 T-helper) immune cells in CRC. These results can be used to guide further research to design novel immunotherapy strategies against $KRAS^{mut}$ CRC.

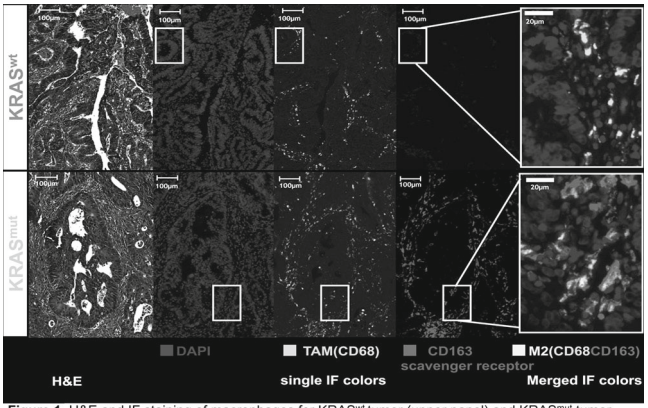


Figure 1. H&E and IF staining of macrophages for $KRAS^{wt}$ tumor (upper panel) and $KRAS^{mut}$ tumor (lower panel) in tumor cores (TC). Middle 3 panels are showing Single IF colors; DAPI, blue; CD68+Tumor associated macrophages (TAM), green; CD163 scavenger receptor, red. Scale bars, 100 microns. Right panel showing merged IF colors; triple positive CD68+CD163+DAPI+cells (M2-macrophages), yellow. Scale bars, 20 microns.

32

Phase 1/2 Trial of Adjuvant Dendritic Cell Vaccine with Chemokine Modulation in Peritoneal Carcinomatosis R. Ramanathan,[1]* M. Girgis,[2] H. Jones,[1] P. Kalinski,[3] J. Tobin,[1] H.A. Choudry,[1] L. Totin,[1] W. Gooding,[1] D.L. Bartlett.[1] *1. Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA; 2. University of California in Los Angeles, Los Angeles, CA; 3. Roswell Park Cancer Institute, Buffalo, NY.*

Introduction: Peritoneal carcinomatosis (PC) has a low response rate to standard chemotherapies. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) improves outcomes, but recurrence is common. This Phase I/II trial evaluates the safety and efficacy of direct intranodal transfer of autologous antigen-loaded polarized type 1 dendritic cell (aDC1) vaccines with chemokine modulation (CKM) after CRS/HIPEC. Methods: Patients undergoing CRS/HIPEC for appendiceal or colorectal primary PC and peritoneal mesothelioma were enrolled. In addition to standard chemotherapy, patients received ultrasound-guided intranodal and intradermal injections of aDC1 vaccine and CKM every four weeks for up to three cycles. CKM consisted of celecoxib, interferon alpha, and rintatolimid. Results: Fifty-six patients were enrolled, with 31 appendiceal primaries, 21 colorectal primaries, and two mesotheliomas. In the Phase I cohort (n=11), low dose and high dose vaccine were tolerated equally with no adverse effects, and high dose were used in the Phase II (n=45). Autologous aDC1 were loaded with tumor antigen. 97% of cells expressed HLA-DR and CD86 suggesting appropriate activation. IL12 production has been correlated with progression free survival (PFS), and mean IL12 production was 3.5 ng/mL per $2x10^4$ aDC1. However, tumor cell recovery from tissue specimens was low, and only 8% of aDC1 were loaded with the target tumor cell to dendritic cell ratio of 3:1. Furthermore, due to low tumor cell yield and low aDC1 recovery after cryopreservation, only 22% of patients were injected with the target dose of $3x10^6$ aDC1. Intranodal and intradermal injection was successful in all patients. There were six grade III-V adverse events. Median PFS for appendiceal primaries was 31 months, colorectal 11 months, and mesothelioma 20 months. Compared to an institutional, matched, historical cohort there was no significant difference in PFS. Conclusions: This study demonstrates the safety and feasibility of intranodal and intradermal injection of aDC1 vaccine and CKM. Improving tumor cell recovery and aDC1 recovery to target ratios and quantities may improve patient outcomes.

33

Machine Learning Algorithm Improves Accuracy of Perioperative Risk Prediction Tools J.H. Terhune,* S.B. Edge, S. Nurkin. *Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Current predictive models utilized to estimate perioperative risks in patients undergoing oncologic surgery provide varied results and often have low correlation with each other, limiting their value in providing an accurate risk assessment. The application of machine learning (ML) or artificial intelligence (AI) to predictive algorithms provides an opportunity to improve upon models presently in use due to their unique ability to constantly refine results as data is added in real time; this is especially relevant in oncology with the increasing

volume of genomic information. We hypothesize that a ML algorithm can outperform the risk assessment tools presently in use to predict perioperative outcomes. We have applied a Machine Learning model (Bitwise Analytics LLC) to colon cancer data from the National Cancer Database (NCDB) through 2015, which included 830,638 patients, of which 761,523 patients had data that was analyzable by the algorithm. We randomly selected 70% of this data to train a ML model; the remaining 30% of the data was used to test the accuracy of the model. The algorithm was tested on overall survival and 30-day readmission data. After applying numerous algorithms and combinations of data, we have achieved ≥90% in predictive accuracy for overall survival and 30-day re-admissions rates. Our predictive model for overall survival after colorectal oncologic resection has an accuracy of 0.890 with an area under the curve (AUC) of 0.956 (Fig 1A). The predictive model estimating 30-day hospital re-admission after resection has an accuracy of 0.917 and an AUC of 0.768 (Fig 1B). As payers increasingly move to a fee-for-value reimbursement strategy, as opposed to fee-for-service, the need to compare an institution's outcomes to those expected for their patient population becomes increasingly relevant. Our ML model provides improved accuracy and AUC in predicting hospital re-admission and overall survival after colorectal surgery compared to the risk calculators presently in use. Furthermore, the model is able to continuously analyze new data as it is added and adapt to advances in the field as they are developing, a distinct advantage over the current risk calculators.

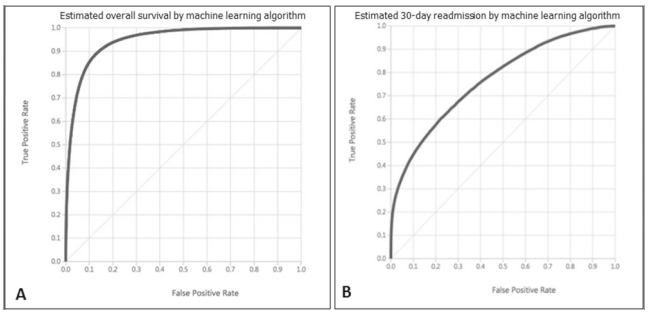


Figure 1: Machine learning algorithm applied to National Cancer Database cohort of patients undergoing colorectal oncologic resection up to 2015. (A) Overall survival curve estimated by the machine learning algorithm has an accuracy of 0.890 and area under the curve (AUC) of 0.956. (B) 30-day re-admission curve estimated by the algorithm with an accuracy of 0.91 and an AUC of 0.768.

34

Health-Related Quality of Life Deterioration Diminishes Benefit of Colorectal Cancer Resection in Older Patients A.M. Blakely,* D. Chanson, L. Wong, S. Sentovich, K. Melstrom, L. Lai, Y. Fong, V. Sun. *City of Hope, Duarte, CA.*

Background: Outcomes of oncologic resection is related to tumor biology as well as patient-reported health factors. However, data regarding changes in functional status and health-related quality of life (HRQOL) before and after surgery are currently lacking. Methods: We identified colorectal cancer patients from the SEER-Medicare Health Outcomes Survey (MHOS) linked database. HRQOL survey data captured physical/mental health, activities of daily living (ADLs), and medical comorbidities. Patients who underwent surgery with 1) baseline HRQOL survey prior to cancer diagnosis and 2) follow-up survey at least one year after diagnosis were selected. Patient, disease, and HRQOL measures were analyzed in regard to overall survival (OS) and disease-specific survival (DSS). Results: Overall, 590 patients were evaluated, of whom 265 (45%) were male. Age at diagnosis was 65-69 years for 98 patients (17%), 70-79 years for 310 (52%), and ≥80 years for 182 (31%). The majority of patients were Caucasian (n=445, 78%); 42 (7%) identified as Hispanic. Stage was I-II for 309 (52%), III for 239 (41%), and IV for 42 (7%). In general, the cohort experienced a decline in physical and mental HRQOL and ADLs as well as an increase in the number of major comorbidities (see Table). Median OS was 83 months. On univariate analysis of ADLs, only decreased ability to feed oneself was associated with increased risk of mortality (HR 2.4, p=0.022). Decreased OS was independently associated with age ≥70 vs. 65-69 years (HR 2.0, p=0.0006), male sex (HR 1.4, p=0.024), more advanced disease (Stage III vs. I-II: HR 1.6, p=0.0006; Stage IV vs. Stage I-II: HR 7.0, p<0.0001), and decline in mental HRQOL (HR 1.5, p=0.0068). Decreased DSS was independently associated with Hispanic race (HR 2.4, p=0.0004) and more advanced disease (Stage III vs. I-II: HR 3.8, p<0.0001; Stage IV vs. Stage I-II: HR 17.4, p<0.0001). Conclusions: The potential overall survival benefit of oncologic surgery is diminished by a decline in physical and mental health. Early identification of older surgical patients at risk for functional and HRQOL declines may in turn optimize oncologic outcomes.

Health-related Quality of Life, Activities of Daily Living, and Co-Morbidity Scores by Survey Time Point

Variable	Baseline	Follow-Up
Physical HRQOL - At or above population mean (score 50+)	182 (31%)	112 (19%)
Physical HRQOL - Below population mean (score<50)	408 (69%)	478 (81%)
Mental HRQOL - At or above population mean (score 50+)	404 (68%)	378 (64%)
Mental HRQOL - Below population mean (score <50)	186 (32%)	212 (36%)
Bathing - No difficulty	539 (91%)	512 (87%)
Bathing - Have difficulty or unable to do	51 (9%)	76 (13%)
Dressing - No difficulty	554 (94%)	527 (89%)
Dressing - Have difficulty or unable to do	36 (6%)	63 (11%)
Eating - No difficulty	576 (98%)	564 (96%)
Eating - Have difficulty or unable to do	13 (2%)	25 (4%)
Getting in and out of chairs - No difficulty	476 (81%)	453 (77%)
Getting in and out of chairs - Have difficulty or unable to do	114 (19%)	135 (23%)
Walking - No difficulty	428 (73%)	394 (67%)
Walking - Have difficulty or unable to do	162 (27%)	195 (33%)
Using the toilet - No difficulty	560 (95%)	539 (92%)
Using the toilet - Have difficulty or unable to do	30 (5%)	50 (8%)
ADL scores - Independence with each ADL = 1 point	5.3 (±1.3)	5.1 (±1.4)
Number of self-reported comorbidities - 0	317 (54%)	241 (41%)
Number of self-reported comorbidities - 1	200 (34%)	205 (35%)
Number of self-reported comorbidities - 2+	73 (12%)	144 (24%)

HRQOL=health-related quality of life; ADL=activities of daily living

35

Measuring Guideline-Concordant Care for Rectal Cancer as a Quality Metric in Colorectal Cancer P.R. Varley,* P. Bou-samra, S. Tohme, C. Shen, A. Tsung. *University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: National Comprehensive Cancer Network guidelines for rectal cancer recommend neoadjuvant therapy (NAT) for all patients with T3-4, N1-2 rectal cancer. We hypothesized that concordance with this guideline may be associated with improved outcomes not only for patients being treated for rectal cancer, but all colorectal cancers. Methods: The National Cancer Database from 2004-2014 was queried for all patients undergoing surgery for Stage I-III colorectal adenocarcinoma. A treatment center's neoadjuvant therapy rate (NATr) was calculated by identifying T3-4, N1-2 patients who did or did not receive NAT. Treatment centers were then divided into tertiles based on NATr. This variable was then used in a stratified, multivariable Cox proportional hazard regression to evaluate impact on overall survival. Results: There were 963 treatment centers with >10 cases available for evaluation, and the median NATr was 83.3% (range 10-100%, IQR 71.4-90.3%). Tertiles for NATr were 0-74.3%, 74.4%-88.2% and ≥88.3%. Median survival with 95% CIs stratified by anatomic location, pathologic stage and NATr tertile are presented in Table 1. As expected, NATr has the most demonstrable effect in patients with Stage III rectal cancer. However in a multivariable Cox regression stratified for primary site, node positivity and T-stage, treatment at the mid- and high-NATr centers was associated with a significant improvement in overall survival when compared to the low NATr centers (HR 0.95, 95% CI 0.949-0.962, p < 0.001 and HR 0.95, 95% cI 0.935-0.958, p < 0.001, respectively). Conclusion: In this study NATr attempts to quantify guideline-concordant care for patients with T3-4, N1-2 rectal adenocarcinoma within a national sample of cancer treatment centers. NATr is strongly associated with survival in patients with Stage III rectal adenocarcinoma, but it also is a significant predictor of survival in patients presenting with colorectal primaries that would not be expected to receive NAT. NATr may therefore be influenced by structural factors within a treatment center that lead to improved patient outcomes, and it may be considered for use as a quality benchmark.

Stage I			
	Low	Middle	High
Right	116.5 (114.4-120.5)	124.2 (120.8-127.2)	119.1 (116.1-122.3)
Transverse	116.5 (109-128.2)	123.4 (116-132.3)	124.5 (118.3-138.9)
Left	147.6 (139.1-*)	152.1 (148.2-*)	147.8 (143.6-*)
Rectosigmoid	144.1 (*-*)	151.8 (*-*)	*
Rectum	132.3 (125.3-144)	147.8 (*-*)	*
Stage II			
	Low	Middle	High
Right	94.1 (91.9-96.7)	98.3 (96.3-100.5)	100.3 (98-103.3)
Transverse	92.4 (87.9-96.2)	96.8 (93.2-102.4)	100.2 (95.5-104.6)
Left	102.1 (98.6-105.4)	109.3 (105.8-113.2)	113.7 (108.9-118)
Rectosigmoid	111.2 (103-123)	126.6 (117.9-136.8)	120.7 (114.3-127.9)
Rectum	100.4 (93.7-106.1)	111.2 (106.4-116)	118.2 (112.5-123.7)
Stage III			
	Low	Middle	High
Right	58.9 (57.2-60.6)	62.7 (60.9-64.7)	67 (65.2-69.3)
Transverse	62.8 (57.7-67.5)	64.9 (61-70.4)	68 (62.9-73)
Left	87.1 (83.6-90.8)	100.5 (97.2-104.6)	102.9 (97.8-107.8)
Rectosigmoid	99.8 (89.3-107.5)	108 (102.5-115.1)	110.4 (104.6-116.2)
Rectum	76 (72.1-79.8)	94 (90.2-97.5)	100.9 (96.1-105.8)

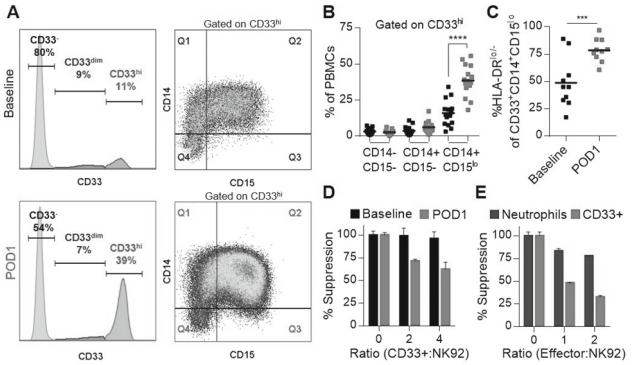


Figure. Immature myeloid cells accumulate after surgery and suppress NK cells in humans. **(A)** Representative histograms and flow plots from a cancer patient at baseline and POD1 **(B)** demonstrating a significant increase in $CD33^+/CD14^+/CD15^{lo}$ myeloid cells, **(C)** with low HLA-DR expression. **(D)** Isolated $CD33^+$ cells from POD1 (red) suppress NK92 cytotoxicity against K562 targets by ~60%, while cells isolated preoperatively (black) are not suppressive. **(E)** Neutrophils (blue, $CD33^+ CD15^{hi}$) isolated on POD1 are significantly less suppressive of NK92 cytotoxicity as compared to $CD33^+$ cells (red) isolated at the same time from the same patients.

36

Immunophenotyping Postoperative Myeloid Derived Suppressor Cells in Cancer Surgery Patients L. Angka,[1] A. Jeong,[2] M. Scaffidi,[1] C. Tanese de Souza,[2] L. Kuhlmann,[3] M. Kennedy,[2] T. Kislinger,[3] R.C. Auer.[1]* *1. Surgery, University of Ottawa, Ottawa, ON, Canada; 2. Ottawa Hospital Research Institute, Ottawa, ON, Canada; 3. University of Toronto, Toronto, ON, Canada.*

Immunosuppression following curative cancer surgery is multifaceted but ultimately predisposes to postoperative infections and cancer recurrence. We have previously demonstrated, in murine studies, that myeloid derived suppressor cells (MDSCs) play a major role in mediating postoperative immunosuppression. These surgery-induced MDSCs were shown to be directly responsible for postoperative Natural Killer (NK) cell dysfunction and increased metastases. We hypothesize that targeting surgery-induced MDSCs in cancer patients will improve post-operative immune function and cancer outcomes. Unfortunately, human MDSCs are challenging to define and surgery-induced MDSCs have not been previously characterized. To investigate unique surface markers on surgery-induced MDSCs, cancer surgery patients (n=28) at a university-affiliated hospital were prospectively enrolled. Peripheral blood mononuclear cells were isolated before and after surgery and assessed for common human MDSC markers (CD33, CD11b, CD14, CD15, HLA-DR, CD124). We observed a large and consistent increase (2.4 fold, $p<0.0001$) in monocytic-MDSCs (Mo-MDSCs, $CD33^+CD14^+CD15^{lo/-}Lin^-$), with an immature phenotype (78.7% $HLA\text{-}DR^{lo}$) on post-operative day 1 (POD1). These POD1 MDSCs potently suppress Natural Killer (NK) cell cytotoxicity ex vivo (53.6% suppression; n=19, $p<0.0001$) while the POD1 neutrophils (which also expand 2.7 fold) are minimally suppressive. To further characterize these surgery-induced MDSCs, we performed a proteomics screen of cell surface proteins from sorted MDSCs before and after surgery, using a glycocapture technique. Upon validating the proteins which were most upregulated following surgery, we report that a unique marker (CDX) was restricted to MDSCs and increased after surgery in all 5 patients tested (44.7 to 67.9%, p=0.06). This is a provocative finding as CDX has been reported as a tumor-associated ligand for multiple immune checkpoint receptors present on NK cells. This study provides characterization of a previously unrecognized population of surgery-induced MDSCs and identifies a novel molecule for perioperative targeting. (Note: CDX is used to protect molecular identity pending patent filing)

37

Patient-Derived Tumor Infiltrating Lymphocytes Can be Reprogrammed and Differentiated to Tumor Mutation-Reactive T-Cells M.L. Good,[1]* N. Tamaoki,[1] T. Maeda,[1] S. Islam,[1] M. Bosch-Marce,[1] M. Kruhlak,[2] S. Pack,[3] N. Bedanova,[3] P. Malekzadeh,[1] D.C. Deniger,[1] R. Yoseph,[1] C. Liu,[4] K. Hanada,[1] P. Robbins,[1] S.A. Rosenberg,[1] R. Vizcardo,[1] N.P. Restifo.[1] *1. Surgery Branch, National Cancer Insitute, NIH, Bethesda, MD; 2. Experimental Immunology Branch, National Cancer Institute, NIH, Bethesda, MD; 3. Experimental Pathology Laboratory, National Cancer Institute, NIH, Bethesda, MD; 4. Transgenic Core, Division of Intramural Research, National Heart, Lung and Blood Institute, NIH, Bethesda, MD.*

BACKGROUND: Adoptive T Cell Therapy (ACT) targeting tumor mutated antigens can mediate durable response in some patients with advanced cancer, but response rates may be limited by the transfer of terminally differentiated effector cells. Induced Pluripotent Stem Cell (iPSC) technology may provide a future strategy to produce high numbers of mutation-reactive naïve T cells for use in ACT. However, mutation-reactive T cell receptors (TCR) have not previously been identified in iPSC generated by reprogramming tumor infiltrating lymphocytes (TIL-iPSC). Moreover, TIL-iPSC-derived T cells will need to be screened for tumor reactivity prior to clinical application. We aim to determine whether TIL-iPSC inherit mutation-reactive TCR and can be differentiated to T cells with preserved specificity. METHODS: TIL were reprogrammed to iPSC and characterized by conventional methods. TIL-iPSC were differentiated to immature T cells using OP9-DLL1 co-culture system, and activation was assessed by co-culture with peptide pulsed antigen presenting cells (APC). RESULTS: Using a T cell line and heterogeneous TIL obtained from the infusion bags of several patients, we could reprogram mutated antigen-specific T cells to iPSC, which retained rearranged TCR against mutant peptides. TIL-iPSC generated from mutant GBAS reactive T cells were differentiated to CD34+CD43+ hematopoietic progenitors and subsequently CD4-CD8- double negative (DN) and CD4+CD8+ double positive (DP) T cells, which both expressed TCR complex. Co-culture of TIL-iPSC-derived T cells with APC resulted in antigen-specific upregulation of 4-1BB, even when DN T cells were used. TIL-iPSC generated from the infusion bag of a patient with regression of metastatic colorectal cancer following ACT targeting mutant KRAS G12D were differentiated to DN and DP T cells, which are being tested for mutation-specific activation. CONCLUSIONS: We have shown that patient-derived TIL-iPSC can be used to produce tumor mutation-reactive T cells. Our goal is to develop a xeno-free method to mass produce TIL-iPSC-derived cancer antigen-specific naïve T cells, which may significantly improve the therapeutic efficacy of ACT.

38

Identification of CD4+ and CD8+ T-Lymphocyte Responses Against TP53 Hotspot Mutations in Patients with Colorectal Cancer

P. Malekzadeh,* D.C. Deniger, A. Pasetto, P. Robbins, M.R. Parkhurs, B.C. Paria, Z. Yu, V. Hill, W. lo, S.L. Goff, S.A. Rosenberg. *Surgery, National Cancer Institute, Bethesda, MD.*

Introduction: TP53 tumor suppressor gene is the most commonly mutated gene in cancer. Certain mutations in the DNA binding domain occur at high frequencies and are termed hotspots. Forty-three percent of colorectal cancers harbor a TP53 mutation, however, investigation into the immunogenicity of TP53 hotspot mutations has not been reported. The primary aim of this study was to evaluate the immunogenicity of TP53 hotspot mutations in colorectal cancer as a prelude to the use of TP53 reactive cells for cell transfer immunotherapy. Methods: Whole-exome sequencing data was evaluated in 71 patients with colorectal adenocarcinoma. A novel technique using minigenes encoding 25 amino acid peptides containing each of the TP53 hotspot mutation flanked by 12 amino acids of wild type were concatenated in tandem to generate a tandem minigene(TMG). Similarly, wild type and mutated peptides corresponding to TP53 mutation were synthesized. Autologous dendritic cells were electroporated with TMGs or pulsed with peptides and co-cultured with tumor infiltrating lymphocytes (TIL) fragments. T-cell responses were measured by 41BB upregulation (flow cytometry) and secretion of interferon-γ using an Enzyme-Linked ImmunoSpot(ELISPOT) assay. Autologous tumor cell lines were generated from mouse xenografts. Allogenic tumor cell lines expressed mutant TP53. Results: Fifty-four (76%) colorectal tumors expressed a TP53 mutation, including 42(78%) missense, 7(13%) stop gain, 4(7%) frameshift, and 1(2%) non-frameshift deletion. Of the 42 tumors that expressed missense mutations, 21(50%) were found to express a hotspot mutation. Eight patients TIL (38%) were immunogenic and elicited either a CD4+ or CD8+ T-lymphocyte response. Autologous and allogenic hotspot mutation expressing tumor cell lines were recognized by reactive T cells. Conclusions: This study demonstrates that TP53 hotspot mutations are immunogenic and specific T cells were able to recognize naturally processed p53 neoepitopes on autologous and allogenic tumor cell lines. Thus, the most commonly mutated gene in cancer represents an attractive candidate for evaluating targeted cell transfer immunotherapies.

Patients with T-cell responses to TP53 hotspot mutations

Patient	Age/Sex	Cancer type	FrTu#	TP53 mutation	T cell type	TP53 neoepitope (mutation)
1	52M	Colon	4141	R175H	CD8	HMTEVVRHC
2	36M	Colon	4196	R175H	CD8	HMTEVVRHC
3	55M	Colon	4252	R175H	CD4	YKQSQHMTEVVRHCPHHERCSDSDG
4	46M	Colon	4285	R175H	CD4	VVRHCPHHERCSDSD/QHMTEVVRHCPHHER
5	44F	Colon	4259	Y220C	CD4/CD8	RNTFRHSVVVPCE/VVPCEPPEV
6	69F	Colon	4268	R248Q	CD4/CD8	YMCNSSCMGGMNQRPILTIITLEDS
7	41F	Colon	4266	R248W	CD8	SSCMGGMNWR
8	49M	Rectal	4273	R248W	CD4	SCMGGMNWRPILTII

39

Surveillance of Low-Grade Appendiceal Mucinous Neoplasms with Peritoneal Metastases After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: Is 5-Years Enough? A Multisite Experience

D. Solomon,[1]* Y.M. Maniar,[1] E.Y. Bekhor,[1] n. DeNicola,[1] L. Totin,[2] m. hofstedt,[1] S.N. Aycart,[1] J. Carr,[1] S. Ballentine,[1] D.R. Magge,[1] B.J. Golas,[1] R.K. Pai,[2] A. Polydorides,[1] D.L. Bartlett,[2] D.M. Labow,[1] H.A. Choudry,[2] U. Sarpel.[1] *1. Surgical Oncology, Icahn School of Medicine at Mount Sinai, Tel Aviv, Israel; 2. School of Medicine, University of Pittsburgh, Pittsburgh, PA.*

Background Low-grade appendiceal mucinous neoplasms (LAMN) are tumors that often present with widespread mucin in the peritoneal cavity (pseudomyxoma peritonei, PMP). Treatment with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is effective, but no recommendations exist regarding interval and duration of post-treatment surveillance. Methods Data from prospectively maintained databases of patients undergoing CRS/HIPEC 2004-2018 at two high-volume institutions were analyzed. Patients who underwent optimal (completeness of cytoreduction, CC0-1) CRS/HIPEC for PMP secondary to LAMN were included. Pathologic examination confirmed the diagnosis; cases of mucinous adenocarcinomas were excluded. Results Overall, 156 patients were included. Median PCI was 18 (IQR1-3 12-23), and 125 (80.1%) patients had CC0 cytoreduction. According to the AJCC grading, implants in 152 patients (97.4%) were classified as acellular mucin or G1, 2 (1.3%) as G2, and 2 (1.3%) as G3. During the follow-up period (median, 36 months, IQR 15-67) 23 patients (14.7%) recurred. All recurrences were peritoneal and occurred within 5 years from index surgery. In the study population, DFS at 1, 3, and 5 years was 95.5%, 83.4%, and 77.4%. Univariate Cox regression analysis showed that higher PCI scores (p<.001), CC1 cytoreduction (p=.005), and higher preoperative levels of CEA (p=.012) and CA-125 (p=.032) correlated with shorter DFS. On multivariate analysis, only higher PCI scores predicted earlier recurrences (p<.001). Among the 23 patients with recurrence median DFS was 21 months (95%CI 14.7, 27.3), and 1-, 3-, and 5-year DFS were 73.9%, 17.4%, and 0%. Conclusions Most patients recurred within 3 years from CRS/HIPEC, and none after 5 years. Earlier recurrence was associated with high PCI, CC1 score, and high pre-op CEA and CA-125. High PCI was the only independently significant variable. This suggests that appropriate surveillance would include tumor markers and imaging modalities every 6 months during the first 3 years, with annual surveillance thereafter until 5 years.

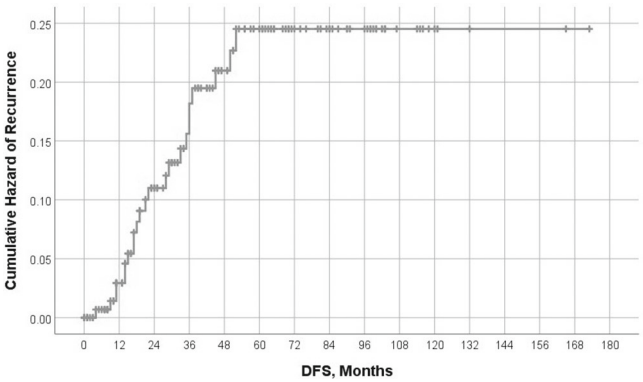


Figure 1. Kaplan Meier analysis on cumulative hazard of recurrence, overall study population

40

Universal Healthcare Coverage Does Not Ensure Adherence to Initial Colorectal Cancer Screening Guidelines

C. McEvoy,[1]* N. Shah,[2] S. Roberts,[2] A. Carroll,[2] T. Platz,[1] C.R. Oxner,[1] R. Butler,[1] R. Ricca.[1] *1. Surgical Oncology, Naval Medical Center Portsmouth, Chesapeake, VA; 2. Health Analysis, Navy and Marine Corps Public Health, Portsmouth, VA.*

Background- Colorectal cancer is the second leading cause of cancer deaths in the United States, and screening tests are underutilized. The aim of this study is to determine the proportion of individuals at average risk who obtained a recommended initial screening test during the first 36 months of screening eligibility in a universal healthcare coverage system. Methods- This is a retrospective cohort study and population-based analysis of active duty and retired military members as well as civilian beneficiaries of the Military Health System. Individuals born 1960 to 1962 and eligible for full health care benefits through the Military Health System on their 50th birthday were evaluated. Individuals meeting surveillance criteria prior to 50th birthday were excluded. Average risk individuals were analyzed. Adherence to the United States Preventive Services Task Force guidelines for initial colorectal cancer screening was determined using Current Procedural Terminology and Healthcare Common Procedure Coding System codes for colonoscopy, sigmoidoscopy, fecal occult blood test, and fecal immunohistochemistry test. Results- We identified 275,665 individuals at average risk. Of these, 105,957 (38.4%) adhered to screening guidelines. An additional 19,806 (7.2%) individuals were screened early between ages 47 to 49. Colonoscopy (82.7%) was the most common screening procedure. Highest odds of screening was associated with being active duty military (OR 3.63, 95% CI 3.43 to 3.85), having highest SES (OR 2.37, 95% CI 2.31 to 2.44), and having managed care insurance (OR 4.36, 95% CI 4.28 to 4.44). Limitations- The primary

limitations are the inherent biases associated with a retrospective data base study including reporting errors due to improper or insufficient medical coding. Conclusions- Universal healthcare coverage does not ensure initial colorectal cancer screening utilization nor does it eliminate disparities. Interventions to increase screening utilization and reduce disparities during initial years of screening eligibility are warranted in this population.

Baseline Demographics Among Patients Who Received Colorectal Cancer Screening Between Ages 47 and 49 (Early), Between 50 and 53, and Those Who Did Not Receive Colorectal Cancer Screening

	Total Average Risk n=275,665	Early Screened (47-49) n=19,806 (7.2%)	Screened Ages 50-53 n=105,957 (38.4%)	Not Screened n=149,902 (54.4%)	p Value
Subject months contributed to study period n	6,784,445	370,142	1,373,663	5,040,640	n/a
Lost to follow-up n (%)	15,056 (5.5)	874 (4.4)	n/a	14,182 (9.5)	n/a
Death n (%)	1514 (0.5)	132 (0.7)	n/a	1,382 (0.9)	n/a
Age at screening, y median (Q1, Q3)	n/a	48.5 (47.7, 49.4)	50.9 (50.4, 51.6)	n/a	n/a
Birth year cohort n (%)					
1960	92,820 (33.7)	6,097 (30.8)	35,089 (33.1)	51,634 (34.4)	<0.001
1961	92,465 (33.5)	6,745 (34.1)	35,605 (33.6)	50,115 (33.4)	
1962	90,380 (32.8)	6,964 (35.2)	35,263 (33.3)	48,153 (32.1)	
Gender n (%)					
Male	136,670 (49.6)	8,998 (45.4)	53,508 (50.5)	74,164 (49.5)	<0.001
Female	138,994 (50.4)	10,808 (54.6)	52,448 (49.5)	75,738 (50.5)	
Race/ethnicity n (%)b					
White non-hispanic	104,639 (37.9)	7,293 (36.8)	44,050 (41.6)	53,296 (35.6)	
Black non-hispanic	32,764 (11.9)	2,773 (14.0)	13,204 (12.5)	16,787 (11.2)	
Asian	8,133 (3.0)	499 (2.5)	3,559 (3.4)	4,075 (2.7)	<0.001
Hispanic	7,351 (2.7)	497 (2.5)	3,037 (2.9)	3, 817 (2.5)	
Other	4,122 (1.5)	305 (1.5)	1,697 (1.6)	2,120 (1.4)	
Unknown	118,656 (43.0)	8,439 (42.6)	40,410 (38.1)	69,807 (46.6)	
Active duty status n (%)c					
Non-active duty	257,457 (93.4)	18,231 (92.1)	95,048 (89.7)	144,178 (96.2)	<0.001
Active Duty	6,142 (2.2)	463 (2.3)	4,006 (3.8)	1,673 (1.1)	
Active duty (partial)	12,066 (4.4)	1,112 (5.6)	6,903 (6.5)	4,051 (2.7)	
Rank or rank of sponsor n (%)d					
Junior enlisted (lowest rank)	88,291 (32.0)	5,482 (27.7)	26,741 (25.2)	56,068 (37.4)	
Senior enlisted (third highest rank)	134,566 (48.8)	10,089 (50.9)	55,088 (52.0)	69,389 (46.3)	
Junior officer (second highest rank)	19,277 (7.0)	1,485 (7.5)	8,105 (7.6)	9,687 (6.5)	
Senior officer (highest rank)	31,697 (11.5)	2,642 (13.3)	15,414 (14.5)	13,641 (9.1)	
Other	1,834 (0.7)	108 (0.5)	609 (0.6)	1,117 (0.7)	

41

Comparison of Immune Tumor Microenvironments in Endoscopic Biopsy Versus Resection Specimen in Colorectal Cancer Subjects

J.L. Campf,[1]* A.T. Hickerson,[1] J.L. Lombardo,[1] L.M. Messersmith,[1] G.M. Williams,[1] D.F. Hale,[1] T.J. Vreeland,[3] T.A. Brown II,[1] J.W. Myers, III,[1] R.O. Brady,[1] R.A. Collins,[1] G.E. Peoples,[2] G.T. Clifton.[1]
1. General Surgery, San Antonio Military Medical Center, Fort Sam Houston, TX; 2. Cancer Vaccine Development Program, San Antonio, TX; 3. MD Anderson Cancer Center, Houston, TX.

Introduction The immune tumor microenvironment (TME) is being explored for prognostic implication, and as a target for novel cancer therapies. In colorectal cancer (CRC), CD3 and CD8+ lymphocytes correlate with prognosis, independent of stage. The relationship between the TME on endoscopic biopsy (EBx) to the resection specimen (RS) in CRC is not well defined. Our aim was to further elucidate this relationship. Methods CRC patients with banked, matched EBx and RS from a single institution from 2007-2017 were selected for evaluation. The CD3 and CD8+ lymphocytes were quantified by immunohistochemistry from the center of the tumor (CT) (defined as a 1mm^{2}area in the center) and the invasive margin (IM) in both the EBx and RS. TMN staging and tumor characteristics from the original pathology report were recorded. Comparison between cell counts was performed with Pearson Correlation and Wilcoxon Signed Rank Test and cell count compared to stage was performed with Spearman Correlation. Results 93 matched samples were evaluated. There was moderate correlation between the EBx and RS in both the CD3+ lymphocyte density (LD) (r=.463 CT and r=.411 IM) and the CD8+ LD (r=.407 CT and r=.406 IM). There was a higher median of CD3+ lymphocytes at the IM (p=.001; 1125, IQR:813-1663 VS 813, IQR:523-1155) and CT (p=.001; 966, IQR:588-1457 VS 455, IQR:214-854) in the EBx compared to the RS, respectively. The median values of CD8+ lymphocytes were similar at the CT (p=.866; 181, IQR:81-363 VS 187, IQR:35-329) and the IM (p=.031; 290, IQR:155-582 VS 378, IQR:188-619) between the EBx and RS, respectively. There was a significant inverse relationship between stage and CD3+ (ρ=-.35; p=.001) and CD8+ (ρ=-.26; p=.013) LD at IM of the RS. There was no significant relationship between CD8 or CD3+ LD to PVI, PNI or grade in the EBx or RS. Conclusion The TME of the EBx is predicative of the TME in the final pathology with moderate overall correlation. This data suggests CD3+ lymphocyte count in the EBx may over estimate the LD in the RS. These limitations should be noted when using the EBx TME to select for neoadjuvant therapy and/or inclusion in clinical trials.

42

Primary Tumor Sidedness is Predictive of Survival in Colon Cancer Patients Treated with Cytoreductive Surgery with or without Hyperthermic Intraperitoneal Chemotherapy: A Multi-Institutional Collaborative Study

N.V. Kotha,[1]* J. Baumgartner,[1] J. Veerapong,[1] J. Cloyd,[2] A. Ahmed,[2] T.E. Grotz,[3] J.L. Leiting,[3] K. Fournier,[4] A. Lee,[4] S. Dineen,[5] S. Dessureault,[5] C.N. Clarke,[6] H. Mogal,[6] M.Y. Zaidi,[7] M.C. Russell,[7] S.H. Patel,[8] J.J. Sussman,[8] L.A. Lambert,[9] R.J. Hendrix,[10] D. Abbott,[11] C. Pokrzywa,[11] B. Lee,[12] K.J. Lafaro,[12] J.B. Greer,[13] N. Fackche,[13] A.M. Lowy,[1] K.J. Kelly.[1] *1. Surgery, University of California San Diego, San Diego, CA; 2. Ohio State University, Columbus, OH; 3. Mayo Clinic, Rochester, MN; 4. MD Anderson Cancer Center, Houston, TX; 5. H Lee Moffitt Cancer Center, Tampa, FL; 6. Medical College of Wisconsin, Milwaukee, WI; 7. Emory University, Atlanta, GA; 8. University of Cincinnati, Cincinnati, OH; 9. University of Utah, Salt Lake City, UT; 10. University of Massachusetts, Worcester, MA; 11. University of Wisconsin - Madison, Madison, WI; 12. City of Hope Cancer Center, Duarte, CA; 13. Johns Hopkins University, Baltimore, MD.*

Introduction Primary tumor sidedness has been demonstrated to impact prognosis and treatment outcome in metastatic colon cancer. The clinical impact of sidedness is not fully understood in colon cancer patients with peritoneal disease treated by cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Methods This is a retrospective cohort study of a multi-institutional HIPEC Collaborative Database of patients with peritoneal surface malignancy undergoing CRS/HIPEC at 12 participating high-volume academic centers between 2000-2017. Survival analysis was conducted with Kaplan-Meier curves (log-rank test) and univariate/multivariate Cox Regression for both Disease-Free Survival (DFS) and Overall Survival (OS). Results A total of 428 patients with colorectal cancer treated with CRS +/- HIPEC were identified. After excluding transverse colon and rectal primary tumors, 375 patients were analyzed, 209 (55.7%) with right-sided and 166 (44.3%) with left-sided primary tumors. Patients with right-sided tumors were more likely to be older, male, have higher peritoneal cancer index (PCI) scores at surgery, and have a perforated primary tumor, but were less likely to have extraperitoneal disease (see Table 1). Patients with complete cytoreduction (CC-0/CC-1), had a median DFS of 16 (95% CI 13.3 – 18.1) vs 24 (95% CI 20.7 – 26.7) months (p=0.086) and median OS of 30 (95% CI 25.3 – 35.5) vs 51 (95% CI 40.5 – 61.9) months (p=0.044) for right- and left-sided tumors, respectively. Multivariate analysis revealed that right-sided primary tumor was an independent predictor of worse DFS (HR 1.66, 95% CI 1.02 – 2.68; p= 0.040) but not OS (HR 1.44 95%, CI 0.92 – 2.24; p=0.108). Conclusion In this study, a right-sided primary tumor was an independent predictor of worse DFS. Relevant primary clinicopathologic criteria, such as tumor sidedness and PCI, should be considered in patient selection for CRS/HIPEC and in stratification for clinical trials.

Univariate and Multivariate Cox-Regression Analyses of Factors Associated with Disease-Free Survival in 317 Patients with Colon Cancer Who Underwent CRS-HIPEC with Complete Cytoreduction

	Univariate Analysis			Multivariate Analysis		
Factor	Hazard Ratio	95% C.I.	P	Hazard Ratio	95% C.I.	P
Right-sided primary tumor	1.38	0.95-2.00	0.088	1.66	1.02-2.68	0.040
Age at surgery	1.01	0.99-1.02	0.325			
Female gender	0.90	0.62-1.29	0.560			
BMI	0.99	0.96-1.02	0.654			
PCI	1.06	1.03-1.08	<0.001	1.05	1.02-1.08	<0.001
Extraperitoneal Disease	1.45	0.93-2.25	0.103	1.69	1.01-2.82	0.028
Poor Differentiation	1.67	1.10-2.53	0.016	1.58	0.99-2.50	0.053
Adjuvant Chemotherapy	1.03	0.68-1.58	0.878			

43

Spatial Characterization of the Metastatic Colon Cancer Immune Microenvironment Identifies Potential Candidates for Immunotherapy J. Lazarus,[1]* T. Maj,[1] J.J. Smith,[2] M. Perusina Lanfranca,[1] L. Delrosario,[1] A. Girgis,[1] I. Kryczek,[1] J. Shi,[1] H. Crawford,[1] H. Nathan,[1] A. Rao,[1] M. Pasca Di Magliano,[1] J. Shia,[2] W. Zou,[1] T. Frankel.[1] *1. Surgery, University of Michigan, Ann Arbor, MI; 2. Memorial Sloan Kettering, New York, NY.*

Anti-programmed death receptor ligand 1 (PD-L1) therapy is currently used for patients with metastatic colorectal cancer and microsatellite instability (MSI) characterized by accumulation of immunogenic neoantigens and enhanced cytotoxic T cell (CTL) infiltration. Using a novel multiplex fluorescent immunohistochemistry platform (mf-IHC), we sought to characterize the immune infiltrate of colorectal liver metastases (CRLM) in MSI and microsatellite stable (MSS) tumors. Formalin-fixed tissue from 177 CRLM were subjected to mf-IHC using tyramide signal amplification allowing phenotyping of epithelial cells (ECs), CTLs, regulatory Tcells (T_{regs}), antigen presenting cells (APCs) and measurement of PD-L1. After multispectral imaging, cell to cell interactions were analyzed by measurement of engagement, intercellular distance and activation. MSI was assessed by staining for DNA damage repair proteins. Measurement of intercellular distances and engagement revealed that when PD-L1$^+$APCs were present in the CRLM tumor microenvironment (TME), CTLs were located closer to immunosuppressive T_{regs} (p=0.0007) which were more abundant. CTLs were less likely to be engaged with ECs (p=0.0007) impairing their function as determined by staining for the degranulation marker LAMP-1 as well as overall survival. Conversely, patients with low PD-L1$^+$APCs and high CTLs had an improved overall survival (p=0.0137). MSI tumors tended to have greater infiltration of CTLs which were more engaged with ECs. A subset of MSS tumors (12%) had similar immune microenvironment profiles to MSI tumors characterized by high CTL infiltration and EC engagement and also exhibited a high frequency of PD-L1$^+$APCs(p=0.0001) suggesting they may benefit from checkpoint therapy. Analysis of the CRLM TME by mf-IHC highlights the important role of PD-L1$^+$APCs in shaping the immunosuppressive cellular infiltrate in MSI and MSS tumors. Adding the spatial dimension immune profiling allowed for identification of a subset of currently untreated MSS patients who may benefit from immune based therapies.

44

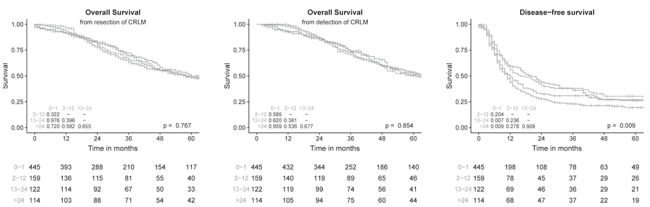
Implementation of Enhanced Recovery After Surgery (ERAS) Improves Outcomes in Patients Undergoing Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy (HIPEC) C. Webb,* R. Day, C.S. Velazco, B. Pockaj, R. Gray, C. Stucky, N. Wasif. *Surgery, Mayo Clinic Arizona, Phoenix, AZ.*

Background. Cytoreduction (CRS) and HIPEC have been associated with increased post-operative complications and a prolonged length of stay (LOS). We report on our experience following implementation of an ERAS program for CRS and HIPEC. Methods. Patients undergoing CRS and HIPEC from 2010-2018 were divided into pre and post-ERAS groups. Modifications in the ERAS group included transversus abdominus plane (TAP) blocks, intra and postoperative fluid restriction, and minimizing use of drains and nasogastric tubes. Results. Out of 130 patients, 49 (38%) were pre-ERAS (33 open, 16 laparoscopic), and 81 (62%) in the ERAS group (58 open, 23 laparoscopic). The groups had no difference in median Peritoneal Cancer Index (PCI) score, mean operative time, or completion of CC0/CC1 resection (p = NS). The ERAS group received less intravenous fluid both in the operating room (5.7 ± 3.0 liters vs. 8.1 ± 4.2 liters, p = <0.001) and during their hospitalization (19.2 ± 18.7 liters vs. 32.8 ± 32.5, p = 0.003, respectively). Median total morphine equivalent use (oral and intravenous) was significantly reduced in the open ERAS versus pre-ERAS group (226.0 mg vs. 415.3 mg, p = .021). Mean LOS was reduced from 10.03 ± 9.05 days to 6.59 ± 4.17 in the ERAS group (p = 0.005). In patients undergoing open CRS and HIPEC mean LOS was reduced from 12.51 ± 9.68 to 8.18 ± 3.58 days (p = 0.004) and from 4.95 ± 4.56 to 2.74 ± 2.46 (p = 0.061) in laparoscopic CRS and HIPEC. Overall complication rate was reduced from 63.3% to 37.0% pre and post-ERAS (p = 0.006), including decreases in re-operations and grades III-IV complications (12.2% to 6.2%, p = 0.330; 24.5% to 16.0%, p = 0.258, respectively). No change in the rates of 30-day readmission or acute kidney injury was seen (p = NS). On multivariable analyses ERAS was significantly associated with a reduction in LOS (-2.89 days, 95% CI -4.84 to -0.94) and complication rate (OR 0.22, 95% CI 0.08-0.57). Conclusions. Implementation of an ERAS program for CRS and HIPEC leads to a reduction in overall intravenous fluids, post-operative narcotic use, complication rates and length of stay.

45

The Disease-Free Interval Between Resection of Primary Colorectal Malignancy and the Detection of Hepatic Metastasis is of Limited Prognostic Value Following Surgical Treatment for Colorectal Liver Metastasis. D.J. Höppener,[1]* P.M. Nierop,[1] B. Galjart,[1] P.B. Olthof,[3] M. van Amerongen,[2] T.M. van Gulik,[3] J.H.W. de Wilt,[2] D. Grunhagen,[1] N.N. Rahbari,[4] C. Verhoef.[1] *1. Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; 2. Radboud UMC, Nijmegen, Netherlands; 3. Amsterdam UMC, Amsterdam, Netherlands; 4. Mannheim University Medical Centre, Mannheim, Germany.*

INTRODUCTION: Time to metastasis in colorectal cancer (CRC) patients is seen as an important prognostic indicator. Recent analysis in metastatic CRC found limited evidence to support this. The current study aims to determine its prognostic value in patients undergoing curatively intended surgical treatment of colorectal liver metastases (CRLM). METHODS: Patients undergoing first surgical treatment for CRLM without extra-hepatic disease who were treated in a single Dutch high volume tertiary referral centre were eligible for inclusion. In addition, data of two other Dutch tertiary referral centres was used for external validation. The disease-free interval (DFI) was defined as time between resection of CRC and detection of CRLM. Baseline characteristics and Kaplan-Meier survival estimates were stratified by DFI. Cox regression analysis was performed for overall (OS) and disease-free survival (DFS) with the DFI in months entered as continuous measure. RESULTS: In total 840 patients were included in the original cohort and 307 in the external validation cohort. Baseline characteristics of the original and the validation cohort were comparable in terms of patient demographics and clinical risk. In both cohorts, patients with shorter DFI were younger, more often had nodal involvement of the primary, more frequently received neo-adjuvant chemotherapy for CRLM, had more CRLM at diagnosis and had a higher proportion of bilobar metastases. Survival analysis corrected for these confounding factors in the original cohort only found the DFI to be prognostic for DFS (Hazard Ratio (HR) [95% Confidence interval (CI)]: 0.992 [0.985-0.999], p=0.022) and not for OS (HR [95%CI]: 0.996 [0.988-1.004], p=0.303). Validation yielded similar outcomes in the external cohort: DFI was prognostic in multivariable analysis for DFS (HR [95%CI]: 0.988 [0.977-0.998], p=0.021) but not for OS (HR [95%CI]: 0.985 [0.969-1.001], p=0.067). DISCUSSION: The DFI is of limited prognostic value following surgical treatment of CRLM.



Kaplan-Meier survival curves for overall survival from resection of colorectal liver metastasis (CRLM), overall survival from detection of CRLM and disease-free survival stratified by the disease-free interval in months. Overall p-value is displayed in the right-hand corner of each graph, p-values of the pairwise comparison of individual strata are reported in the table on the left-hand corner of each graph, and the numbers at risk per stratum are reported in the table below each graph.

46

Organ Preservation in Rectal Cancer Patients Treated with Total Neoadjuvant Therapy F.F. Quezada,* R.M. Jimenez-Rodriguez, I. Hameed, S. Patil, J.J. Smith, J. Garcia-Aguilar. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Retrospective case series suggest that watch-and-wait (WW) is a safe alternative to total mesorectal excision (TME) in selected patients with a clinical complete response (cCR) after chemoradiotherapy (CRT). Because treatment strategies vary widely and total numbers of patients treated at different institutions have not been reported, the proportion of rectal cancer patients who can potentially benefit from WW is not known. Here, we report the results of a treatment strategy incorporating WW in a cohort of rectal cancer patients treated with total neoadjuvant therapy (TNT). Methods: Consecutive patients with stage II/III rectal adenocarcinoma treated with TNT from 2012 to 2017 by a single surgeon were included. TNT consisted of mFOLFOX6 (8 cycles) or CapeOX (5 cycles) either before or after CRT (5600 cGy in 28 fractions with sensitizing fluorouracil or capecitabine). Tumor response was assessed with a digital rectal exam, endoscopy, and MRI according to predefined criteria. Patients with a cCR were offered WW, and patients with residual tumor were offered TME. WW and TME patients were compared based on intention to treat, using the chi-square or rank sum test. Relapse-free survival (RFS) was evaluated by Kaplan-Meier analysis. Results:A total of 108 patients were included: 64 (59%) had an incomplete clinical response; 4 of the 64 patients declined surgery or had local excision, and 60 underwent TME. The remaining 44 patients (41%) had a cCR and underwent WW. On average, patients in the WW group were older and had smaller, more distal tumors. Median radiation dose, number of chemotherapy cycles, rate of adverse events, or length of follow-up (28 months) did not differ between the TME and WW groups. Five (11%) of the 44 WW patients had local tumor regrowth, at a median of 14 (4–25) months after TNT; 2 of the 5 had distant metastasis. Six (10%) of the 60 TME patients had a pathological complete response. RFS did not differ between the TME and WW groups (log rank P= 0.09). Conclusions: Approximately 40% of patients with stage II/III rectal cancer treated with TNT achieve a clinical complete response and can benefit from a WW approach with the aim of preserving the rectum.

47

Predicting Risk of Recurrence After Colorectal Cancer Surgery in the United States: An Analysis of a Special Commission on Cancer National Study S. Zafar,[1]* C. Hu,[1] R.A. Snyder,[2] A. Cuddy,[1] Y. You,[1] L.M. Lowenstein,[1] R.J. Volk,[1] G.J. Chang.[1] *1. Surgical Oncology, MD Anderson Cancer Center, Houston, TX; 2. Dept. of Surgery, University of South Carolina School of Medicine-Greenville Health System., Greenville, SC.*

Introduction Follow-up testing after surgical treatment of colorectal cancer (CRC) is routinely performed to detect cancer recurrence. We aimed to develop a risk model for recurrence after definitive treatment of stage I-III CRC using data from a nationally representative database. And to develop an individualized web-based tool to guide medical discussion and decision-making. Methods A random sample of patients who underwent definitive resection for stage I-III CRC between 2006 and 2007 at Commission on Cancer (CoC) accredited centers were included. Data regarding first recurrence was abstracted from medical records through 2012 as part of a CoC Special Study and merged with the National Cancer Database. Multivariable cox regression was used to test for factors associated with cancer recurrence, stratified by stage. Clinically relevant or statistically significant variables were included in the model. Model performance was tested by c statistics and calibration plots. Hazard Ratios were utilized to develop an individualized web-based recurrence prediction tool. Results A total of 8,249 patients from 1,175 centers were include. The mean age was 65 years, and 52% were female. 80% of patients had colon cancer and 36.8% had stage III disease. Over 5 years of follow up, 1,656 (20.1%) patients recurred, of which 307 (18.5%) had locoregional, 1,189 (71.8%) had distant, and 200 (12.1%) patients had local and distant recurrences. Median time to recurrence was 16 months. The final predictive models displayed excellent discrimination and calibration with concordance indexes of 0.7. The model included 12 variables and is individualized for tumor site, stage, and time since surgery. Output is displayed numerically and graphically with an icon array (Figure 1). Conclusions Using primarily abstracted recurrence data from a random sample of patients treated for CRC at CoC accredited centers across the United States, we successfully created and tested an individualized CRC recurrence risk assessment tool. This web-based decision support tool can be used by physicians and patients to understand and guide management discussions.

Figure 1: Screenshot of the web-based individualized colorectal cancer recurrence decision support tool

48

Pelvic Exenteration for Locally Advanced and Recurrent Colorectal Adenocarcinoma: Aggressive Surgical Resection Provides Excellent Outcomes N.A.N. Kumar,* R.S. Shinde, K. Verma, A. Desouza, V. Ostwal, R. Engineer, A. Saklani. *Surgical oncology, Tata Memorial Hospital, Mumbai, India.*

Background: Pelvic exenteration (PE) is indicated in locally advanced or recurrent rectal cancers in order to achieve R0 resection. The survival outcomes differ with patient, tumor characteristics and high volume centers. Objective: The aim was to assess the perioperative and long-term survival outcomes of patients undergoing PE for locally advanced or recurrent colorectal cancers (CRC) and to evaluate the prognostic factors affecting the survival outcomes. Patients and Methods: This was a retrospective analysis of prospectively collected data. All consecutive patients who underwent PE for colorectal adenocarcinoma from May 2013 to July 2018 were included. The short-term measures were perioperative outcomes, postoperative complications and histo-pathological characteristics. The Long-term outcome measures were overall survival (OS), disease-free survival (DFS) and prognostic factors affecting survival. The log rank test and Cox proportional hazard model were used for univariate and multivariate analysis respectively. Results: Out of 115 patients, 95 (82.6%) were primary and 20 (17.4%) were recurrent CRC. The preoperative, perioperative and histopathological characteristics are shown in Table 1. At a median follow up of 13.6 months (1-75 months), 8 patients (6.9%) developed local recurrence and 30 (26.08%) developed distant recurrence. The estimated 2 year and 3 year DFS was 62.9% and 44.2% respectively. The estimated 2 year and 3 year OS was 66.9% and 57.6% respectively. On multivariate analysis, the important prognostic factors affecting DFS were nodal stage (0.004), tumor regression grade (TRG) (0.043) and complication rate (p=0.026) and important prognostic factors affecting OS were poor differentiation (0.001), complication rate (0.016) and recurrence rate (p=0.001). Conclusions: Pelvic exenteration improves an R0 resection rate in locally advanced and recurrent CRC with good short-term and long-term outcomes. The poor prognostic factors affecting survival were nodal stage, poor differentiation, TRG, complication rate and recurrence.

Preoperative, Perioperative and Histopathological characteristics

Characteristics	n=115, (%)
Preoperative details	
Age (year), mean	45.16 (19-71)
Gender Male Female	. 63 (54.8) 52 (45.2)
Differentiation Well/Moderate Poor	. 75 (65.2) 40 (34.8)
Signet ring cell Histology	19 (16.5)
cT stage cT4a cT4b	. 37 (34.3) 71 (65.7)
cN stage cN0 cN1 and above	. 14 (12.2) 101 (87.8)
Mesorectal fascia (MRF) involved	112 (97.4)
Lateral pelvic lymph node (LPLN) involved	39 (33.9)
Neoadjuvant Treatment Neoadjuvant chemo-radiotherapy Short course radiotherapy Neoadjuvant chemotherapy	108 (93.9) 79 (68.7) 16 (13.9) 72 (62.6)
Perioperative details	
Total pelvic exenteration Posterior exenteration	71 (61.7) 44 (38.3)
Sphincter preservation surgery (Supralevator)	29 (25.2)
Additional procedures Pelvic lymph node dissection Multivisceral resection CRS+HIPEC(PCI<5) Sacrectomy Posterior vaginal wall resection Plastic reconstruction	. 37 (32.2) 25 (21.7) 02 05 (4.3) 21 (18.3) 33 (28.7)
Open Laparoscopic Robotic	91 (79.1) 16 (13.9) 08 (7.0)
Duration Surgery, (min), mean Blood loss, (mL), Median Blood transfused, (mL), median Hospital stay, (days), median	509.10 (180-800) 1500 (150-11000) 250 (0-3800) 12 (5-94)
Complications Clavien–Dindo (CD) grade CD II CD IIIa CD IIIb and IV CD V	62 (53.9) 37 (32.17) 10 (8.7) 14 (12.17) 01 (0.86)
Perineal wound infection	36 (31.3)
Readmission in 30 days	13 (11.3)
Histopathological Characteristics	
Resection type R0 R1 (CRM involved)	. 99 (86.08) 16 (13.92)

CRS=Cyto-reductive surgery; HIPEC=Hyperthermic intra-peritoneal chemotherapy;PCI=Peritoneal cancer index; CRM=Circumferential resection margin;pCR=Pathological complete response;TRG=Tumour regression grade;EMVI=Extramural venous invasion

49

Associated Prognostic Factors to Regrowth and Recurrences in Rectal Cancer Patients Treated with Total Neoadjuvant Chemo-radiotherapy (TNCR) and Watch and Wait (W&W) Policy P. Luna-Perez,[4]* M. RAMIREZ,[1] P. LUNA-MERLOS,[2] R. SILVA,[1] N. SALAZAR,[3] S. RODRIGUEZ.[1] *1. Hospital de Oncología, Ciudad de México, Mexico; 2. INCAN, Ciudad de Mexico, Mexico; 3. IMSS YUCATAN, Mérida, Mexico; 4. Hospital Metropolitano, Cd de Mexico, Mexico.*

Background. Approximately 8-30% of rectal cancer patients undergoing neoadjuvant chemoradiation achieve pathological complete response, which has been associated with low rate of local recurrence and long-term survival. In such patients, surgery has been associated with high morbidity, that has lead to a watch and wait policy. However, is highly controversial, due to clinical complete response (cCR) does not correlated with complete pathological response. Due to this, we need identify factors associated with the tumor and treatment. Objective. To analyze factors associated with regrowth and recurrence in a group of patients with rectal cancer achieving cCR after TNCR. Materials and methods. Between 2012 and 2016, 720 patients with stage II-III rectal adenocarcinoma were treated with neoadjuvant chemoradiation. All patients received neoadjuvant Capecitabine +/- oxaliplatinum(OX) and 50.4 Gy (CT/RT) +. Responder patients received at least 6 cycles of Capecitabine +/- OX. cCR was defined as no residual tumor by digital rectal examen, endoscopy and MRI. The outcome and factors associated with recurrence were analyzed by means of logistic regression analysis and survival was estimated with Kaplan-Meier method. Results. Were 25 males and 20 females, mean age was 62 yrs. Mean distance from distal tumor margin to the anal verge was 4.1 Cm. MRI evaluation before TNCR was: Stage II= 24 and III= 21. 39 patients received TNCR. Median time to evaluate cCCR was 6 weeks. Median follow-up was 42 months, 35 patients (77%) had no recurrence; eight (17.7%) had regrowth (all of them were surgically treated) and two (4.4%) had distant recurrences. 5-year disease-free survival was 82%. Associated factor with regrowth and recurrence were: pre-treatment CEA (p= 0.01), MRI pretreatment Stage (p=0.01) and complete TNCR (p=0.04). Conclusion. For rectal cancer patients who achieved cCR after TNCR, W&W policy is safe. Identification of factors associated with the tumor and treatment are powerful tool to identify patients with high risk of regrowth and recurrence. In such patients intensive surveillance should be performed.

50

Oncologic Outcomes of Minimally Invasive Treatment for Early Colorectal Cancer: Comparison of Endoscopic Resection and Laparoscopic Surgery S. Bae,* W. Jeong, S. Baek. *Keimyung University Dongsan Medical Center, Daegu, Korea (the Republic of).*

Aim: The aim of our study was to compare the oncologic outcomes between endoscopic and laparoscopic treatment for early colorectal cancer. Method: The study group included 127 patients who underwent an endoscopic treatment and 38 patients who underwent a laparoscopic surgery for early colorectal adenocarcinoma between January 2010 and December 2013. Results: As to the histopathological diagnoses, 114 (89.8%) carcinomas in the ESD group were mucosal to sm1 and 13 (10.2%) were sm2 or deeper carcinomas and 17 cases (13.4%) with high risk underwent an additional surgery in endoscopic group. The mean operation time, time to soft diet, and length of stay was significantly shorter in the endoscopic group than in the laparoscopic group. The 4-year overall survival rates of the endoscopic group and laparoscopic groups were 90.4% and 98.0%, respectively (p=0.246), and the 4-year disease-free survival rates were 90.4% and 97.5% (p=0. 378), respectively. Systemic recurrences occurred in 2 patients (1.6%) in endoscopic group and 1 (2.0%) patient in laparoscopic group and local recurrence combined to systemic recurrence occurred in 1 patient (0.8%) in endoscopic group. Conclusion: Endoscopic resection for early colorectal cancer can be performed safely, with long-term oncological outcomes comparable to those obtained with laparoscopic surgery.

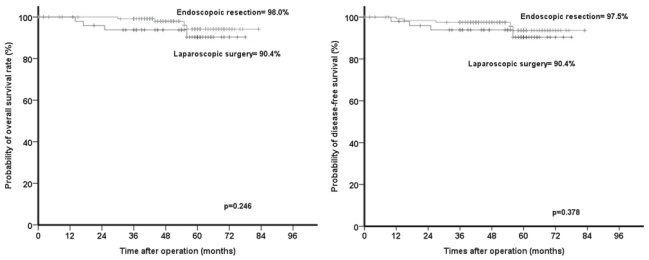


Figure 1. Comparison of the 4-year overall survival and disease-free survival rates between the laparoscopic and open groups

51

Adjuvant Chemotherapy Does Not Affect Relapse-Free Survival in Patients with Stage II & III Rectal Cancer After Neoadjuvant Chemoradiation and Total Mesorectal Excision R.K. Voss,[1]* D.D. Klaristenfeld,[2] J.C. Lin,[2] J.H. Ruan,[2] W.H. Tseng,[2] M.H. Al-Temimi,[2] M.S. Tam,[2] M.J. Sherman,[2] M.J. Tomassi.[2] *1. UC San Diego Medical Center, San Diego, CA; 2. Kaiser Permanente, San Diego, CA.*

Introduction: NCCN guidelines for rectal cancer recommend neoadjuvant chemoradiotherapy followed by surgery and adjuvant chemotherapy for stage II & III rectal cancer. However, the absolute benefit of adjuvant chemotherapy after neoadjuvant chemoradiation and total mesorectal excision (TME) remains unknown. Methods: A retrospective chart review was performed of all Southern California Kaiser Permanente patients with stage II & III rectal cancer who underwent chemoradiation followed by surgery from 2005-2016. Demographics, pre- and post-treatment stage, surgical data, treatment information, and recurrence data were collected. Relapse-free survival (RFS)

was calculated, and multivariate adjusted analysis was performed to identify factors associated with disease relapse. Results: 348 stage II and 514 stage III patients were included (n=862), and 682 patients (79.1%) underwent adjuvant chemotherapy. The mean patient follow-up after TME was 63.0 months (range 3-160). The most common adjuvant regimens were FOLFOX (34%), capecitabine (29%), and CAPEOX (28%). Univariate analysis showed that pre-treatment clinical stage did not predict RFS (P=0.50), but yp stage was an excellent predictor of RFS ($P=1 \times 10^{-21}$). Multivariate logistic regression revealed that yp stage and en bloc resection were the only clinical variables that significantly predicted disease recurrence (Table 1). The addition of adjuvant chemotherapy did not improve RFS (P=0.09). Subgroup analyses were performed to analyze the benefit of adjuvant chemotherapy based on different clinical variables (e.g. demographics, clinical stage, yp stage, type of chemo), and notably, no significant reduction in RFS was seen in any subgroup. Conclusions: In patients with stage II & III rectal cancer treated with neoadjuvant chemoradiotherapy then TME, yp stage was a better predictor of long-term oncologic outcome than pre-treatment stage. Moreover, adjuvant chemotherapy did not improve RFS in any studied group in this large cohort. Future studies should confirm these results and delineate the oncologic benefit of adjuvant chemotherapy in this population.

Table 1	Number	Mean Follow Up (Months)	Relapse Free Survival (Months)	%	Univariate Analysis HR (95%CI)	Multivariate Analysis Adjusted HR (95% CI)
Overall	862	63	178	79.4%		
Year of Diagnosis					1 (0.96-1.05)	
Sex						
Male	534	62.6	107	80.0%	Reference	Reference
Female	328	63.6	71	78.4%	1.1 (0.81-1.48)	0.99 (0.73-1.36)
Age at Diagnosis					1 (0.99-1.02)	1.01 (1-1.02)
Age 19-49	163	65.2	33	79.8%		
Age 50-70	527	64.3	107	79.7%		
Age 71-89	172	57	38	77.9%		
Pre-radiation Stage						
Stage 2 (TxN0)	348	67.3	70	79.9%	Reference	
Stage 3 (TxN1)	433	64.1	90	79.2%	1.06 (0.77-1.44)	
Stage 3 (TxN2)	81	38.5	18	77.8%	1.49 (0.89-2.51)	
Type of Surgery						
LAR	620	64.5	117	81.1%	Reference	Reference
APR	213	60.3	53	75.1%	1.39 (1-1.92)	1.19 (0.85-1.67)
Hartmann	22	55.9	3	86.4%	0.72 (0.23-2.25)	0.87 (0.27-2.85)
Exenteration	7	33.6	5	28.6%	**7.19 (2.93-17.67)**	**3.63 (1.25-10.56)**
En Bloc Resection						
No	802	63.5	155	80.7%	Reference	Reference
Yes	60	57	23	61.7%	**2.37 (1.53-3.67)**	**1.76 (1.04-2.98)**
Surgical yp Stage						
CPR/Tis	192	69.8	11	94.3%	Reference	Reference
Yp Stage 1	232	64.5	24	89.7%	1.97 (0.97-4.02)	2.00 (0.98-4.1)
Yp Stage 2	209	59.6	52	75.1%	**5.33 (2.78-10.21)**	**4.85 (2.51-9.34)**
Yp Stage 3	229	58.9	91	60.3%	**9 (4.81-16.82)**	**9.05 (4.79-17.09)**
Downstaging						
No downstaging	327	60.6	122	62.7%	Reference	
Some downstaging	343	61.6	45	86.9%	**0.31 (0.22-0.44)**	
CPR	192	69.8	11	94.3%	**0.12 (0.07-0.22)**	
Adjuvant Chemo						
No	200	69	34	83.0%	Reference	Reference
Yes	662	61.2	144	78.2%	1.38 (0.95-2)	1.15 (0.76-1.74)
Adjuvant Agent						
None	202	68.6	36	82.2%	Reference	
FOLFOX	225	60.4	64	71.6%	1.79 (1.19-2.7)	
5-fu	49	85.5	11	77.6%	1.12 (0.57-2.2)	
capecitabine	192	63.7	29	84.9%	0.86 (0.53-1.4)	
CAPEOX	187	53.5	35	81.3%	1.18 (0.74-1.87)	
oxaliplatin	3	26.6	2	33.3%	10.92 (2.61-45.68)	
FOLFOX+Avastin	4	92.7	1	75.0%	1.39 (0.19-10.16)	

LAR=low anterior resection, APR=abdominoperineal resection, CPR=complete pathologic response

Table 1

52

Evaluation of Health-Related Quality of Life After Cytoreductive Surgery/HIPEC for Mucinous Appendiceal Cancer: Results of a Multicenter Randomized Trial Comparing Oxaliplatin and Mitomycin E. Levine,[1] O. Moaven,[1]* K.I. Votanopoulos,[1] D.L. Bartlett,[2] P. Shen,[1] P. Mansfield,[3] G. Russell,[1] K. Perry,[1] R. McQuellon,[1] J.H. Stewart.[4]
1. Wake Forest University, Winston-Salem, NC; 2. University of Pittsburgh Medical Center, Pittsburgh, PA; 3. MD Anderson Cancer Center, Houston, TX; 4. University of Illinois, Chicago, IL.

INTRODUCTION: The aim of this study is to evaluate health-related quality of life (HRQOL) using patient-reported outcomes in patients with mucinous appendiceal neoplasms who underwent Cytoreductive surgery (CRS) with HIPEC as part of a randomized trial. METHODS: In this prospective multi-center study, mucinous appendiceal cancer patients with evidence of peritoneal dissemination who underwent CRS were intraoperatively randomized to receive mitomycin(40mg) or oxaliplatin (200mg/M2) for HIPEC. Functional Assessment of Cancer Therapy Neurotoxicity (FACT/GOG-NTX) questionnaire was utilized to assess HRQOL. Repeated measures mixed models with an unstructured variance matrix were applied to longitudinally assess changes in HRQOL. RESULTS: FACT-G and all its subscales including physical well-being (PWB), functional well-being (FWB), and social well-being (SWB) declined significantly at 12 weeks ($p < 0.05$ for all), but returned to the baseline range afterward. PWB was associated with overall survival (HR 0.92; 95%CI 0.86-0.98, $p<0.05$). After adjusting for differences at baseline, there was no difference in the FACT-G score between the two treatment arms. There was a trend toward improved trial outcome index (TOI) in oxaliplatin group (p=0.05). The TOI is a summary index responsive to change in physical/functional outcomes. Lack of energy was significantly higher in mitomycin arm ($p < 0.05$). Pain was significantly less in oxaliplatin group ($p<0.05$) and patients ability to work was significantly higher in oxaliplatin group ($p<0.05$). CONCLUSIONS: Negative impact of CRS/HIPEC on quality of life is significant in the first few months after surgery but recovers to baseline afterward. Some aspects of physical well-being are better sustained with oxaliplatin vs. mitomycin, while there is no overall difference and no difference in neurotoxicity.

54

Use of Preoperative Induction Chemotherapy for Advanced Stage Oral Cavity Squamous Cell Carcinoma S.R. Popat,[1]* A.S. Popat.[2]
1. Otolatyngology - Head & Neck Surgery, University of Bufalo, Buffalo, NY; 2. Canisius High School, Buffalo, NY.

Oral cavity squamous cell carcinoma (OC-SCCa) accounts for nearly 1/3 of all head and neck squamous cell cancers in the US however with significant international geographic variation due to carcinogen exposure and availability. The mainstay of treatment for resectable disease had been surgery with post-operative radiation based on specific clinical and pathologic features. Survival rates have little improved prior to the use of concurrent postoperative chemo-radition. Since 2009, we have employed induction chemotherapy (ICT) as an option to be added to the comprehensive treatment of OC-SCCa. A review of our outcomes was conducted. Patients/Methods: Retrospective review from 2010 -2016 of patients with stage IV OC-SCCa with minimal 24 month follow-up who received ICT and with no previous history of treated head & neck SCCa. 59 patients were identified however 13 met inclusion criteria. All received 2 to 3 cycles of ICT consisting of cisplatin and either fluorouracil and/or a taxane. Following IHC, all underwent surgical resection. Results: Survival from OC-SCCa was 100% with 11 patients NED and 2 patients DOC/NED. Median survival was 48.3 months. Three patients had ICT complications but recovered and proceeded to surgery. There were 3 surgical complications in 2 patients. Historic literature based on AJCC data has survial at 4 years to be approximately 29%. Conclusions: Though the study size is small, ICT demonstrated excellent tumor response in our patient population with enduring and superior disease free survival. A larger multicenter trial would be required to confirm these results and outline chemotherapy drug selection.

55

Prediction of Survival for Pancreatic Neuroendocrine Tumors: A Systematic Review of Clinical Tools G. Ho,[1]* K. Beyfuss,[1] A. Mahar,[2] S. Myrehaug,[1] D. Chan,[3] C. Law,[1] J. Hallet.[1] *1. Surgery, University of Toronto, Toronto, ON, Canada; 2. University of Manitoba, Winnipeg, MB, Canada; 3. Royal North Shore Hospital, Sydney, QLD, Australia.*

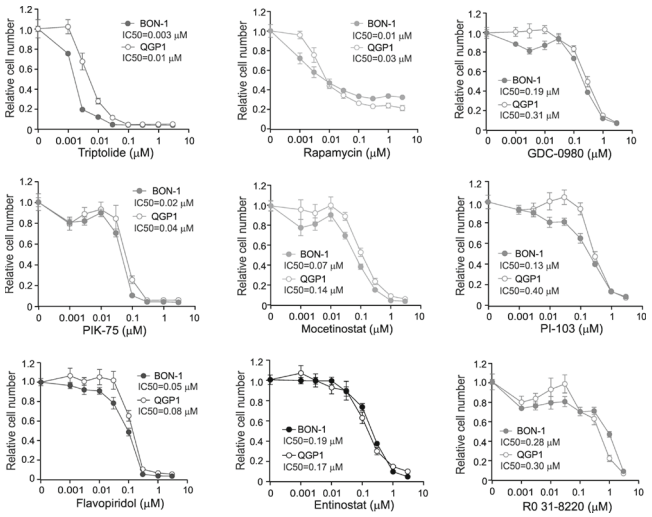
Background:Individual prognostication can support the management of pancreas neuroendocrine tumours (PNET). Clinical prediction tools aggregate patient and disease information to predict outcomes. Little is known about PNET prediction tools' accuracy and utility. We sought to evaluate the quality of prediction tools in PNET. Methods: We systematically searched the literature for studies reporting development or validation of tools predicting survival for PNET. We evaluated the tools using the Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies guidelines and the American Joint Committee on Cancer (AJCC) acceptance criteria for risk models. Results: We identified 12 tools to predict survival in PNET, including 11 for resected PNET. Three tools were endorsed staging classifications (ENETS, AJCC, and WHO). All were developed on patients diagnosed back to 1980-90s. They included 2 to 5 prognostic factors; the majority excluded key factors such as age and sex. Tumor stage and grade

were most commonly included. Nine tools were designed to predict overall survival, and three for both disease-specific and recurrence-free survival. One tool underwent bootstrapping internal validation with a "good" calibration (c-statistic: 0.74). Seven tools were externally validated; calibration was evaluated in 4 studies (c-statistics range: 0.60-0.77), discrimination in one with area under the curve (0.77) and in others with separation of survival curves. Validation samples relied on unknown or small(<100) number of events. No tool met AJCC acceptance criteria for risk models (range: 4 to 9 criteria met over 13). Conclusions: Existing tools cannot be confidently used for PNET prognostication in current clinical practice. Patient-level and non-pathologic disease factors should be included for more personalized prognostication. Better quality tools should be developed and validated following best methodology practices for predictive tools development and validation. Such tools are important to support more individual and accurate estimate of disease course, selection of therapy, patient counselling, and risk-stratification.

56

Gene Expression Changes and Potential New Therapies for Metastatic Pancreatic Neuroendocrine Tumors A. Scott,[1]* B. Darbro,[1] M. Weitz,[2] P. Breheny,[2] B. Brown,[2] T. Braun,[2] G. Li,[2] P. Ear,[2] U. Shaik Amjad,[2] C. Kaemmer,[2] C. Maharjan,[2] D. Quelle,[2] A. Bellizzi,[1] J. Dillon,[1] T. O'Dorisio,[1] J. Howe.[1] *1. Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA; 2. University of Iowa, Iowa City, IA.*

Introduction Pancreatic neuroendocrine tumors (PNETs) are uncommon malignancies noted for their indolent growth, propensity to metastasize, and comparatively favorable prognosis. Although both the number of treatment options and the median survival have increased in the last several decades, most patients will die of metastatic disease, and new systemic therapies are needed to improve outcomes. Methods Tissue samples were obtained from primary tumors, lymph node and liver metastases from 20 patients with sporadic, well-differentiated PNETs. Transcript profiling was performed using RNA-Seq, and gene expression was compared between primary tumors and metastases. Genes which were highly overexpressed in only lymph nodes or liver metastases were filtered out to help eliminate tissue-specific genes unrelated to metastasis. Ingenuity Pathway Analysis (IPA) was used to identify pathways involved in the progression to metastasis, and the Broad Connectivity Map (CMAP) was used to identify drugs likely to be effective based upon expression profiles from tumor cells treated with these agents. CMAP scores were used to select nine drugs for validation in vitro using two PNET cell lines (BON1, QGP1). Results A total of 610 genes were significantly over or under expressed in metastases compared to the primary tumors. IPA predicted altered activity of biological pathways involving histone modification, cell cycle checkpoints, DNA repair, the PI3K/mTOR/AKT pathway and p53 in the metastases compared to primary tumors. Inhibitors of members of these pathways, including the proto-oncogene MDM2, cyclin dependent kinases 1/2/4, mTOR, PI3K, DNA-PK, PKC and histone deacetylases, were identified through CMAP. All but one of these were highly cytotoxic in PNET cell lines (Fig 1). Discussion We have employed a complementary bioinformatics approach to identify novel therapeutic agents for PNETs by analyzing gene expression changes in metastatic tumors. The validity of this strategy was supported in vitro using two PNET cell lines. Additional in vivo evaluation of these compounds using PNET xenograft models will be important for confirming their clinical utility.



Dose response curves in BON and QGP1 for nine drugs predicted to have activity against metastatic PNETs. Cell viability was assayed five days following treatment.

57

Timing of Peritoneal Dissemination of Gastroenteropancreatic Neuroendocrine Tumors Does Not Affect Survival A.M. Blakely,[1]* O.S. Eng,[2] P. Ituarte,[1] G. Singh,[1] M. Raoof,[1] B. Lee.[1] *1. City of Hope National Medical Center, Duarte, CA; 2. University of Chicago, Chicago, IL.*

Background: About 5% of patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) develop peritoneal metastasis (PM). Prior studies have shown that PM from GEP-NETs is associated with worse survival. However, timing of PM and prognostic factors for this patient population remain poorly defined. Methods: California Cancer Registry was queried for all GEP-NETs with PM, years 2000-2012. Metastases were considered synchronous when occurring within 6 months of diagnosis. Patient, disease, and treatment variables were analyzed using nominal logistic regression for timing of PM and Cox proportional hazards model for overall survival (OS). Results: Overall, 692 patients with GEP-NETs and PM were identified. Median age was 62 years, 51.3% were male. Most NETs originated in the small bowel (48.0%), followed by colon (19.2%), pancreas (15.3%), appendix (10.7%), stomach (4.4%), and rectum (4.0%). Positive nodes were identified in 389 patients (56.2%). Median follow-up was 34 months (IQR 12-65). PM was metachronous in 183 patients (26.4%) at median time 24 months. Liver metastases developed in 341 patients (49.3%) overall, of which 227 were synchronous, while 114 were metachronous at median 24.5 months. Fewer than 10% developed lung, bone, or brain metastasis. Synchronous PM was more likely with nodal involvement (OR 2.1, p=0.022) and synchronous liver metastasis (OR 9.4, p<0.0001). Timing of PM was not associated with primary site. Decreased OS (see Table) was associated with age >80 years (HR 3.8, p<0.0001), non-small bowel origin, high grade (HR 4.3, p<0.0001), unresected primary site (HR 1.8, p<0.0001), and synchronous liver metastasis (HR 1.8, p<0.0001). Synchronous vs. metachronous PM was not associated with OS (HR 0.85, p=0.16). Conclusions: Peritoneal metastases most often originate from NETs of the small bowel. Overall, half have concomitant lymph node or liver involvement. Timing of PM was not associated with overall survival, as other disease factors better reflected tumor biology. The presence of PM should not by itself discourage GEP-NET debulking surgery.

Multivariate Cox proportional regression analysis of patient, disease, and treatment factors with overall survival as outcome measure

Variable		N (%)	Hazards Ratio	p Value
Age, years	18-44	60 (8.7)	Ref	-
	45-59	226 (32.6)	0.87	0.47
	60-80	346 (50.0)	1.4	0.061
	>80	60 (8.7)	3.8	<0.0001
Primary site	Small bowel	332 (48.0)	Ref	-
	Colon	133 (19.2)	2.1	<0.0001
	Pancreas	106 (15.3)	1.8	0.0003
	Appendix	74 (10.7)	3.2	<0.0001
	Stomach	23 (4.4)	2.9	<0.0001
	Rectum	21 (4.0)	1.8	0.057
Tumor size	≤2 cm	165 (23.8)	Ref	-
	2.1-5 cm	238 (34.4)	1.2	0.12
	>5 cm	113 (16.3)	1.3	0.11
	Tx	176 (25.4)	1.4	0.023
Tumor grade	I	144 (20.8)	Ref	-
	II	54 (7.8)	1.4	0.14
	III	106 (15.3)	4.3	<0.0001
	Unspecified	388 (56.1)	1.5	0.0076
Node status	Positive	389 (56.2)	Ref	-
	Negative	61 (8.8)	0.95	0.78
	Nx	242 (35.0)	1.3	0.054
Primary site resection	Yes	529 (76.4)	Ref	-
	No	163 (23.6)	1.8	<0.0001
Peritoneal metastasis	Synchronous	509 (73.6)	Ref	-
	Metachronous	183 (26.4)	0.85	0.16
Liver metastasis	Did not occur	351 (50.7)	Ref	-
	Synchronous	227 (32.8)	1.8	<0.0001
	Metachronous	114 (16.5)	1.1	0.41

58

Improved Survival in Resected Midgut Neuroendocrine Tumors with Liver-Only Metastases: Is there Benefit in Resection of the Primary? N. Manguso,* J. Lee, J. Gong, A. Hendifar, R. Tuli, A. Gangi. *Cedars-Sinai Medical Center, Los Angeles, CA.*

Background: Management of metastatic midgut neuroendocrine tumors (NET) remains controversial. The benefit of resection of the primary tumor only is unclear and is often only advocated for select patients, usually for palliation. We evaluated patients with midgut NETs with liver metastasis in the National Cancer Data Base (NCDB) to determine if resection of the primary tumor only affected survival outcomes. Methods: The NCDB was queried to identify patients with liver only metastatic midgut NETs between 2010 and 2015. Patients who underwent surgery for liver metastasis were excluded. The cohort was separated into two groups, those who underwent resection of the primary tumor and those who did not. Patient demographics, tumor characteristics and outcomes were compared between the groups. The primary outcome was overall survival (OS). Results: 1952 patients with median age of 63 were identified. Median tumor size was 2.4 cm. Of these, 1,295 (66.0%) patients underwent resection of the primary tumor and 667 (34.0%) did not. Those undergoing resection were younger (median age 63 vs 65, p<0.001) and had smaller tumors (median 2.3 cm vs 3.0 cm, p<0.001). With respect to clinical tumor stage, those with T1-2 tumors were significantly less likely to undergo resection compared to those with T3-4 tumors (58.5% vs 89.7%, p<0.001). Median follow up time was 42.8 months. A total of 483 deaths occurred in the entire cohort with a 5-year OS of 60.8%. The 5-year OS for patients undergoing resection of the primary tumor was 65.9% and 49.3% for those not undergoing resection (p<0.001). When patients were grouped based on T-stage there was no survival difference with resection versus no resection for stages T1 (p=0.07) or T2 (p=0.40), however, 5-year survival was better in the resection group for T3 (67.5% vs 37.2%, p<0.001) and T4 tumors (59.8% vs 21.5%, p<0.001). Conclusions: Patients with liver only metastatic midgut neuroendocrine tumors had an OS advantage when the primary tumor was resected. These patients may benefit from surgical resection and should be evaluated for surgery at the time of diagnosis, especially with higher t-stage tumors.

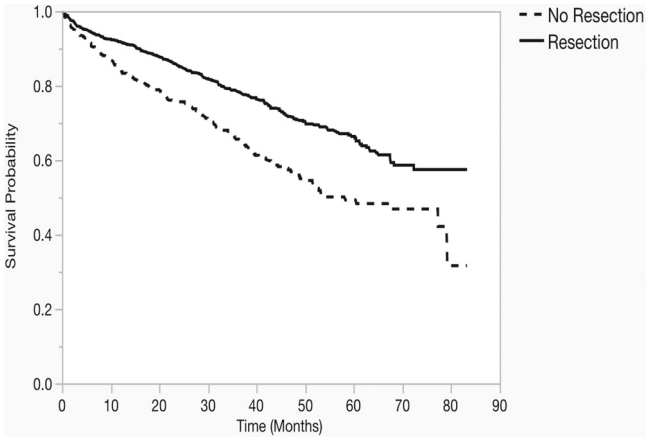


Figure: Overall Survival of Liver only metastatic midgut NET undergoing resection versus no resection

59

Primary Cardiac Angiosarcoma: A Contemporary Review of the Mayo Clinic Experience W.S. Sorrells,* S.P. Bagaria, M. El-Sayed, K. Landolfo, S. Jacob, I. Makey, S. Pham, M. Thomas. *Department of General Surgery, Mayo Clinic Florida, Jacksonville, FL.*

Background: Primary cardiac angiosarcoma is a rare disease with unclear outcomes. We aimed to review our contemporary experience with primary cardiac angiosarcomas. Methods: Retrospective review of our institutional cancer registry identified patients diagnosed with primary cardiac angiosarcoma from 2000 to 2016. Patient characteristics, treatment strategies and outcomes were analyzed. Results: A total of 21 primary cardiac angiosarcomas were identified. The mean age at diagnosis was 46 years (range, 23 to 77) with a female predominance (66.7%). Surgical biopsy was the most common method of diagnosis (76.2%). The most common location was the right atrium (76%) followed by the right ventricle (9.5%). The majority of tumors were high grade (86%). Only 10 patients (47.6%) presented with localized disease and 11 patients (52.4%) presented with metastasis. The most common site of metastasis was the lung (67%), followed by liver and spine (19% each). Only 10 patients (47.6%) underwent attempted resection. Of those, 3 underwent an R0 resection, 1 underwent an R1 resection, 3 underwent an R2 resection, and 3 were found to be unresectable. Median overall survival for the entire cohort was 10 months with a 5-year overall survival rate of 10%. Median overall survival for those who underwent surgical resection was 11.5 months and for those who underwent an R0 resection was 144 months. One patient with R0 resection has survived greater than 10 years. To our knowledge, 10-year survival has never before been reported for cardiac angiosarcoma. Discussion: Primary cardiac angiosarcoma remains a rare disease with poor overall survival. Complete surgical resection remains the only option for cure but may not be possible due to advanced disease at the time of diagnosis.

Variable	Number (n)	Percentage (%)
Sex		
Male	7	33
Female	14	67
Age (years)		
20-29	3	14.3
30-39	5	23.8
40-49	5	23.8
50-59	3	14.3
60-69	4	19
70-79	1	4.8
Race		
Non-Hispanic White	15	71.4
Non-Hispanic Black	1	4.8
Hispanic	0	0
Other	5	23.8
Location		
Right Atrium	16	76.2
Right Ventricle	2	9.5
Right Atrium and Ventricle	2	9.5
Pericardium	1	4.8

60

Improved Adherence to ATA Medullary Thyroid Cancer Treatment Guidelines L. Philipp,* J. Sharma, T. Gillespie, C. Weber, S.G. Patel, N.D. Saunders. *Emory University, Atlanta, GA.*

Introduction The 2009 American Thyroid Association (ATA) guidelines for medullary thyroid cancer (MTC) were created to unify national practice patterns. Surgery remains the cornerstone of MTC management, and evidence-based recommendations reflect the national standard for quality patient care. We present an appraisal of national adherence to the ATA surgical and adjuvant therapy guidelines from 2009-2013. Methods National Cancer Database (NCDB) records were queried for all MTC cases, 2009-2013, for retrospective, cross-sectional analysis. 2009 ATA recommendations (R) for allocation and extent of surgery (R61-R66), cytotoxic chemotherapy (R53), radioactive iodine (RAI) (R56), and EBRT (R92-R100) were analyzed. NCDB cases were examined for adherence to each guideline, and overall congruence with the set of recommendations. Logistic regression was used to determine predictors of discordance. Results 2700 MTC cases with requisite data were identified. 2466 had M0 disease, and 234 had M1 disease. Among M0 cases, 448 had advanced locoregional disease. 71.6% (n=1772) of M0 cases adhered to R61-66. 66.2% (n=1336) of M0 cases without advanced local disease were adherent to R61-63 recommending TT+LND. 86.1% underwent TT, and 71.3% had some LND, while 8.8% (n=178) were not adherent to either guideline. R65 allows limited surgery for advanced M0 cases, though 12 had no surgery. R64-R66 collectively include full, limited, or no surgery for M1, therefore all 234 were adherent. Collectively, 74.3% of all cases adhered to R61-R66. A total of 223 cases had adjuvant treatments discordant from R83, R85, and R92-R100. RAI and/or cytotoxic chemotherapy was employed in 189 cases. EBRT was used as adjuvant or monotherapy in 59 cases. Overall, 1827 (67.7%) cases followed ATA recommendations. Patient factors predicting discordant treatment were increasing age, female sex, and localized disease without extrathyroidal extension. Conclusion Surgical and adjuvant treatments of MTC were discordant from 2009 ATA guidelines in 32.3% of cases from 2009-2013, most often in cases with localized, non-invasive disease. This appears to be an improvement from previous data showing 41% not receiving recommended surgical therapy.

Table 1: National Adherence to 2009 ATA Guidelines for Surgical Management of MTC

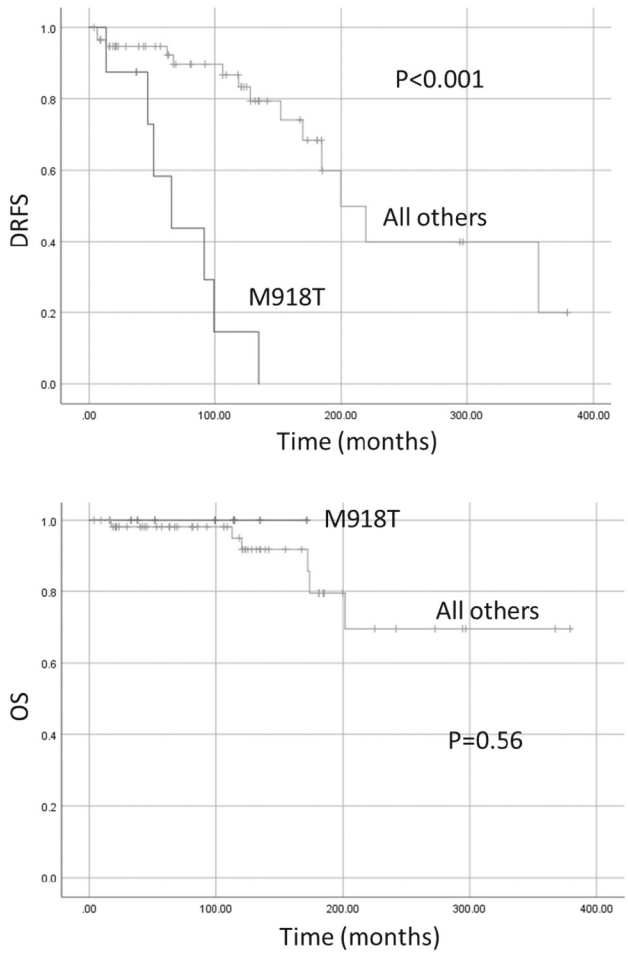
	M0 (-Adv)		M0 (+Adv)		M1	
Surgical Management	n	%	n	%	n	%
Total thyroidectomy + LND	1336	66.2%	385	85.9%	105	44.9%
Total thyroidectomy (-LND)	401	19.9%	26	5.8%	5	2.1%
Subtotal thyroidectomy + LND	27	1.3%	10	2.2%	0	0.0%
Subtotal thyroidectomy (-LND)	23	1.1%	3	0.7%	1	0.4%
Limited resection + LND	64	3.2%	7	1.6%	11	4.7%
Limited resection (-LND)	100	5.0%	5	1.1%	2	0.9%
No surgery + LND	12	0.6%	2	0.4%	12	5.1%
No surgery (-LND)	55	2.7%	10	2.2%	98	41.9%
ATA Recommendation					**Adherent**	**Discordant**
Recommendations 61-63: Patients with MTC with no evidence of advanced local invasion, and no distant metastases (M0) should undergo total thyroidectomy + [some] lymph node dissection					1336	682
Recommendations 64-66: In the presence of advanced local or distant disease, less aggressive neck surgery may be appropriate					670	12
Recommendations 61-66: Appropriate surgical management					*2006*	*694*
Recommendation 83: Routine use of cytoxic chemotherapy is discouraged						123
Recommendation 85: Postoperative radioactive iodine is not recommended						68
Recommendations 92-100: Appropriate use/timing of external beam radiation					190	59
Recommendations 83, 85, 92-100: Adjuvant therapy						*223*

61

Long-Term Oncologic Outcomes After Curative Resection of Familial Medullary Thyroid Carcinoma P.M. Spanheimer,* R.A. Ghossein, M.M. Tuttle, R.J. Wong, A.R. Shaha, I. Ganly, B. Untch. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Germline RET mutations confer risk of medullary thyroid carcinoma (MTC) and are associated with varying aggressiveness. We sought to characterize long term outcomes in patients with germline RET mutations and MTC. Methods: Sixty-six patients were identified from 1986 to 2017 who underwent curative thyroidectomy for MTC and had positive genetic test for RET germline mutation. Fourteen (21%) were prophylactic intent with discovery of MTC on pathology. Recurrence and survival were assessed using Kaplan-Meier estimates and correlated with clinicopathologic features using log-rank, Fisher's exact, or T-tests. Results: At median follow-up of 147 months (9-379), overall survival (OS) of the cohort was 93% at 10 years; median tumor diameter was 1.7 cm (range 0.1-8.9), preoperative calcitonin (Ct) was known in 46 patients (median 78, [0-37,590]). Lymph node (LN) dissection was performed on 52 (79%) and was positive in 37 patients (56%). Locoregional recurrence (LR)-free survival was 62% at 10 years; 19/22 (86%) patients with LR required repeat neck operation. Distant recurrence (DR)-free survival was 73% at 10 years and 36% at 20 years. On univariate analysis, predictors of DR were tumor size (p=0.007), positive LNs (p=0.02), LR (p<0.001), and postop Ct (p=0.01). Fifteen patients (23%) were treated with tyrosine kinase inhibitors after DR. In prophylactic-intent patients (n=14), two (14%) developed DR at 128 and 152 months and there were no deaths at median follow up of 115 months. Eight patients (12%) had ATA highest risk (M918T) mutations, 10 (15%) had high risk, 16 (24%) had moderate risk, and 32 (48%) were unknown. Patients with high, moderate, and unknown risk mutations had similar rates of LR, DR, and OS. M918T mutation-bearing patients had 10-year DRFS of 0% compared to 83% in all others (p<0.001), but equivalent 10-year OS (100% vs 92%, p=0.6). Conclusion: Structural recurrence is common in patients with germline RET mutations and MTC and can occur greater than 10 years after initial treatment; however, OS remains high even after distant recurrence. Care for these patients should focus on surveillance strategies and long-term control of structural disease.

Figure 1: Distant Recurrence Free Survival (DRFS) and Overall Survival (OS) by RET mutation.



62

Socioeconomic Factors are Associated with Disparities in the Management of Differentiated Thyroid Cancer J.Y. Liu,[1]* S.G. Patel,[2] C. Weber,[2] C.Y. Ko,[1] J. Sharma,[2] A.D. Yang,[3] N.D. Saunders.[2] *1. American College of Surgeons, Chicago, IL; 2. Emory University, Atlanta, GA; 3. Northwestern University, Chicago, IL.*

INTRODUCTION: Disparities exist within healthcare, however the effects of socioeconomic status (SES) on the management of differentiated thyroid cancer remains poorly defined. Our aim was to describe the impact of SES on access to care and treatment for patients with thyroid cancer and determine if disparities exist. METHODS: Patients who underwent thyroidectomy for papillary or follicular thyroid cancer were identified from the 2015 National Cancer Data Base. SES variables evaluated included insurance status, income, level of education, city type, and distance from treating facility. Stage of presentation, time to treatment, facility volume, academic vs non-academic facility, and radioactive iodine (RAI) and central lymph node dissection (CLND) utilization were compared within each SES variable using hierarchical multivariable logistic regression models. RESULTS: There were 355,331 patients analyzed from 1338 hospitals. Patients with government or no insurance, lower income, less education, and who travelled >50 miles to their treatment facility were all associated with a higher stage at diagnosis (all p<0.05). Patients without insurance had longer time from diagnosis to treatment (28.11 d vs 19.22 d private insurance; p=0.03). Furthermore, patients with lower income, less education, and from rural cities were less likely to be seen at a high volume and/or academic institution whereas patients traveling >50 miles to their treatment facility were more likely to be seen at a high volume and/or academic institution (all p<0.05)(Table 1). Patients with no insurance and less education were less likely to receive RAI when indicated, whereas patients from rural cities were more likely to receive RAI (all p<0.05). Prophylactic CLND occurred less often in patients with government or no insurance, lower income, and less education (all p<0.05). CONCLUSIONS: Patients with lower SES experience a significant disparity in their stage at diagnosis, time to treatment, type of facility they are treated at, and utilization of RAI and CLND. Further research is necessary to determine whether this disparity impacts important short and long term outcome measures.

Factors associated with treatment of differentiated thyroid cancer at high vs low volume institutions.

	High Volume (%)	Low Volume (%)	OR	95% CI	P Value
INSURANCE					<0.01
None	29.32	70.68	1.96	1.41-2.72	
Government	37.99	62.04	1.27	1.15-1.40	
Private	44.15	55.85	REF	REF	
INCOME					<0.01
<$38,000	34.76	65.24	2.05	1.52-2.78	
$38,000 - $47,999	35.68	64.32	1.98	1.50-2.62	
$48,000 - $62,999	39.72	60.28	1.61	1.31-1.98	
$63,000 +	49.76	50.24	REF	REF	
% DID NOT GRADUATE FROM HIGH SCHOOL					<0.01
21% +	36.82	63.18	1.71	1.32-2.20	
13% - 20.9%	39.32	60.68	1.52	1.28-1.81	
7% - 12.9%	41.58	58.42	1.36	1.21-1.54	
<7%	48.18	51.82	REF	REF	
CITY TYPE					<0.01
Rural	28.50	71.50	2.30	1.48-3.56	
Urban	31.46	68.54	1.87	1.41-2.48	
Metro	43.83	56.17	REF	REF	
DISTANCE					<0.01
50 + miles	61.31	38.69	0.43	0.33-0.56	
<50 miles	40.19	59.81	REF	REF	

63

Microscopic Extrathyroidal Extension and BRAFV600E Status Improve PTC Recurrence Prediction by AJCC 8th Edition Staging K.J. Nicholson,[1]* S. Carty,[1] K. McCoy,[1] P. Manroa,[2] M. Nikiforova,[2] Y. Nikiforov,[2] L. Yip.[1] *1. Surgery, University of Pittsburgh, Pittsburgh, PA; 2. University of Pittsburgh, Pittsburgh, PA.*

Introduction: While papillary thyroid cancer (PTC) incidence is increasing, many tumors are indolent and pose a low risk for recurrence following resection. Although it was present in the American Joint Committee on Cancer 7th edition (AJCC 7) cancer staging, the recent 8th edition (AJCC 8) removed microscopic extrathyroidal extension (microETE) from the differentiated thyroid cancer staging criteria. The study aim was to assess the association of AJCC 7 and 8 with PTC recurrence. Methods: A previously described database of 1,353 PTC patients with molecular marker testing data was updated to include interval follow-up data and recurrence (defined as histologic disease at ≥6 months post-thyroidectomy). Patients with <6 month follow-up were excluded. Data were analyzed by logistic regression and c-indices were generated from receiver-operator curves. Results: Mean length of follow-up was 66.8 months (range 6.0-131.0). Recurrence was observed in 6.3% of patients at a mean of 25.9 months after surgery (range 7.3-113.4). MicroETE was histologically present in 27.2% of PTC and BRAF V600E mutations were identified in 44.4%. By multivariable analysis, a higher stage by AJCC 7 (p<0.001) or 8 (p=0.043), as well as the presence of microETE (p=0.002) or BRAF V600E mutation (p<0.001), were independently associated with recurrence. The c-index to discriminate recurrence for AJCC 7 alone was 0.615, but rose to 0.724 with the addition of BRAF V600E mutation. The recurrence discrimination for AJCC 8 was 0.523 and lower than for AJCC 7, but improved to 0.650 with the inclusion of microETE, and to 0.726 with both microETE and BRAF V600E mutation. Conclusions: Examined in a large cohort of patients with a mean long-term follow-up of >5 years, AJCC 7 staging was a better discriminator for PTC recurrence than AJCC 8 staging. For both AJCC 7 and 8, the addition of BRAF V600E mutation status distinguished PTC that was more likely to recur. Because the AJCC system was optimized for mortality, which occurs uncommonly in PTC, consideration of microETE and BRAF V600E may offer particular utility in personalizing postoperative PTC management and surveillance strategies.

64

Whole Genome Copy Number Variation for the Classification of Tumors by Cell of Origin C.M. Court,* S. Sho, p. winograd, b. dipardo, L. Liu, H. Tseng, V. Agopian, T. Graeber, J. Tomlinson. *UCLA, Los Angeles, CA.*

Introduction: Somatic copy number variations (CNVs) are increasingly recognized as important genetic drivers in many cancer types. We first investigated the ability of whole genome CNV profiles to correctly identify the cell of origin and then determined if CNV profiles obtained from circulating tumor cells (CTCs) in the blood could be used to determine the location of the primary tumor. Methods: Whole genome CNV data was obtained from The Cancer Genome Atlas (TCGA). Low-resolution whole genome sequencing was used to establish CNV profiles for CTCs from 16 patients with liver and lung cancer. Results: A total of 10478 samples from 32 tumor types were used to develop a pan-cancer CNV dataset. Dimensional reduction analysis revealed a wide range of clustering between tumor types, with some cancers showing no similarity between samples and others demonstrating closely related copy number profiles. A radial basis support vector machine was used to develop a predictive model for classifying tumor site of origin and demonstrated an overall accuracy of 0.59 (95% CI: 0.56 – 0.61). Limiting the analysis to just the 17 cancer types that demonstrated condensed clustering, the accuracy of the predictive model improved to 0.82 (95% CI: 0.79 – 0.84). Our cell of origin classification model correctly identified the primary tumor site for 29/40 (72.5%) CTCs and identified at least 1 CTC correctly for 13/16 (81.3%) patients with lung or liver cancer. Conclusion: CNVs are genetic drivers for many tumors and whole genome CNV profiles demonstrate distinctive cell of origin patterns for many tumor types. CNV profiling of CTCs demonstrates potential utility for identifying the location of the primary tumor from the blood.

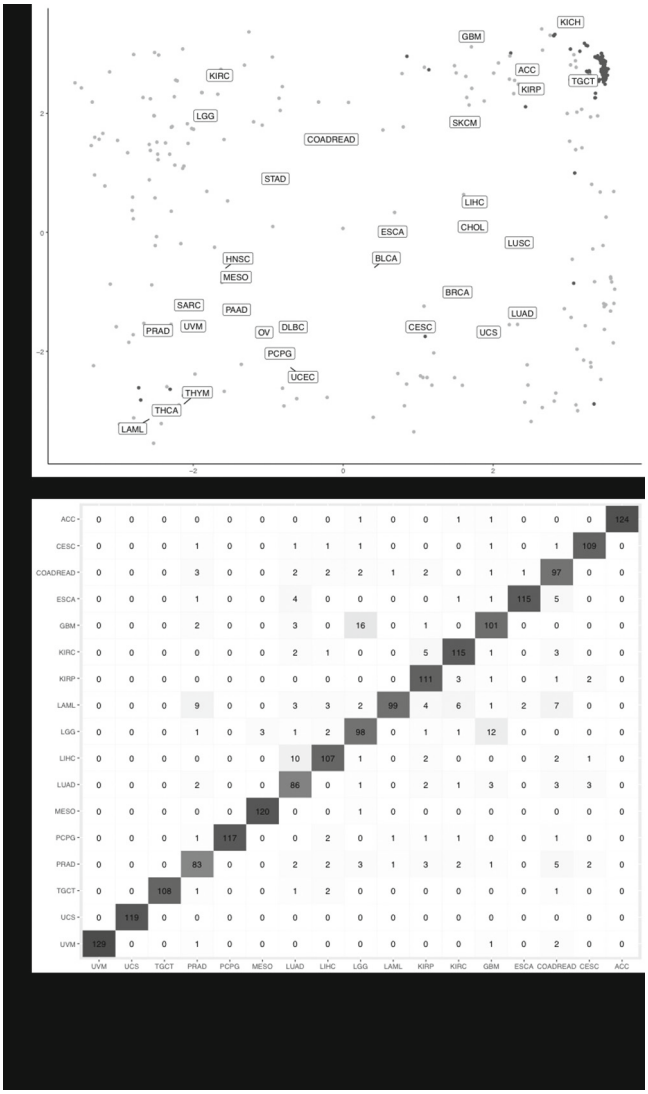
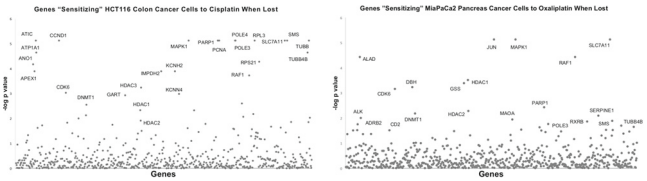


Figure 1. (A) copy number variations at all genes for the 32 cancer types were transformed using t-SNE into a 2-dimensional space. The mean of all samples for each cancer type is plotted as well as the individual samples for the best clustering (TGCT — Blue) and worse clustering (ESCA — Pink) cancer types. B) TCGA class prediction confusion matrix for the final cancer classification model.

65

Harnessing the Power of CRISPR/Cas9 to Discover Novel, Synthetically-Lethal FDA-Approved Drug Combinations for Gastrointestinal Malignancies E. Dogeas,* G. Shi, Y. Xie, J.T. Mendell, M. Augustine. *Surgery, University of Texas Southwestern Medical Centre, Dallas, TX.*

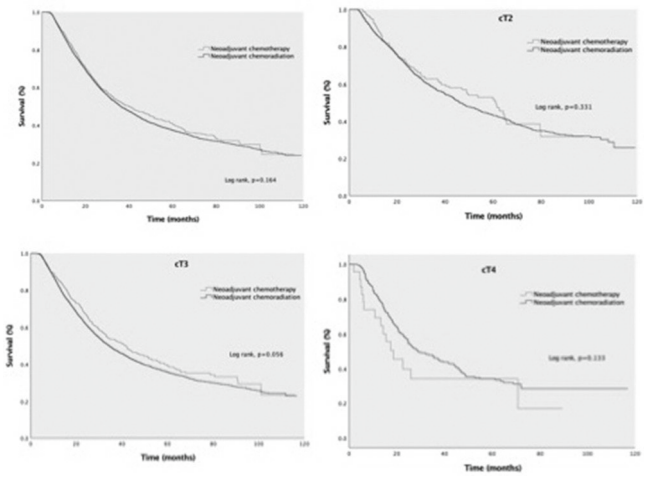
Introduction: With the cost of antineoplastic drug discovery rising exponentially, existing FDA-approved pharmacologic agents present a readily available, untapped resource that could be combined with current standard-of-care chemotherapy to enhance its efficacy. We sought to harness the CRISPR-Cas9 gene-editing technology to discover novel, synthetically-lethal drug combinations against gastrointestinal malignancies. Methods: A focused single-guide RNA (sgRNA) library against 650 genes targeted by FDA-approved drugs was designed and constructed. The MiaPaCa-2 pancreatic and HCT116 colon cancer cell lines were transduced with the library and treated with constant dose platinum chemotherapy. Genomic DNA was extracted from surviving cells and guide sequences were amplified and sequenced. MAGeCK statistical analysis identified significantly depleted guides in the treated cells. Secondary validation was performed with in vitro dual-drug combination testing. The Bliss independence model was applied to determine synergy. The efficacy of selected drug combinations was tested in a mouse xenotransplant model of pancreatic adenocarcinoma (PDAC). Results: Several genes, common between the two cell lines, were identified to confer sensitivity to platinum agents when lost. (Figure) The FDA-approved drugs, based upon the highly ranked genes from the screen (DNMT, PARP, HDAC, POLE and CDK4/6) demonstrated strong synergy with platinum in in vitro binary testing. Finally, the combination of the CDK4/6 inhibitor, palbociclib, with oxaliplatin exhibited greater in vivo anti-tumor activity than each drug alone in the mouse PDAC model. Conclusion: We successfully developed a CRISPR/Cas9 based in vitro to in vivo preclinical pipeline to identify novel, synthetically-lethal drug combinations against gastrointestinal malignancies with readily-available FDA-approved agents. By bypassing the lengthy and costly phase of new drug development, our platform can deliver novel and highly-promising drug combinations for clinical trial investigation.



66

Utility of Radiation After Neoadjuvant Chemotherapy for Surgically Resectable Esophageal Cancer F. Macedo,* B. Azab, N. Song, D. Yakoub, N. Merchant, D. Franceschi, A.S. Livingstone. *Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL.*

INTRODUCTION: Neoadjuvant chemotherapy (NAC) is the gold standard approach for locally advanced esophageal cancer (EC), however the addition of radiation remains largely controversial. We sought to investigate the role of neoadjuvant radiation in resectable EC by comparing outcomes of patients who underwent neoadjuvant chemotherapy with (NACR) or without radiation (NAC) using a large nationwide cohort. METHODS: National Cancer Data Base (NCDB) was queried for patients with non-metastatic EC between 2010 and 2014. Kaplan-Meier, log-rank and Cox multivariable regression analysis were performed to calculate overall survival (OS). Logistic regression was used to identify factors associated with 90-day mortality and complete pathological response (pCR). RESULTS: A total of 12,546 EC patients who underwent neoadjuvant therapy were included: the majority were males (84%), Caucasians (90.3%), and had adenocarcinoma (81.1%), cT3 (60.6%) and cN1 (49.1%). 11,269 (89.8%) patients had NACR, whereas 969 (7.7%), NAC alone. pCR rate was 14.1% (19.2%, NACR vs. 6.3%, NAC, p<0.001). Neoadjuvant radiation was an independent predictor for improved pCR [HR 0.305, 95% CI 0.205-0.454, p<0.001], however OS was similar in patients undergoing NAC with or without radiation (35.9 vs. 37.6 months, respectively, p=0.393, Fig 1A). This persisted regardless of tumor staging (Fig. 2B-D). There was a trend towards worse 90-day mortality after radiation (8.2%, NACR vs. 7.7%, NAC; HR 1.410, 95% CI 0.975-2.038, p=0.068). In Cox regression, controlling for patient and disease-related factors, neoadjuvant radiation was an independent predictor of worse OS (HR 1.322, 965% CI 1.177-1.485, p<0.001). CONCLUSIONS: This is the largest study comparing NACR versus NAC in resected EC. The addition of radiation to neoadjuvant chemotherapy is associated with improved pathological response rates, however it had deleterious effects in long-term and possibly, short-term survival. Our findings suggest that NAC without radiation may be the optimal neoadjuvant therapy in resectable EC, however further evidence with randomized clinical trials is warranted.



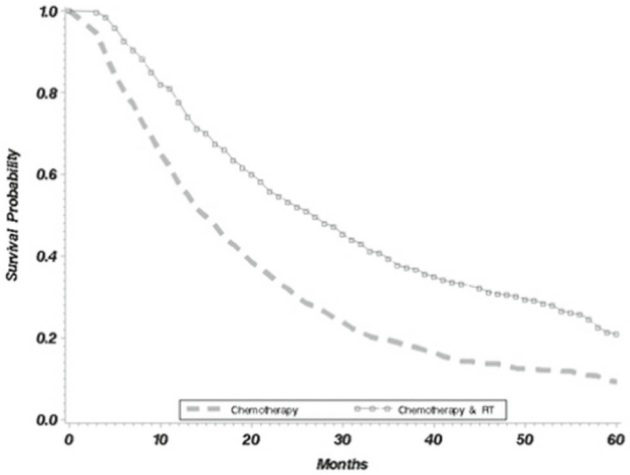
67

The Addition of Chemoradiation to Chemotherapy for Node-Positive Gastric Cancer is Associated with Improved Survival

A.M. Altman,* A. Sheka, S. Marmor, M. Reynolds, E. Lou, J. Hui, T. Tuttle, E. Jensen, J. Denbo. *Surgery, University of Minnesota, Minneapolis, MN.*

The ARTIST trial randomized gastric cancer patients who underwent curative-intent gastrectomy with D2 lymphadenectomy to adjuvant chemotherapy (CT) or CT plus chemoradiation (CRT) and found that the addition of CRT did not improve disease-free survival (DFS). However, subgroup analysis suggested that patients with nodal metastases (LN+) may have had an improved DFS from CRT. The purpose of the present study was to evaluate the impact of postoperative CRT among LN+ gastric cancer patients using a population-based study. We used the Surveillance, Epidemiology and End Results-Medicare linked data to identify patients with LN+ gastric adenocarcinoma who underwent upfront surgical resection. Patients who received adjuvant CT alone were compared to those who received adjuvant CT and CRT. Multivariable logistic regression was used to determine factors associated with receipt of CRT. Five-year overall survival (OS) was estimated with the Kaplan-Meier method and Cox proportional hazards modeling. A total of 2,409 pateints underwent upfront surgical resection and were found to have LN+ disease; 309 (13%) received adjuvant CT alone, and 407 (17%) received adjuvant CT + CRT. Factors associated with an increased odds of receipt of CRT were earlier year of diagnosis and younger age ($p \leq 0.05$). Median OS for all patients with LN+ gastric cancer was 15 months, while median OS was 20 months for patients who received CT alone compared to 27 months for patients who received CT + CRT ($p \leq 0.05$, Figure). After adjusting for known prognostic factors, we found that recent diagnosis (2009-2013), older age (75 years and older), T stage III/IV and Charlson comorbidity index were associated with an increase in the hazard ratio for death ($p<0.05$) while extent of lymphadenectomy (>15 nodes) and receipt of CRT were associated with a decreased hazard ratio for death ($p<0.05$). Patients with LN+ gastric adenocarcinoma who underwent upfront surgical resection and received CT + CRT had improved survival compared to CT alone, regardless of extent of lymphadenectomy. These data suggest that CRT should be a component of adjuvant therapy for LN+ gastric adenocarcinoma.

Figure 1: Kaplan Meier overall survival curves for patients with lymph node positive gastric adenocarcinoma treated with chemotherapy or chemotherapy and chemoradiation. Median overall survival is 20 months for those treated with chemotherapy and 27 months for those treated with additional chemoradiation ($p \leq 0.05$).



68

Resection Margin Distance in Extra-Hepatic Cholangiocarcinoma: How Much Is Enough?

A. Rahnemai-Azar,[1]* S.M. Ronnekleiv-Kelly,[1] D. Abbott,[1] C. Ethun,[10] G. Poultsides,[2] T. Tran,[2] R. Fields,[3] B.A. Krasnick,[3] R. Martin,[4] C.R. Scoggins,[4] K. Idrees,[5] C.A. Isom,[5] I. Hatzaras,[6] R. Shenoy,[6] P. Shen,[7] J.D. Perkins,[8] T. Pawlik,[9] S. Maithel,[10] S. Weber.[1] *1. Department of Surgry, Division of Surgical Oncology, University of Wisconsin School of Medicine and Public Health, Madison, WI; 2. Department of Surgery, Division of Surgical Oncology, Stanford University School of Medicine, Palo Alto, CA; 3. Department of Surgery, Division of Surgical Oncology, Washington University School of Medicine at St. Louis, St. Louis, MO; 4. Department of Surgery, Division of Surgical Oncology, University of Louisville School of Medicine, Louisville, KY; 5. Department of Surgery, Division of Surgical Oncology, Vanderbilt University School of Medicine, Nashville, TN; 6. Department of Surgery, Division of Surgical Oncology, NYU School of Medicine, New York City, NY; 7. Department of Surgery, Division of Surgical Oncology, Wake Forest University School of Medicine, Winston-Salem, NC; 8. Department of Surgery, University of Washington, Seattle, WA; 9. Department of Surgery, Division of Surgical Oncology, The Ohio State University Wexner Medical Center, Columbus, OH; 10. Department of Surgery, Division of Surgical Oncology, Emory University Winship Cancer Institute, Atlanta, GA.*

Background: Surgical resection is required for the curative treatment of patients with extra-hepatic cholangiocarcinoma (EH-CCA). The objective of this study was to determine if the distance of surgical margin was associated with outcome. Methods: Patients who underwent curative-intent resection for EH-CCA, including distal- and perihilar CCA, between 2000 and 2015 at 10 hepatobiliary centers across the U.S. were evaluated using prospectively collected data. Cox proportional hazard model was utilized to evaluate the influence of the extent of the margin on the outcome. Results: 538 patients with EH-CCA who underwent curative-intent resection were included: 383 (71%) undergoing R0 resection, 153 (28%) undergoing R1 resection, and 2 with R2 resection. A negative surgical margin (R0) was associated with improved recurrence-free (RFS) and overall survival (OS) (RFS: 10.5% vs 3.6% (R1) and OS: 25.8% vs 9.3% (R1). Subsequently, further analysis on 161 patients with complete data on distance of resection margin, all undergoing R0 resection, was performed to assess the impact of extent of margin on the outcome. On multivariable analysis, the resection margin distance, analyzed as a continuous variable, was not associated with either improved RFS (RR 1.00, 95% CI 0.96-1.05; p 0.71) or OS (RR 0.99, 95%CI 0.96-1.01; p 0.49). Increasing age, increased tumor size, and LN metastasis were identified as independent predictors of OS; while RFS were mainly dependent on tumor size and LN metastasis (Table 1). Conclusion: Achieving R0 resection improves

OS for EH-CCA tumors, and obtaining additional margin does not confer any additional clinical benefit. Increasing age, tumor size, and LN metastasis are independent predictors of RFS and OS, but increased margin width is not associated with improvement in either.

Table 1. Multivariable analysis of factors affecting overall survival of patients with extra-hepatic CCA who underwent surgical resection, with significant factors noted in bold.

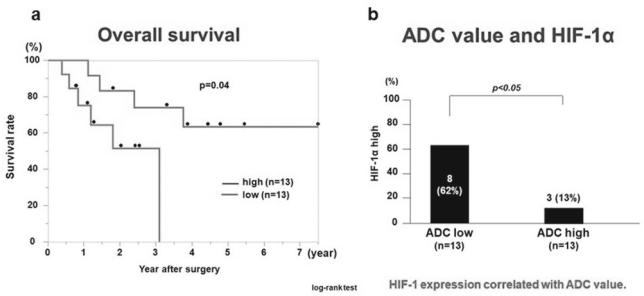
Variable	RR	CI
Closest margin distance	0.99	0.96- 1.01
Preoperative biopsy	0.68	0.44- 1.06
Male gender	1.40	0.92- 2.19
Lymphovascular invasion	1.32	0.83- 2.12
Perineural invasion	0.79	0.51- 1.28
Age	1.03	1.01- 1.05
Tumor size	1.02	1.00- 1.03
Lymph node positive	1.87	1.21- 2.89

69

Prognostic Prediction of Mass-Forming Intrahepatic Cholangiocarcinoma from Diffusion Weighted Image of Magnetic Resonance Image S. Yamada,* M. Shimada, Y. Morine, s. imura, T. Ikemoto, S. Iwahashi, Y. Saito, T. Yoshimoto, M. Nishi, C. Takasu. *Surgery, Tokushima University, Tokushima, Japan.*

Background: It has been reported that diffusion weighted image (DWI) of MRI could estimate the malignancy of tumor non-invasively. However, there are few reports about intrahepatic cholangiocarcinoma (IHCC). We herein evaluate apparent diffusion coefficient (ADC) in MRI-DWI as the prognostic factor. Method: Patients who underwent hepatic resection for mass forming type IHCC were enrolled in this study (n=26). MRI scans were conducted on Signa HDe 1.5T or Signa Explorer 1.5T (GE healthcare, USA). Using DWI (b value: 0, 20, 800s / mm^2), ADC map was made (SYNAPSE VINCENT, FUJIFILM, Japan). Patients were divided into two groups (ADC high; n=13 ADC low; n=13 cut off: median), and clinicopahological factors were compared between two groups. Immunohistochemistry staining of HIF-1α in tumor tissue was also performed, and divided into high and low expression along with previous report (Cancer Res. 2014) Results: In ADC low group, there were more old patients compared with ADC high group (p=0.03). There was no significant difference in gender, tumor location, stage, tumor markers, vessel invasion, and lymph node metastasis. Overall survival rate in ADC low group was significantly worse than ADC high group ($p<0.05$). In univariate analysis, tumor location (hilar), stage (III, IV), portal vein invasion, ADC low were detected as prognostic factors for overall survival ($p<0.05$). In multivariate analysis, tumor location (hilar), portal vein invasion, ADC low were detected as independent prognostic factors. Furthermore, ADC low group showed higher rate of HIF-1α high expression compared with ADC high group. Conclusion; In IHCC, DWI-ADC low was independent prognostic factor, and correlated with HIF-1α expression. MRI may estimate prognosis of IHCC, as well as evaluation of the tumor.

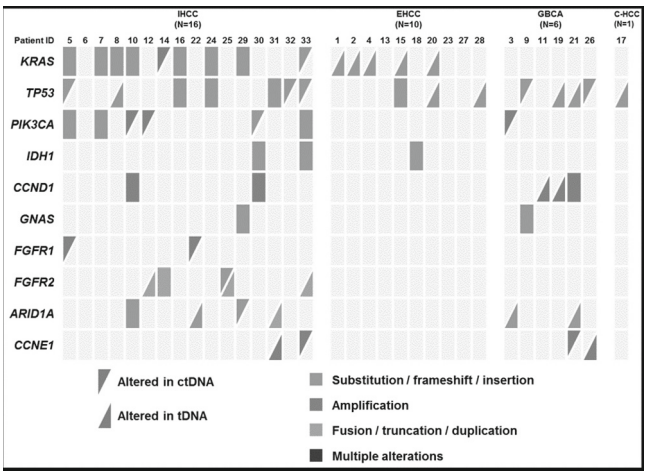
Figure 1



70

Biliary Tract Cancers Frequently Possess Concordant Genomic Alterations in Circulating and Tissue-based Tumor DNA R. Okamura,* R. Kurzrock, R.J. Mallory, P.T. Fanta, A.M. Burgoyne, B.M. Clary, S. Kato, J.K. Sicklick. *Center for Personalized Cancer Therapy, Moores Cancer Center, University of California, San Diego, San Diego, CA.*

Background: Biliary tract cancers have dismal prognoses even when cytotoxic chemotherapy is administered. To further develop clinically useful precision treatment approaches, we used next generation sequencing (NGS) to analyze the genomic landscape of these cancers in circulating tumor DNA (ctDNA) from plasma and tissue-based tumor DNA (tDNA) from tumor tissue. Methods: We performed comprehensive genomic profiling (Foundation Medicine; Guardant) for both ctDNA and tDNA of 33 biliary tract cancer patients. Frequency and concordance of genomic alterations in the two CLIA-certified NGSs assays were assessed. Variants of unknown significance were excluded. Results: This study included patients with intrahepatic cholangiocarcinoma [N=16], extrahepatic cholangiocarcinoma [N=10], gallbladder cancer [N=6] and cholangiohepatocellular carcinoma [N=1]. Seventy percent of patients (23/33) had ≥1 alteration in ctDNA [median number of alterations/patient: 2 (range, 0-9)], while all patients had ≥1 alteration in tDNA [median number of alterations/patient: 3 (range, 1-9)]. Across all tumor types, the most common ctDNA and tDNA alterations occurred in KRAS (N=9, 27%), TP53 (N=9, 27%), and PIK3CA (N=7, 21%) versus KRAS (N=12, 36%), TP53 (N=10, 30%), and CDKN2A/B (N=10, 30%), respectively. The concordance between ctDNA and tDNA was 79% for KRAS, 67% for TP53, and 88% for PIK3CA genomic alterations while there was 100% gene variant concordance for IDH1 and GNAS. When assessed by tumor biopsy site (primary [N=26] vs metastatic [N=7]), ctDNA results were more concordant with metastatic site tDNA than primary tumor tDNA (KRAS: 100% vs 73%, TP53: 71% vs 65%, PIK3CA: 100% vs 85%). Conclusions: Evaluation of ctDNA and tDNA by NGS is feasible in biliary tract cancer patients and for the first time we report high concordance rates between these results. Moreover, ctDNA results were more concordant with metastatic tumor DNA than primary tumor DNA, suggesting that these tests are complimentary rather than mutually exclusive. Further studies are warranted to assess the application of these assays for pharmacologically targeting biliary tract cancers.

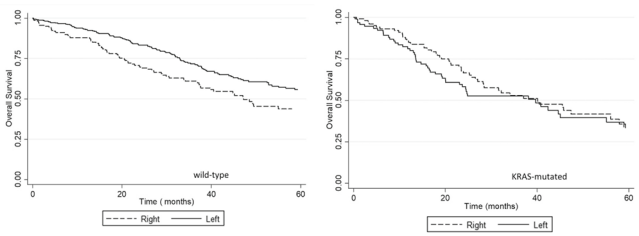


Comparison between ctDNA and tDNA sequencings for the commonly altered genes [N=33]. Abbreviations: ctDNA, circulating tumor DNA from plasma; tDNA, tissue-based tumor DNA; IHCC, intrahepatic cholangiocarcinoma; EHCC, extrahepatic cholangiocarcinoma; GBCA, gallbladder cancer; C-HCC, cholangiohepatocellular carcinoma.

71

The Prognostic Role of Primary Tumor Site Differs Among Patients with Colon Cancer Liver Metastases According to the KRAS Mutational Status G. Margonis,[1]* N. Amini,[1] S. Buettner,[1] N. Andreatos,[1] D. Wagner,[2] S. Kazunari,[3] J. Wang,[1] G. Sun,[3] A. Pulvirenti,[11] A. Beer,[4] C. Kamphues,[5] D. Morioka,[6] I. Løes,[7] K. Imai,[8] J. He,[1] T. Pawlik,[9] K. Kaczirek,[4] G. Poultsides,[10] P. Lønning,[7] R. Burkhart,[1] I. Endo,[6] H. Baba,[8] H. Mischinger,[2] F. Aucejo,[3] M. Kreis,[5] C. Wolfgang,[1] M. Weiss.[1] *1. Johns Hopkins University School of Medicine, Baltimore, MD; 2. Medical University of Graz, Graz, Austria; 3. Digestive Disease Institute, Cleveland Clinic, Cleveland, OH; 4. Medical University of Vienna, Vienna, Austria; 5. Charite Campus Benjamin Franklin, Berlin, Germany; 6. Yokohama City University Graduate School of Medicine, Yokohama, Japan; 7. University of Bergen and Haukeland University Hospital, Bergen, Norway; 8. Graduate School of Medical Sciences, Kumamoto, Japan; 9. The Ohio State University Wexner Medical Center, Columbus, OH; 10. Stanford University School of Medicine, Stanford, CA; 11. Memorial Sloan Kettering Cancer Center, New York, NY.*

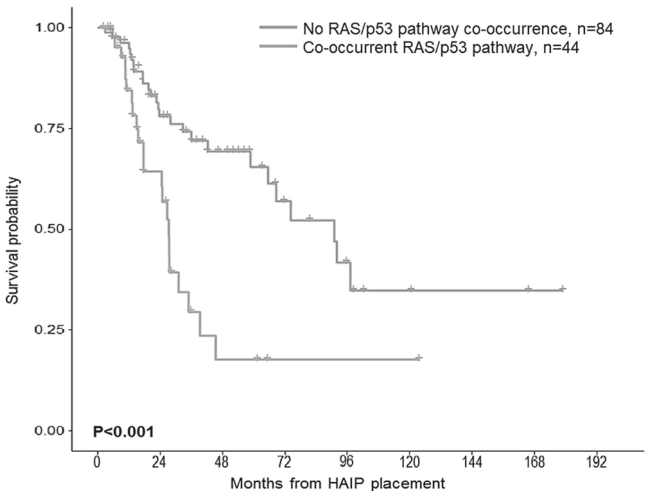
Introduction: Although some studies have demonstrated that patients with colon cancer liver metastases (CLM) from a right sided primary cancer fare worse, others have found equivocal outcomes of CLM patients with right vs left sided primary tumors. In the light of recent evidence from unresectable metastatic colon cancer suggesting that tumor laterality predicts survival only in those with KRAS wild-type tumors, we aimed to examine the prognotic role of tumor laterality in CLM after stratifying by the KRAS mutational status. Methods: We retrospectively identified 1137 patients with known primary colon cancer site and KRAS mutational status who underwent hepatic resection for CLM between 2000 and 2015. Patients with rectal or transverse colon tumors were excluded from analysis. The prognostic impact of right (RS) vs left sided (LS) primary colon cancer was determined after stratifying by the KRAS mutational status. Results: 277 patients had an RS (38.6%) and 441 (61.4%) had a LS tumor. Roughly two thirds of tumors were KRAS wild type (n = 516, 71.9%), while 28.1% (n = 202) had KRAS mutations. Median and 5-year overall survival (OS) of the entire cohort was 55 months and 46.6%, respectively. In the entire cohort, RS was associated with worse 5-year OS compared with LS (39.4% vs. 51.0%%) and remained significantly associated with worse OS in the multivariable analysis (hazard ratio (HR) 1.41, 95 % CI 1.06-1.88; P = 0.02). In wild-type patients, a worse OS associated with an RS tumor was evident in univariable analysis (5-year OS: RS, 43.8% vs LS, 55.7%; P = 0.02) and persisted in multivariable analysis (HR 1.52, 95 % CI 1.10-2.11; P = 0.01). In contrast, tumor laterality had no impact on OS, even in the univariable analysis, among patients with KRAS mutated tumors (5-year OS: RS, 32.8% vs. LS, 34.0%; HR 0.84, 95 % CI 0.57-1.24; P = 0.38). Conclusions: This study demonstrated, for the first time, that in CLM the prognostic role of primary tumor side differs according to the KRAS mutational status. Right-sided tumors were associated with worse survival only in CLM patients with wild-type tumors (Figure).



72

A Distinct Genomic Profile is Associated with Conversion to Resection and Survival in Initially Unresectable Colorectal Liver Metastasis J. Datta,[1]* R.R. Narayan,[1] W. Chatila,[1] D.A. Goldman,[1] G. Mithat,[1] N. Schultz,[1] V.P. Balachandran,[1] J.A. Drebin,[1] P.J. Allen,[2] T.P. Kingham,[1] W.R. Jarnagin,[1] N.E. Kemeny,[1] M.I. D'Angelica.[1] *1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Duke University, Durham, NC.*

INTRODUCTION: Up to 80% of patients with colorectal liver metastasis are initially unresectable (IU-CRLM). Combination hepatic artery infusion (HAI) and systemic (SYS) chemotherapy allows conversion to resection (CTR) with associated long-term overall survival (OS) in a subset of patients. Genomic correlates of CTR and OS in IU-CRLM have not been previously explored. METHODS: We reviewed IU-CRLM patients receiving HAI/SYS chemotherapy who underwent next-generation sequencing encompassing >400 genes. False discovery rate-adjusted (q-value) Fisher's exact test compared gene and signaling pathway-level alterations - filtered for known driver variants - between CTR and unresectable (UR) cohorts. Kaplan-Meier and unadjusted Cox methods assessed associations with OS from HAI initiation. RESULTS: Of 128 IU-CRLM patients, 51 (40%) underwent CTR at median 6 months from HAI initiation. CTR and UR cohorts differed in SYS chemotherapy exposure prior to HAI and disease-free interval between primary and CRLM diagnosis, but not clinical risk score or presence of extrahepatic disease. Median and 5-year OS for the overall cohort was 66 months and 51%, respectively; median follow-up among survivors was 26 (range, 2-179) months. CTR was associated with decreased risk of death (HR 0.23, 95% CI 0.1-0.5, P<0.001). The most frequently altered genes were APC (80%), TP53 (77%), and KRAS (37%). Mutual exclusivity of RAS and p53 pathway-level alterations (P=0.008) was associated with CTR. When examining OS, patients harboring RAS pathway-level alterations demonstrated worse OS (P=0.002, q=0.02). Moreover, co-occurrence of RAS with p53 pathway-level alterations was associated with worse OS (median 27 vs. 91 months, P<0.001, q<0.001; Figure) vs. non-co-occurrent cohorts. At the gene-level, class I/II BRAF mutations (median 18 vs. 69 months, P<0.001, q<0.001) correlated with worse OS. CONCLUSION: An association between co-occurrence of p53 and RAS pathway-level alterations with CTR and OS is observed in this selected cohort of IU-CRLM patients receiving HAI/SYS chemotherapy. This novel signal needs to be validated in future studies.



73

Cytolytic Activity Score as a Favorable Biomarker of Hepatocellular Carcinoma H. Takahashi,[1]* T. Kawaguchi,[2] K. Takabe.[1] *1. Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY; 2. Department of Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan.*

Background: Ongoing clinical trials with immune checkpoint inhibitors (CPIs) for hepatocellular carcinoma (HCC) have revealed that identification of the respondents is imminent need. As cytolytic activity score (CYT), defined by Granzyme A (GZMA) and Perforin (PRF1) expression, is a useful tool to assess the anticancer immunity, we aimed to examine the immune landscape of HCC using CYT. Method: Three hundred seventy-one HCC patients in The Cancer Genome Atlas (TCGA) were analyzed. CIBERSORT and TIMER were used to estimate intra-tumoral immune cell composition, and Gene Set Enrichment Analysis (GSEA) was conducted. Kaplan-Meier curve for overall survival (OS), disease free interval (DFI), progression free interval (PFI), and disease-specific survival (DSS) were obtained, and Cox Progression Hazards model was used for multivariable analysis. Results: High CYT was associated with high levels of activated CD8+ T cells, gamma-delta T cells, M1 macrophages, and memory CD4+T cells by both CIBERSORT and TIMER. The levels of immune checkpoint molecules (ICMs), including programmed death-1 (PD-1), programmed death-ligand 1 (PD-L1), PD-L2, cytotoxic T-lymphocyte-associated protein 4 (CTLA4), lymphocyte-activation gene 3 (LAG3), T cell immunoglobulin and mucin domain 3 (TIM3), indoleamine 2,3-dioxygenase 1 (IDO1), and IDO2, correlated significantly with CYT ($p< 0.0001$). CYT-high HCCs strongly enriched gene sets related with innate immune system, such as Defense Response and Immune Response by GSEA. CYT-high HCC patients had significantly improved DFI, PFI, DSS, and OS ($p= 0.01$, 0.003, 0.026, and 0.005, respectively), compared to CYT-low HCC patients. Multivariate analysis demonstrated high CYT was an independent protective factor for prognosis in patients with HCC. Conclusions: CYT-high HCC is associated with significantly improved survival secondary to enhanced immunity and increased cytolytic activity by T cell and M1 macrophage. Given strong correlation, further study to determine CYT as a potential predictive biomarker for CPIs is warranted.

74

Disparities in Treatment Utilization for Early Stage Hepatocellular Carcinoma in the Veteran Patient Population P.M. Polanco,[1]* M. Chansard,[1] C. Ahn,[1] E. Mortensen,[2] H. Zeh,[1] A. Yopp.[1] *1. Surgery, University of Texas Southwestern Medical Center, Dallas, TX; 2. University of Connecticut, West Hartford, CT.*

Introduction:The incidence of hepatocellular carcinoma(HCC) has significantly increased in the Veterans health system. While often diagnosed at a late stage, early stage HCC(ES-HCC) should receive curative intent therapies when clinically appropriate. The aim of this study is to identify patient and hospital factors associated with disparities in the utilization of curative intent treatments for ES-HCC in the Veteran population. Methods:VA Corporate Data Warehouse was used to identify all patients diagnosed with HCC from 2001-2015. ES-HCC patients (stages I /II, AJCC 7ed) were the study cohort. Demographics, ICD-9 codes, CPT codes, Child scores, MELD, laboratory data, hospital data and year of treatment were used to identify clinically relevant factors. Initial (first) therapy was categorized as curative treatment [(CT) resection, ablation or transplant], non-curative treatment [(NCT)transarterial embolization or chemotherapy] and no treatment (NT). A series of univariate logistic regressions tested factors for inclusion in a stepwise multivariate(MVA) logistic regression model. Outcomes include overall treatment utilization and receipt of CT versus NCT/NT. Results: A total of 18,265HCC patients were identified, of which 9504 were ES-HCC (5359 stage I, 4145 stage II). Of this, 15%(1456), 51%(4812) and 34%(3236) received CT, NCT or NT respectively. Initial MVA revealed that stage II, presence of Non-alcoholic fatty liver disease, early study period (2001-2005), Child C, higher MELD, lower complexity and Southwest hospitals were significantly associated with higher risk of NT(Table1A). Subsequent MVA revealed that significant factors associated with decreased utilization of CT versus NCT/NT were:stage II, Hispanic race, latter study period(2011-2015), Child B score, higher MELD score, lower complexity hospitals and hospitals in the Midwest, West and Southeast regions(Table 1B). Conclusion:Our study reports the largest cohort of veteran patients with ES-HCC. Only a small fraction of patients received CT. Several patient and hospital factors are associated with significant disparities in overall treatment utilization and curative intent therapies for ES-HCC.

Table 1: Stepwise multivariate logistic regression model

TABLE 1A: OUTCOME: Any Treatment (n = 6268) vs No Treatment (n = 3236)				
VARIABLE	OR	CI	p	T3 Error
HCC STAGE				
Stage I	Reference			
Stage II	1.241	1.088 - 1.416	p= .0013	
NAFLD/NASH	0.724	0.585 - 0.897	p= .0031	
YEAR OF DIAGNOSIS				
2001 - 2005	Reference			p< .0001
2006 - 2010	1.639	1.347 - 1.994	p= .0024	
2011 - 2015	1.747	1.429 - 2.135	p< .0001	
CHILD PUGH SCORE				
A	Reference			p< .0001
B	0.643	0.554 - 0.747	p= .5088	
C	0.369	0.273 - 0.499	p< .0001	
MELD SCORE	0.947	0.929 - 0.966	p< .0001	
VA HOSPITAL REGION				
Northeast	Reference			p< .0001
Midwest	0.882	0.719 - 1.082	p= .0723	
West	1.498	1.215 - 1.848	p< .0001	
Southwest	0.788	0.636 - 0.977	p= .0015	
Southeast	0.953	0.788 - 1.151	p= .4477	
VA HOSPITAL COMPLEXITY				
High	Reference			p< .0001
Low	0.718	0.623 - 0.828	p<.0001	
TABLE 1B: OUTCOME CT (n = 1456) vs NCT/NT (n = 8048)				
VARIABLE	ADJUSTED OR	95% CI	p	T3 Error
HCC STAGE				
Stage I	Reference			
Stage II	0.524	0.447 - 0.615	p<.0001	
RACE				
White	Reference			p= .0277
Black	1.213	1.010 - 1.456	p= .0562	
Hispanic	0.8	0.616 - 1.038	p= .0225	
Other	1.142	0.737 - 1.769	p= .5218	
Cirrhosis	1.225	1.041 - 1.440	p= .0144	
YEAR OF DIAGNOSIS				
2001 - 2005	Reference			p< .0001
2006 - 2010	0.614	0.493 - 0.765	p= .0715	
2011 - 2015	0.506	0.402 - 0.636	p< .0001	
CHILD PUGH SCORE				
A	Reference			p= .0409
B	0.787	0.654 - 0.948	p= .2836	
C	0.811	0.520 - 1.265	p= .6809	
MELD SCORE	0.944	0.919 - 0.971	p< .0001	
VA HOSPITAL REGION				
Northeast	Reference			p< .0001
Midwest	0.446	0.344 - 0.578	p< .0001	
West	0.794	0.636 - 0.990	p= .0168	
Southwest	0.674	0.526 - 0.865	p= .8086	
Southeast	0.524	0.42 - 0.655	p= .0034	
VA Hospital Complexity				
High	Reference			p= .0002
Low	0.708	0.592 - 0.847	p= .0002	

75

Detailed Analysis of Margin-Positivity and Local Recurrence Following Pancreaticoduodenectomy C.A. McIntyre,* C. Zambirinis, A. Pulvirenti, J. Chou, G. Mithat, V.P. Balachandran, T.P. Kingham, M.I. D'Angelica, J.A. Drebin, W.R. Jarnagin, P.J. Allen. *Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: The association between a positive surgical margin and recurrence following pancreatic cancer (PDAC) resection has been reported, yet assessment of the specific location of the positive margin and site of local recurrence has not. We aimed to investigate whether site of margin positivity was associated with the site of local recurrence after pancreaticoduodenectomy. Methods: A prospectively maintained database was queried for patients who underwent R0/R1 pancreaticoduodenectomy for PDAC between 2000-2015. The bile duct, pancreas, stomach/duodenum, anterior capsule, and posterior (uncinate) margins were routinely assessed. Postoperative imaging was reviewed for site of first recurrence, and local recurrence was defined as located in the remnant pancreas, surgical bed, or retroperitoneal site outside of the surgical bed. Associations between pathologic variables and cumulative incidence of site of local recurrence were evaluated using competing risks methods and compared using Gray's test. Results: During this period, 891 patients underwent pancreaticoduodenectomy for PDAC. With a median follow up of 25 months, 354 patients recurred at distant sites, 197 had an isolated local recurrence, 193 had local and distant recurrences, and 147 remained free of disease for >6 months. The 5-year cumulative incidence rates (CIR) of local recurrence (n=390) after surgery were: remnant pancreas, 4% (95%CI:3-5%); surgical bed, 35% (32-39%); and 4% (3-6%) within the retroperitoneum outside of the surgical bed. None of the sites of positive margin were associated with specific sites of local recurrence with the exception of the posterior margin, which was associated with surgical bed recurrence (5yr CIR: 46% vs 32%,

p<0.01). Lymph node positive disease was associated with surgical bed recurrence (38% vs 29%, p=0.006), and increasing tumor size trended towards this outcome (HR:1.08, 95%CI:0.99-1.18, p=0.085). Conclusion: In this study, only a positive posterior margin was associated with local recurrence, specifically within the surgical bed. As other tumor factors were also associated with this type of recurrence, the overall influence of margin on local recurrence is limited.

76

No Advantage of Neoadjuvant Therapy for Clearly Resectable Pancreatic Cancer R.J. Vidri,[1]* W.T. Olsen,[3] D.E. Clark,[3] T.L. Fitzgerald.[2] *1. Surgery, St. Mary's Regional Medical Center, Portland, ME; 2. Maine Medical Center, Portland, ME; 3. Division of Surgical Oncology, Tufts University School of Medicine-Maine Medical Center, Portland, ME.*

Introduction Neoadjuvant therapy is the standard of care for locally advanced and borderline resectable pancreatic cancers. However, the role of neoadjuvant therapy remains controversial for clearly resectable tumors. Methods Retrospective cohort study using the National Cancer Database (2006-2014) of subjects with T1-T2 tumors encompassing Stage I-II pancreatic cancer. An "intention to treat analysis" was performed utilizing time and treatment-sequence variables within the database. Subjects were then classified as intended to have upfront resection (UR) or neoadjuvant therapy (NAT). Inverse probability weighting was used to reduce potential bias. Kaplan-Meier and Cox proportional-hazard models were used for survival analysis. Results A total of 19,621 subjects were included. Median follow-up was 15.6 months. 4,858 (24.8%) subjects had T1 and 14,763 (75.2%) had T2 tumors. 11,080 (56.5%) subjects were intended to have UR and 8,541 (43.5%) NAT. In the UR group, 7,842 (70.8%) patients underwent surgery and completed adjuvant treatment; the remaining 3,238 (29.22%) did not receive adjuvant treatment. Of those intended to receive NAT, 6,965 (81.65) received only chemotherapy, and 1,576 (18.5%) proceeded to complete the intended regimen with surgical resection. There was no difference in 30 and 90-day mortality between those undergoing UR or NAT (2.1% vs 2.67%, p=0.2). Median survival for those who underwent UR and received adjuvant therapy was 26 months, compared to 20 months for those who did not receive adjuvant therapy (p=0.015). Subjects in the group NAT who underwent resection had a median survival of 26.3 months, compared to 9.3 months in those who did not proceed to surgery (p<0.001). [Figure 1] Conclusions Patients with clearly resectable pancreatic cancer have similar survival irrespective of the timing of systemic therapy and surgery. However, given the high attrition rate of neoadjuvant treatment regimens, overall survival may be compromised for patients who do not proceed to surgery; making it potentially detrimental. A properly designed clinical trial will be required to define the role for neoadjuvant therapy for clearly resectable pancreatic cancer.

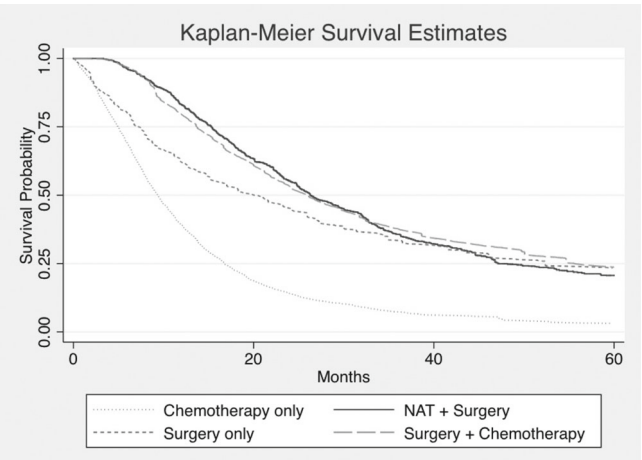


Figure 1. Overall survival by treatment regimen for subjects with stage I and II pancreatic cancer. Plot is truncated at 60 months.

77

Long-Term Follow-up of FOLFIRINOX Induction Therapy for Locally Unresectable Pancreatic Ductal Adenocarcinoma (PDAC) N. Cohen,[1]* C.A. McIntyre,[1] D.A. Goldman,[1] G. Mithat,[1] E. Sadot,[2] E. O'Reilly,[1] A. Varghese,[1] K. Yu,[1] V.P. Balachandran,[1] M.I. D'Angelica,[1] J.A. Drebin,[1] T.P. Kingham,[1] P.J. Allen,[3] W.R. Jarnagin.[1] *1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Rabin Medical Center, Petach Tikva, Israel; 3. Duke University School of Medicine, Durham, NC.*

Introduction: We previously reported that patients with initially locally unresectable PDAC who received induction FOLFIRINOX therapy and ultimately underwent surgical resection had improved survival compared to patients who remained unresectable. Median follow-up was 12 months (range 3-37) in all patients, and median overall survival (OS) had not been reached in the resected patients. Herein, we present 5-year follow-up of this cohort. Methods: A prospectively-maintained database was queried for patients with locally unresectable PDAC treated with induction FOLFIRINOX at our institution between 2010-2013. Local unresectability was adjudicated at a multidisciplinary tumor board. Comparisons between resected and unresected patients were made with Fisher's Exact test and the Wilcoxon Rank Sum test. OS was measured from the start of FOLFIRINOX until death, progression-free survival (PFS) and recurrence-free survival (RFS) were estimated from the start of FOLFIRINOX until clinical or radiologic progression/recurrence or death; patients without the event of interest were censored at last follow-up. Kaplan Meier plots were used to visualize survival outcomes overall and by resection status. Results: The final cohort consisted of 101 patients with locally unresectable PDAC treated with induction FOLFIRINOX, of whom 32 underwent resection and 69 remained unresectable. Median follow-up of survivors was 63.4 months (range: 13.9-84.3). In resected patients, median OS was 35.7 months (95%CI:24.3-58.0 months) and 5-year OS was 25.4% (95%CI:11.1-42.5%). Median RFS was 17.8 months (95%CI:14.0-22.9 months) and 5-year RFS was 12.9% (95%CI:4.1-27.0%). In unresected patients, median OS was 17.0 months (95%CI:14.7-23.0 months) and 5-year OS was 1.4% (95%CI:0.1-6.9%). Median PFS was 10.1 months (95%CI:7.2-13.3 months) and 5-year PFS was 1.4% (95%CI:0.1-6.9%). Conclusion: Patients with initially locally unresectable PDAC treated with induction FOLFIRINOX who underwent resection had 5-year OS 25.4%. Despite poor 5-year survival, patients who remained unresectable had improved short-term outcomes compared to historical benchmarks.

Long-Term Follow-Up of FOLFIRINOX Induction Therapy for Locally Unresectable Pancreatic Ductal Adenocarcinoma

	Overall Survival		Recurrence/Progression-Free Survival	
	Survival Estimate	[95% CI]	Survival Estimate	[95% CI]
Resected Patients n=32				
Median (months)	35.7	[24.3-58.0]	17.8	[14.0-22.9]
1 Year	93.8%	[77.3%-98.4%]	77.4%	[58.4%-88.5%]
3 Year	48.6%	[30.4%-64.6%]	12.9%	[4.1%-27.0%]
5 Year	25.4%	[11.1%-42.5%]	12.9%	[4.1%-27.0%]
Unresected Patients n=69				
Median (months)	17.0	[14.7-23.0]	10.1	[7.2-13.3]
1 Year	73.9%	[61.8%-82.7%]	40.6%	[29.0%-51.8%]
3 Year	11.6%	[5.4%-20.3%]	2.9%	[0.5%-9.0%]
5 Year	1.4%	[0.1%-6.9%]	1.4%	[0.1%-6.9%]

78

Hospice Utilization Among Patients Dying from Pancreatic Cancer A. Paredes,* J.M. Hyer, E.W. Beal, K. Merath, M. Dillhoff, A. Ejaz, J. Cloyd, A. Tsung, T. Pawlik. *Surgery, The Ohio State University Wexner Medical Center, Columbus, OH.*

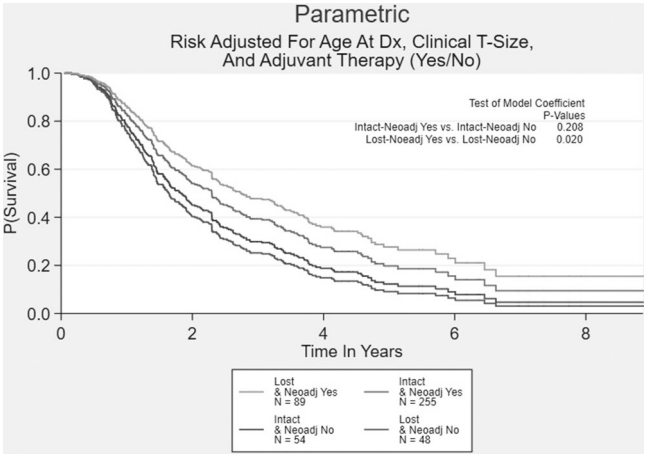
Background: Use of hospice services among patients with pancreatic cancer after pancreatic resection remains unknown. We sought to assess patterns of hospice utilization and impact of hospice use relative to patterns of life sustaining measures among patients with pancreatic cancer who previously underwent pancreatic surgery. Methods: The Medicare Standard Analytic Files identified patients diagnosed with pancreatic cancer who underwent pancreatic resection, survived index hospitalization and died within 2013-2015. Outcomes included overall hospice use at time of death, early hospice enrollment (>4 weeks prior to death) and late hospice enrollment (initiation within 3 days of death). Logistic regression analysis was used to determine factors associated with hospice use. Results: 2,582 patients with pancreatic cancer underwent resection

in 2013. By December 31, 2015, 550 patients had died (21.3%). Among patients who died, median age was 74 yrs (IQR 70-79), Charlson comorbidity index score was 8 (IQR 4-9), and most used hospice services prior to death (N= 353, 64.2%). Among patients who died, overall median time to death was 150.5d (IQR 79-235d); median time to death was 103d (IQR 39-200d) for non-hospice users vs. 176d (IQR 100- 247d) for hospice users (p<0.001). Patients who did not utilize hospice were more likely to receive total parenteral nutrition (17.8% vs. 9.3%) and be intubated prior to death (22.3% vs 2.8%) (both p<0.05). Overall, 16.6% (N=77) of patients initiated hospice services within 3 days of death, whereas 20.3% (N=97) initiated hospice services at least 4 weeks prior to death. Median (IQR) survival of late hospice users was 140d (57-217d) versus 214d (154-276d) for early hospice users (p < 0.001). Factors associated with hospice utilization included female sex (OR: 1.49, 1.04-2.13) and Charlson score ≥ 3 (OR: 1.65, 1.02-2.66). Conclusion: Despite attempts a curative-intent resection, many patients with pancreatic cancer succumb to their disease. Among patients who died, two-thirds of patients utilized hospice services after pancreatic resection. Identification of factors to inform conversations about hospice use may enhance end-of-life care.

79

SMAD4 Loss is a Predictor of Neoadjuvant Treatment Response in Pancreatic Ductal Adenocarcinoma R. Ramanathan,[1]* J. Hodges,[1] A. Al-Abbas,[1] C. Buchholz,[1] A. Singhi,[1] H. Zeh,[2] M.E. Hogg,[1] A.H. Zureikat.[1] *1. Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA; 2. UT Southwestern, Dallas, TX.*

Introduction SMAD4 is frequently mutated in pancreatic ductal adenocarcinoma (PDAC). Loss of SMAD4 has been associated with adverse outcomes. This study investigates the association of SMAD4 loss with response to neoadjuvant chemotherapy (NAC) and survival in PDAC. Methods In patients undergoing pancreatectomy for PDAC between 2008 and 2018, SMAD4 status was classified by immunohistochemistry in resected specimens as preserved, partial loss, or complete loss. For analysis, preserved and partial loss of SMAD4 were categorized as intact, and compared to complete loss. NAC regimens were categorized as 5FU-based and gemcitabine-based (Gem). Response to NAC was assessed by percent change in CA 19-9. Non-secretors of CA 19-9 were excluded. Results Of the 470 patients, 139 (29.6%) had loss of SMAD4. 331 had intact SMAD4, with 111 (23.6%) partial loss and 220 (46.8%) preserved SMAD4. 361 patients received NAC: 236 (65.4%) Gem-based regimens, 87 (24.1%) 5FU-based regimens, and 38 (10.5%) with both. Patients with SMAD4 loss had greater median pre-NAC CA19-9 (433.6 vs 295.6 U/mL, p=0.05). SMAD4 loss was also associated with larger mean reduction in CA 19-9 compared to intact (71.1% vs. 36.0%, p<0.01). 5FU-based NAC was associated with greater reduction in CA 19-9 than Gem (57.8% vs. 52.5%, p=0.01). Multivariable analysis adjusting for age, pre-NAC CA 19-9 and tumor size revealed that SMAD4 loss (p<0.01) and 5FU-based NAC (p=0.01) were independently associated with greater CA 19-9 reduction. Adjusting for age, tumor size and receipt of adjuvant therapy, NAC was associated with improved overall survival (OS) in SMAD4 loss (p=0.02), but not in the SMAD4 intact cohort (p=0.21) (Figure). Furthermore, 5FU-based NAC was associated with improved OS compared to Gem in SMAD4 loss (p=0.05), while no OS difference was observed between chemotherapies in the SMAD4 intact cohort. Conclusions Loss of SMAD4 is independently associated with greater CA 19-9 response to NAC, with 5FU based NAC providing the largest reductions in CA19-9. Furthermore, NAC in those with SMAD4 loss is associated with improved OS, with evidence that 5FU-based NAC provides greater survival benefit than Gem-based regimens.



80

Factors Associated with Disease Progression or Performance Status Decline in Patients Undergoing Neoadjuvant Chemotherapy for Localized Pancreatic Head Adenocarcinoma A. Paniccia,[1]* A.L. Gleisner,[2] M. Zenati,[1] A. Al-Abbas,[1] R. Schlabach,[1] K. Lee,[1] M.E. Hogg,[1] H. Zeh,[1] A.H. Zureikat.[1] *1. Surgery - Surgical Oncology, UPMC, Pittsburgh, PA; 2. University of Colorado, Aurora, CO.*

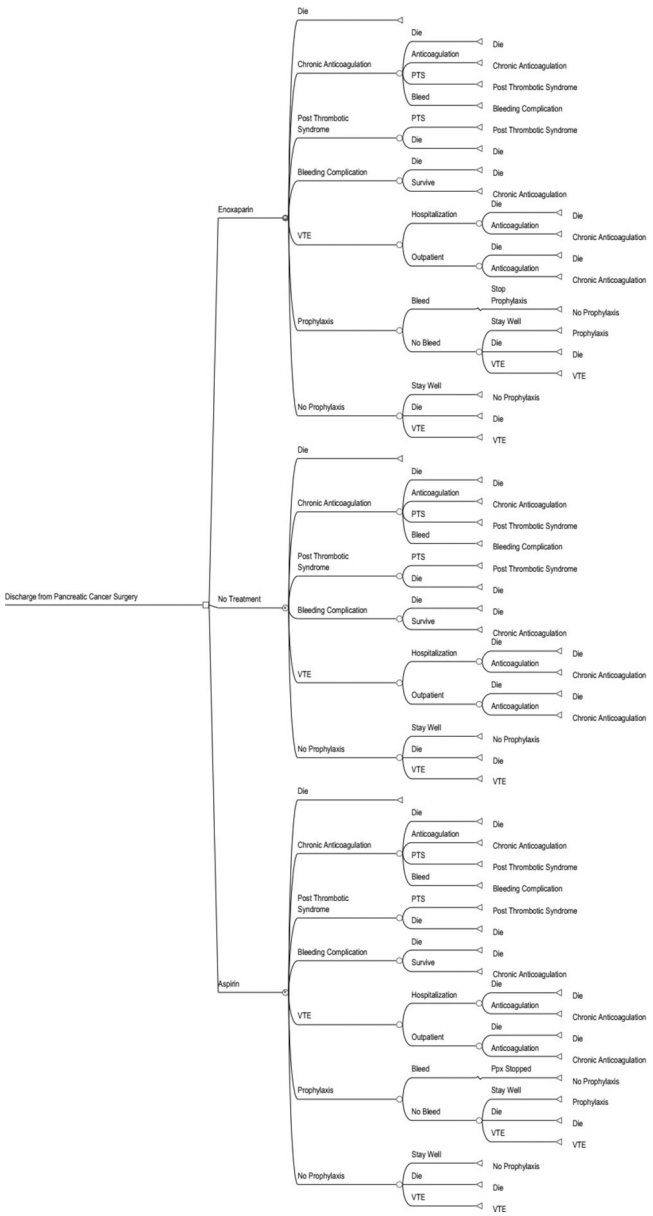
Introduction: Neoadjuvant chemotherapy (NT) is increasingly administered to patients with localized pancreatic head adenocarcinoma (PDAC). However, a significant portion of NT patients do not undergo resection either due to disease progression or performance status decline. We sought to identify predictors of disease progression or performance status decline during NT. Methods: All consecutive patients with localized PDAC who received NT at a tertiary referral center were identified. Univariate and Cox multivariate (MVA) analysis were performed to identify factors associated with disease progression (on imaging or at time of anticipated resection) or performance status decline preventing surgical resection. Results: Between 2005 and 2017, 479 patients diagnosed with PDAC underwent NT; 69.3% proceeded to surgery, 27.8% had disease progression, and 7.1% experienced performance status decline without disease progression on imaging. Median overall survival was 27.9 (95%CI 23.2-32.3), 12.8 (95%CI 11.2-14.1), and 6.9 (95%CI 4.9-11.2) months for the resected, disease progression and performance status decline groups, respectively (p<0.0001). On MVA, predictors of disease progression were EUS tumor size (OR 1.83, 95%CI 1.03–3.26), unplanned change in NT regimen (OR 3.05, 95%CI 1.19–7.80), hospital admission during NT (OR 2.75, 95%CI 1.54–4.92), CA19.9 response (OR 0.26, 95%CI 0.14–0.47) and biliary stent placement prior to NT initiation (OR 0.42, 95%CI 0.22–0.78). On MVA, predictors of performance status decline during NT were increasing age (OR 1.07, 95% CI 1.01 – 1.14), presence of diabetes (OR 4.58, 95% CI 1.53-13.73), EUS tumor size (OR 10.36, 95% CI 1.49 – 71.72), and hospital admission during NT treatment (OR 20.15, 95% CI 4.26 – 95.29). Conclusion: This analysis identifies several predictors of disease progression and performance status decline during NT for PDAC. These data provide further insight into which factors can be leveraged in order to successfully pursue various treatment strategies for localized PDAC.

81

Cost-effectiveness of Post-Discharge Thromboprophylaxis Following Resection for Pancreatic Cancer P.R. Varley,* K.J. Smith, A. Tsung. *University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Guidelines for post-discharge thromboprophylaxis exist based on data from randomized clinical trials indicating substantial reduction in VTE for patients receiving low molecular weight heparin (LMWH) for up to 28 days following discharge. Despite the evidence, there is poor adherence to these guidelines. We hypothesized that perceived cost of post-discharge thromboprophylaxis is a significant barrier, and we therefore sought to evaluate the cost-effectiveness of various treatment strategies for patients following pancreatic surgery. Methods: A Markov cost-effectiveness model was created comparing three potential post-discharge treatment strategies for patients

undergoing resection for pancreatic cancer: (1) enoxaparin 40mg once daily, (2) aspirin 81mg once daily, and (3) no treatment (Figure 1). Post-discharge VTE rate was directly estimated from the NSQIP PUF. Lifetables for patients undergoing resection for pancreatic cancer were generated from the National Cancer Database. Results: No treatment was eliminated through dominance in patients with stage I-III cancer. In the comparison of all three treatment strategies, aspirin was the most cost-effective therapy in patients of all stages. The ICERs for LMWH were $212,155, $414,851, and $462,463 for stage I-III patients, respectively. In an analysis limited to enoxaparin vs. no therapy, ICER for LMWH was $78,909/QALY, $143,611/QALY and $186,243/QALY for stage I, II and III patients. Thus at a willingness to pay threshold of $100,000/QALY, enoxaparin was the preferred strategy only in stage I patients. This indicates that the cost-effectiveness of enoxaparin is linked to expected stage-specific survival following resection of pancreatic adenocarcinoma. Conclusions: Post-discharge thromboprophylaxis is a cost-effective strategy in patients undergoing resection for pancreatic cancer, though selection of therapy depends on the projected survival following surgery. Though aspirin is not recognized in current guidelines as an option for thromboprophylaxis, it represents a promising, pragmatic option for those patients who do not receive enoxaparin.



82

Toll-like Receptor IV Signaling Inhibits Pancreatic Cancer Progression by Innate and Adaptive Immune Response

A. Ferrantella,* S. Kurtom, B. Giri, M. Tarique, P. Sharma, V. Sethi, P. Roy, H.K. Jacob, S. Lavania, A. Saluja, V. Dudeja. *Surgery, University of Miami, Miami, FL.*

Background: Despite studies suggesting that an immune response can be generated against pancreatic cancer, current immunotherapeutic strategies have not been effective. In this study, we evaluated toll-like receptor 4 (TLR4) activation as a strategy to provoke an anti-tumor response against pancreatic cancer. Methods: KPC pancreatic cancer cells were injected into the pancreata of wild-type C57BL/6 (WT) mice, and the tumors were surgically resected after 25 days. Following resection, the mice were randomized to receive lipopolysaccharide (LPS, 5mg/kg) or vehicle i.p. twice weekly, and the mice were followed for cancer recurrence. In a separate experiment, KPC cancer cells were injected into the spleens of WT and Rag1-knockout mice, and the mice were subsequently randomized to receive LPS or vehicle twice weekly. Liver metastases were measured at the endpoint, and immunophenotyping was performed by flow cytometry. Finally, subcutaneous tumors were induced in WT mice using MC38 colon cancer or Braf-Pten melanoma cell lines. After 15 days, the mice were randomized to receive either LPS or vehicle twice weekly, and tumor volumes were serially measured. Results: Activation of TLR4 significantly reduced cancer recurrence following tumor resection, and the median survival was more than double. Liver metastases were drastically suppressed by administration of LPS in WT mice, but there was no effect in Rag1-knockout mice, which lack mature T and B cells. In addition to promoting the classically activated (M1) macrophage phenotype, we observed a significant reduction in the pro-tumorigenic myeloid-derived suppressor cell (MDSC) populations, which are known to suppress T cell activity. TLR4 activation similarly decreased the growth of colon cancer and melanoma, suggesting that this strategy can be effective in other cancers. Conclusion: Our findings demonstrate that TLR4 ligation modulates the innate and adaptive immune systems to suppress the progression of pancreatic cancer. Elucidating the mechanism of this anti-tumor response could lead to identification of novel therapeutic targets, either alone or in combination with contemporary immunotherapeutic strategies.

83

Pancreatic Cancer Micrometastases Contribute to Niche Evolution Through Secretion of Loxl-2 R.I. Ayabe,[1]* M.M. Wach,[1] S.M. Ruff,[1] A. Ahn,[1] E. van Beek,[2] S. Sinha,[1] J.L. Davis,[1] J.M. Hernandez.[1] *1. Surgical Oncology Program, NIH, Bethesda, MD; 2. Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Although recent work has centered on premetastatic niche establishment through exosomes released by the primary tumor, the role of extravasated tumor cells in niche evolution remains understudied. We therefore sought to evaluate the impact of micrometastatic pancreatic cancer cells on the target organ matrix. Methods: We designed and implemented a novel negative selection screen to isolate dormant variants of KPC cells (from Pdx-Cre, $KRas^{G12DLSL}$, $Tp53^{R172HLSL}$ mice) that lack the ability to form liver metastases following splenic injection. We then compared the transcriptomes and secretomes of dormant and fully metastatic cells. Sphere-forming assays were undertaken with and without the addition of extra-cellular matrix proteins. In vivo inhibitor experiments were conducted in nude mice following splenic injection of tumor cells. Statistical analyses were completed using GraphPad Prism. Results: Comparison of the transcriptomes and secretomes of dormant and metastatic cells revealed that metastatic cells significantly upregulate the production and secretion of the collagen crosslinking enzyme, Loxl-2 ($p<0.001$). Analysis of an isolated "escape" dormant clone (revertant phenotype), which acquired the ability to form liver metastasis revealed secretion of Loxl-2 at levels similar to metastatic cells. In evaluating micrometastases by immunofluorescence, nascent tumor cells activate local collagen-producing cells before invading hepatic parenchyma. Accordingly, metastatic cells, but not dormant cells, were able to form tumor spheres in the presence of collagen, but no other ECM proteins. Treatment of metastatic cells with AB0023, an inhibitor of Loxl-2, resulted in reduced sphere formation ($p = 0.001$). Mice treated with AB0023 after splenic injection of tumor cells experienced significantly longer survival compared those treated with a control antibody (undefined vs 24 days, $p = 0.04$). Conclusion: Micrometastatic cells contribute to niche formation through stromal activation and collagen crosslinking. Interruption of matrix remodeling through enzymatic inhibition may be a reasonable strategy for adjuvant therapy after resection of pancreatic cancer.

84

Neutralization of Stromal Dickkopf-3 (DKK3) Inhibits Tumor Progression and Prolongs Survival in Pancreatic Adenocarcinoma

R. Hwang,[9]* L. Zhou,[6] H. Husted,[6] T. Moore,[6] M. Lu,[3] D. Deng,[4] Y. Liu,[8] V. Ramachandran,[5] T. Arumugam,[5] C. Niehrs,[2] H. Wang,[8] P. Chiao,[7] J. Ling,[7] M. Curran,[1] A. Maitra,[8] M. Hung,[7] J.E. Lee,[6] C. Logsdon.[5] *1. University of Texas M.D. Anderson Cancer Center, Immunology, Houston, TX; 2. DKFZ German Cancer Research Center, Heidelberg, Germany; 3. Medabome Inc., Fremont, CA; 4. Baylor College of Medicine, Houston, TX; 5. University of Texas M.D. Anderson Cancer Center, Cancer Biology, Houston, TX; 6. University of Texas M.D. Anderson Cancer Center, Surgical Oncology, Houston, TX; 7. University of Texas M.D. Anderson Cancer Center, Molecular & Cellular Oncology, Houston, TX; 8. University of Texas M.D. Anderson Cancer Center, Pathology, Houston, TX; 9. University of Texas M.D. Anderson Cancer Center, Surgical Oncology and Breast Surgical Oncology, Houston, TX.*

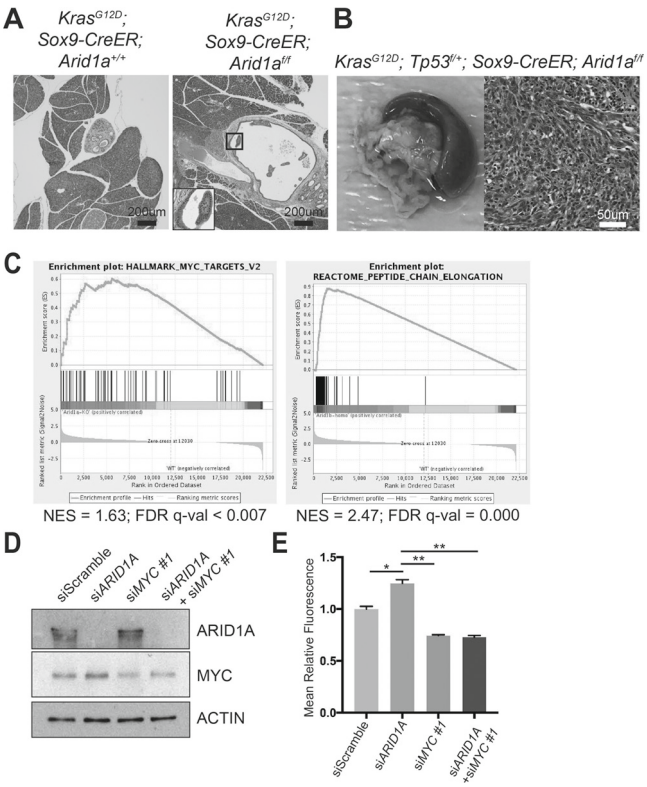
Pancreatic ductal adenocarcinoma (PDAC) has a dismal prognosis, and whether its abundant stromal infiltrate contributes to its aggressiveness is unclear. We have shown that Dickkopf-3 (DKK3) is produced by pancreatic stellate cells and is present in 58% of human PDAC samples on tissue microarray at 4.5-fold levels compared to normal pancreas by expression profiling. DKK3 stimulates PDAC growth ($p<0.0001$), invasion ($p<0.0001$), and resistance to chemotherapy ($p<0.001$) with both paracrine and autocrine mechanisms through NF-kB activation. In this study, genetic ablation of DKK3 by shRNA in a syngeneic orthotopic model resulted in 3.8-fold reduction in tumor growth ($p<0.05$). Neutralization of DKK3 in an autochthonous model of PDAC (P48-Cre; Kras $^{LSL\text{-}G12D}$;Trp53$^{fl/fl}$; Dkk3$^{-/-}$) also inhibited tumor growth and more than doubled survival compared to wild type C57/BL6 mice (68 days vs. 63 days; p=0.0002). Mice with at least partial depletion of DKK3 had 80% reduction in risk of death (HR 0.21, 95%CI 0.09-0.47; p = 0.0002). Compared to pancreatic tumors from wild-type mice at the same age, tumors from DKK3-null mice contained more pre-invasive PanIN lesions, fewer invasive carcinomas and lower levels of Ki-67 ($p<0.001$), collagen 1 ($p<0.05$) and α-SMA indicating a reduction in proliferating cells and activated stroma. Treatment with a novel DKK3 blocking monoclonal antibody (mAb) inhibited PDAC progression and prolonged survival by 43% compared to isotype control mAb (p=0.005, HR 0.24, 95%CI 0.01-0.30). Neutralization of DKK3 induced a peritumoral infiltration of CD3+ and CD8+ T cells (2.4 and 4-fold vs. C57/BL6) with increase in the T-cell markers granzyme B and IL-2 (p=0.005 and p=0.01). Genetic ablation of DKK3 improved response to immune checkpoint inhibition with αCTLA4 with reduction in tumor growth and a significant improvement in survival (p=0.0003; HR 0.20, 95%CI 0.004-0.13), whereas treatment with αCTLA4 had no effect compared to PBS. Taken together, these results suggest that DKK3 neutralization may be effective as a single targeted agent or in combination with immunotherapy for PDAC.

85

Pancreatic Ductal ARID1A Loss Induces Intraductal Papillary Mucinous Neoplasm Formation and Aberrant MYC Mediated Protein Translation

I. Nassour,[1]* S. Xiao,[1] S. Zhang,[1] X. Sun,[1] L. Nguyen,[1] J. Chuang,[1] L. Peng,[1] J. Shen,[2] H. Zhu,[1] S. Wang.[1] *1. Surgery, University of Texas Southwestern, Dallas, TX; 2. Stanford University, Stanford, CA.*

Introduction: Intraductal papillary mucinous neoplasms (IPMN) arise from pancreatic duct cells and can transform to pancreatic ductal adenocarcinoma (PDAC). ARID1A mutations are common in IPMN and PDAC but the effects of these alterations are not well characterized. We aimed to delineate the role of ARID1A in IPMN formation. Methods: We generated transgenic mice with mutations in pancreatic duct cells using the Sox9-CreER system. KrasG12D; Sox9-CreER; Arid1af/f mice and KrasG12D; Tp53f/+; Sox9-CreER; Arid1af/f mice were given tamoxifen (TAM) at 4 weeks of age to induce the mutations. Transgenic mice that were wild-type for Arid1a were used as controls. We used siRNA to knock down ARID1A and MYC in immortalized human pancreatic ductal epithelial (HPDE) cells. Protein synthesis was quantified based on incorporation of the fluorescently-labeled puromycin analog O-propargyl-puromycin. Fluorescence was measured by flow cytometry. Results: 52 weeks after TAM, KrasG12D; Sox9-CreER; Arid1af/f mice had mucinous cystic lesions that resembled early IPMN (Fig A). By incorporating Tp53 loss, we found KrasG12D; Tp53f/+; Sox9-CreER; Arid1af/f mice developed cystic lesions and large pancreatic tail PDAC (Fig B). RNA-sequencing of Arid1a-null murine pancreata showed that gene networks associated with MYC activity and protein translation were highly expressed (Fig C). ARID1A knockdown in HPDE cells led to increased MYC expression and protein synthesis. To test if MYC was responsible for the increase in translation due to ARID1A loss, we performed concurrent knockdown of ARID1A and MYC and found that returning MYC to baseline levels in the setting of ARID1A loss led to a reduction of protein synthesis comparable to the levels seen in cells with MYC knockdown alone (Fig E). This suggests that MYC, in part, mediates the control of protein translation by ARID1A. Conclusions: ARID1A loss in pancreatic ductal cells lead to the formation of cysts reminiscent to human IPMN. Mechanistically, ARID1A loss led to increased MYC expression and elevated protein synthesis. Protein synthesis may be a therapeutic target for restraining IPMN growth and transformation.



(A) 52 weeks after tamoxifen induction, Kras^{G12D}; Sox9-CreER; Arid1a$^{f/f}$ mice formed large cystic lesions.
(B) Kras^{G12D}; Trp53$^{f/+}$; Sox9-CreER; Arid1a$^{f/f}$; ROSA26-LSL-tdTomato mice formed pancreatic ductal adenocarcinoma. The tumor was grossly red due to Tomato expression, confirming ductal origin.
(C) Gene set enrichment analysis of RNA-seq of Arid1a-null pancreata showed that MYC target and protein synthesis gene signatures were highly overexpressed. NES = normalized enrichment score; FDR = false discovery rate.
(D) Western blot demonstrating partial knockdown of MYC with siMYC in the setting of ARID1A knockdown in human pancreatic ductal epithelial (HPDE) cells.
(E) HPDE cells were treated with O-propargyl-puromycin and treated with siScramble (n = 8), siARID1A (n = 3), siMYC (n = 7), and siARID1A and siMYC (n = 3). Quantification of relative fluorescence is shown. *P < 0.05, **P < 0.01.

86

Model of Patient-Specific Mixed Melanoma/Lymph Node Organoid for Predicting Immunotherapy Response: Feasibility Study
K.I. Votanopoulos,[1]* H. Sivakjumar,[2] S. Forsythe,[2] A. Mazzocchi,[2] J. Aleman,[2] L. Miller,[1] E. Levine,[1] P. Triozzi,[1] A. Skardal.[2] *1. General Surgery- Surgical Oncology, Wake Forest University, Winston-Salem, NC; 2. Wake Forest Institute for Regenerative Medicine, Winston Salem, NC.*

Introduction:We have hypothesized that engineering a combined lymph node/melanoma organoid from the same patient, will create a mixed tumor/node organoid, allowing for individual patient tumor, stroma and immune system to remain viable for personalized immunotherapy screening. Methods:Surgically obtained matched melanoma and lymph node biospecimens from the same patient, were transferred to the laboratory, washed with saline, antibiotic, and red blood cell lysis buffer. Biospecimens were dissociated, and incorporated into an ECM-based hydrogel system and biofabricated into 3D patient-specific mixed melanoma/node organoids. Cells were not sorted for tumor, as to preserve tumor heterogeneity, including stroma and immune cell components. Organoid sets, were screened in parallel with nivolumab, pembrolizumab, ipilimumab, and dafrafenib/trametinib for 72 hours. Quantification of live/dead staining and metabolism assays, recorded relative drug efficacy in killing melanoma cells for a particular patient. Light microscopy, immunohistochemistry and next generation sequencing (NGS) were used to compare tumor melanoma cells with organoid melanoma cells. Results:Biospecimens from 5 stage III and IV melanoma patients were applied for mixed organoid development between September 2017 and June 2018. Successful establishment rate of viable organoid sets was 80%(4/5). Average time from organoid development to initiation of immunotherapy testing was 7 days. Organoid response to immunotherapy was similar to patient clinical response in 75%(3/4) patients. The fourth patient's organoids exhibited a 50% melanoma killing by nivolumab while the patient clinically progressed on the drug. Response to trametinib for a BRAF wild patient with melanoma harboring a MEK pathway was suggested by organoid testing prior to NGS and verified by clinical response upon treatment. Conclusion:Development of 3D mixed immune-enhanced tumor/node organoids is a feasible platform, allowing individual patient immune system and tumor cells to remain viable for studying of personalized immunotherapy and targeted therapy response.

87

Overexpression of CX3CL1 and Its Receptor, CX3CR1 Associates with Increased Infiltration of CD8 T-Cells and Dendritic Cells, and Better Prognosis in Melanoma
H. Takahashi,[1]* W. He,[1] L. Spokauskaite,[2] K.H. Eng,[1] A. Witkiewicz,[2] F. Ito.[1] *1. Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY; 2. Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Introduction: Accumulating evidence has shown that an inflammatory microenvironment plays a major role in cancer development. CX3CL1 (fractalkine) is a transmembrane, mucin/chemokine hybrid molecule expressed on the surface of inflamed endothelial cells, while its receptor CX3CR1, is expressed on immune cells such as natural killer (NK) cells, monocytes, and T cells. The recruitment of immune cells from circulation into the tumor microenvironment (TME) has emerged as a pivotal factor in cancer progression as well as a predictive factor of response to immunotherapy; however, there are some conflicting data as to expression of the CX3CL1-CX3CR1 axis in tumors and prognosis. In the present study, we aimed to study association between expression of CX3CL1-CX3CR1and prognosis as well as other genomic expression in patients with skin cutaneous melanoma, utilizing publicly available large data set The Cancer Genome Atlas (TCGA). Method: Genomic and clinical data of patients with melanoma were obtained from TCGA. The cohort was classified into to two groups based on the CX3CL1-CX3CR1 expression. Kaplan-Meier survival curve for overall survival (OS) was then plotted. Furthermore, correlation between CX3CL1-CX3CR1 and other immune cell associated genes were investigated. Results: There were 479 patients in skin cutaneous melanoma cohorts in TCGA. OS was significantly better in high expression of CX3CL1 and CX3CR1 in tumors (p= 0.0066 and 0.0031, respectively). Additionally, expression of CX3CL1 and CX3CR1 in melanoma was significantly correlated with genes associated with adaptive immune cells including cytotoxic CD8 T cells (CD8a, TBX21, and EOMES), plasmacytoid dendritic cells (DCs) (CLEC4C), and myeloid cDC1 (CLEC9A and XCR1). Furthermore, higher expression of CX3CR1 correlates with increased expression of co-inhibitory receptors, PD-1 (PDCD1), TIM3 (HAVCR2), TIGIT, and LAG3. Conclusion: Higher expression of the CX3CL1- CX3CR1 axis in melanoma correlates with increased T cell and DC infiltration and improved prognosis. CX3CL1-CX3CR1 might serve as an indicative of a T cell and DC-inflamed TME.

88

Predictive Gene Signatures in Metastatic Melanoma: Management Implications for the Surgeon
R. Essner,[1]* K. Gong,[2] D. Kaufman,[3] N. Deng,[3] J. Hong.[3] *1. Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA; 2. UCLA Medical Center, Los Angeles, CA; 3. Cedars-Sinai Medical Center, Los Angeles, CA.*

BACKGROUND: The development of immune checkpoint inhibitors and signal pathway targeted agents have revolutionized the treatment of metastatic melanoma. Surgical resection is reserved for patients with limited disease or for palliation of symptoms. Yet the current methods of selecting patients for resection are primarily based on clinical judgment. We evaluated the utility of a molecular gene microarray to predict patient outcome from resected tissue specimens. METHODS: We performed a retrospective review of patients with melanoma undergoing surgical resection for potential curative intent and prospectively collected tissue specimens of primary or metastatic melanoma. Extracted RNA was used to generate cDNA for microarray analyses. Genes were tested based on survival outcome and similarities in gene function. Patients were followed for melanoma-specific death. RESULTS: Ninety patients underwent surgical resection: 40 with primary tumors (PT), 15 with lymph node (LT) and 35 with distant metastases (MT). Most patients were men (60%); median age was 57 years. Primary tumors (PT) were mostly on the extremities (45%) and trunk (25%) whereas the metastases (MT) were mostly subcutaneous (28.6%), small bowel (14.3%), or lung (14.3%). From the 17,000 genes evaluated, we identified thirteen unique genes: TM7SF2, CYP27B1, CYP51A1, SC5DL, that are related to steroid biosynthesis and PPP2R1A, WNT4, CCND1, CSNK2A1, APC2, PPP3CB, PPP3CC, PRKACA, TCF7L2 that related to the Wnt signal transduction pathway that had significantly ($p=0.035$) different expression in metastatic vs. primary melanoma. When the 13-gene profile was examined together, the 5-year survival of patients with resected metastases was 90+/-3% vs 50+/-7% ($p<0.0001$) for patients lacking the profile. Age, gender or metastatic site were not predictive of survival. CONCLUSION: We identified a 13-gene molecular profile from resected melanoma specimens that predicts outcome after surgery. The genes selected were based on common function and prediction of patient outcome. This gene profiling may be important step in understanding which patients should be selected for surgical resection of advanced disease.

89

Chromosome 1q21.3 Copy Number Gain is Associated with Increased Epidermal Differentiation Complex Gene Expression in Melanoma
K.M. Leick,* J.M. Obeid, S. Bekiranov, C.L. Slingluff. *Surgery, University of Virginia, Charlottesville, VA.*

Introduction: We have identified a set of 20 genes encoding proteins that mediate mechanical barrier function through cell adhesions. Overexpression of these barrier molecule genes (BMGs) is associated with decreased immune signatures in tumor and worse overall survival. These BMGs are concordantly expressed with epidermal differentiation complex (EDC) genes, which are important for terminal differentiation of keratinocytes. All 34 EDC genes and 4/20 BMGs are located at chromosome 1q21.3, a susceptibility locus in melanoma. We hypothesized that copy number gain at 1q21.3 contributes to upregulation of BMG/EDC genes in patients with metastatic melanoma. Methods: Copy number data and RNA-seq data from 354 patients with metastatic melanoma were available from the Cancer Genome Atlas. Our gene set included BMG/EDC genes at chromosomal locus 1q21.3. Patient copy number data were visualized using clustered copy number profiles. Associations of 1q21.3 amplification with overall patient survival were assessed using Kaplan Meier curves and log-rank tests. Boxplots and Wilcoxon rank sum test were used to assess associations of 1q21.3 copy number gain with mRNA levels. Results: In 354 patients with metastatic melanoma, 54% (191 patients) had copy number gains encompassing 1q21.3, while 4% (14 patients) had deletions and 42% (149 patients) were diploid (Fig. 1a). Of the patients with 1q21.3 copy number gains, 93.7% (179 patients) were triploid and the remaining 6.3%

(12 patients) were tetraploid. Significantly shorter survival occurred in cases with four copies of 1q21.3 compared to diploid cases (Fig. 1b, P=0.0198). There was no significant survival difference between triploid and diploid cases. Additionally, 1q21.3 locus amplification was associated with higher mRNA levels for BMG/EDC genes in 61% of patients (Fig. 2c, P=0.0469). Conclusions: Our data suggests chromosome 1q21.3 copy number gain is a source of increased BMG/EDC expression and is a poor prognostic factor in melanoma. Identification of regulatory targets may provide opportunities to enhance immunogenicity within the tumor microenvironment through modulation of BMG/EDC gene expression.

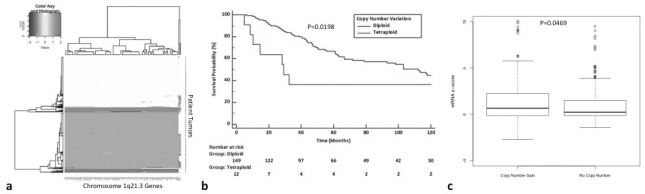
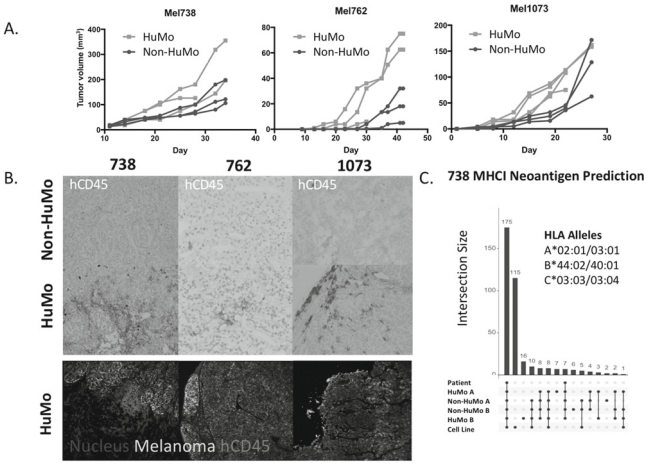


Fig. 1

90

Development of a Fully Autologous Humanized Mouse Model of Melanoma B.A. Krasnick,[1]* M. Chiorazzi,[3] Y. Bi,[1] Z. Skidmore,[1] J. Martinek,[2] P. Ronning,[1] F. Marches,[2] O. Griffith,[1] M. Griffith,[1] P. Goedegebuure,[1] K. Palucka,[2] R. Flavell,[3] R. Fields.[1] *1. Surgery, Washington University in St. Louis, St. Louis, MO; 2. The Jackson Laboratory for Genomic Medicine, Farmington, CT; 3. Yale University, New Haven, CT.*

Introduction: Syngeneic mouse models of cancer have proven to be invaluable in cancer research, but have inherent limitations secondary to their inability to study human tumors. Patient derived xenografts have utilized human tumors implanted into immunodeficient mice. This lack of an immune system enables engraftment, but creates a model with limited translational value. Utilizing the MISTRG6 mouse system, with knocked in human genes for M-CSF, IL-3, SIRPα, thrombopoietin, GMCSF, and IL6, we have created a humanized, fully autologous, mouse model of melanoma to study melanoma immunobiology. Methods: We collect tumor, bone marrow (BM), and peripheral blood from consenting patients undergoing resection of stage IIIC+ melanoma. The BM $CD34^+$ stem cells are isolated and injected into MISTRG6 mice. At 8 weeks, flow cytometry is performed to characterize the $\%CD45^+$ human hematopoietic cells ($hCD45^+$). Mice with ≥5% $hCD45^+$ cells are considered humanized (HuMo) and are subsequently engrafted with autologous mel. Immunohistochemistry (IHC) and immunofluorescence (IF) are used to characterize the melanoma tumor. Exome and RNA sequencing are performed for genomic, transcriptomic, and neoantigen (neoAg) profiling. Results: Melanoma growth of three consecutive human melanoma samples in HuMo mice was accelerated as compared to matched tumors grown in non-humanized (non-HuMo) mice (Figure 1A). We observed hCD45 staining (IHC and IF) in tumors from HuMo, with no staining in non-HuMo tumors ($p<0.0001$, Figure 1B). Exome sequencing revealed a strong correlation of somatic mutations between parental, humanized, and non-humanized tumors (≥75% shared for all samples). Neoag prediction is also preserved between samples (Figure 1C). Conclusion: A HuMo fully autologous mouse model allows for evaluation of cancer immunotherapeutics in human melanoma, as well as therapeutics relying on the targeting of neoAgs. In addition, melanoma growth acceleration appears to occur as a $hCD45^+$ infiltrate dependent phenomenon, with the precise mechanism currently under investigation. This model has the potential to develop a precision-medicine approach to the treatment of patients with solid tumors in the era of immunotherapy.



A, Melanoma (Mel) tumor growth in humanized (HuMo, pink) appears accelerated as compared to non Humanized (Non-HuMo, blue) mice (Patient IDs 738, 762, 1073). B, Representative human CD45 (hCD45) IHC for Non-HuMo(top) and HuMo(middle) tumors, as well as IF images for HuMomice with nuclear stain (blue), melanoma stain (green, gp100/Mart-1/tyrosinase), and hCD45 stains (red). C, MHCI neoantigenprediction and overlap for melanoma 738 samples (patient tumor, all xenografts, and cell line).

91

Age-Related Changes in Tumoral Angiogenesis Drive Melanoma Metastasis and Response to Targeted Therapy B. Ecker,[1]* A. Kaur,[1] M. Middleton,[2] G. Karakousis,[1] A. Weeraratna.[3] *1. Surgery, University of Pennsylvania, Philadelphia, PA; 2. University of Oxford Department of Oncology, Oxford, United Kingdom; 3. Wistar Institute, Philadelphia, PA.*

Background: Older patients with melanoma are at increased risk for the development of incurable visceral metastases, although a mechanistic basis for age-related changes in tumor dissemination that underlie such inferior clinical outcomes is not fully known. Methods: Disease-free survival of AVAST-M trial patients receiving bevacizumab or observation for non-metastatic melanoma was analyzed with respect to patient age by Kaplan-Meier methodologies. Angiogenic markers of human melanoma samples were analyzed by immunohistochemistry and by query of mRNA expression in the TCGA. In vitro, human microvascular endothelial cells were treated with conditioned media from human dermal fibroblasts from young (<40) and aged (>55) healthy donors from the Baltimore Longitudinal Study of Aging and proliferation and angiogenesis measured. In vivo, yumm1.7 xenografts were established in young (8 weeks) and aged (52 weeks) C57/BL6 mice (#556, Charles River), including young mice treated with rsFRP2 and aged mice treated with anti-sFRP2 antibody. Tumor angiogenesis and visceral metastatic burden was quantified by immunohistochemistry. Findings: Increasing age was associated with reduced expression of VEGF and its receptors (VEGFR1, VEGFR2) in human melanoma samples, which corresponded with decreased efficacy of bevacizumab therapy in the AVAST-M clinical trial. In contrast, the proangiogenic protein sFRP2 was increasingly expressed by dermal fibroblasts in aged human skin, where aged fibroblast conditioned media was sufficient to stimulate microvascular endothelial cell angiogenesis in vitro and could be neutralized with α-sFRP2. In a murine model of cutaneous melanoma, the addition of rsFRP2 to young tumor-bearing mice was sufficient to increase tumor angiogenesis and rates of visceral metastasis to that observed in aged mice, while the treatment of aged mice with α-sFRP2 antibody decreased both tumor angiogenesis and rates of visceral metastasis. Interpretation: Patient age is an important angiogenic determinant of the local peritumoral environment, which may have important therapeutic implications for utilization of anti-angiogenesis approaches in melanoma.

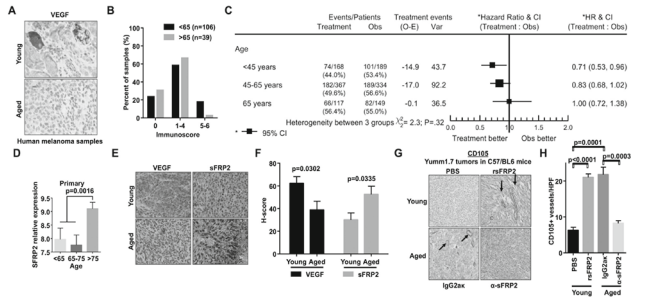


Figure 1. A. Representative VEGF immunohistochemistry of primary human melanoma samples from AVAST-M study patients (magnification 400x); B. Quantification in VEGF expression (n=145), stratified by age (>65 years: 3% vs. <65 years: 18%, p=0.0174); C. Age-stratified analysis of disease-free survival in melanoma patients randomized to bevacizumab therapy or observation (n=1,324; age <45 years: HR 0.71, 95% CI 0.53-0.96; age >65 years: HR 1.00, 95% CI 0.72-1.38); D. Age-stratified TCGA analysis of sFRP2 mRNA expression of cutaneous primary melanoma (n=104); E. Representative VEGF and sFRP2 immunohistochemistry of Yumm 1.7 melanoma tumors five weeks following intradermal injection in young (8 weeks) and aged (52 weeks) C57/BL6 mice (n=10/arm; magnification 400x); F. Quantification in VEGF and sFRP2 expression in serial tumor sections; G. Representative CD105 immunohistochemistry of primary Yumm 1.7mcherry murine tumors in young C57BL/6 mice treated with PBS or rSFRP2, and aged mice treated with α-SFRP2 antibody or IgG2aκ control; H. Quantification of CD105-positive vessel density.

92

False Positive Results and Incidental Findings with Annual CT or PET/CT Surveillance in Asymptomatic Patients with Resected Stage III Melanoma A. Nijhuis,[1]* M. Dieng,[2] S. Lord,[2] J. Dalton,[1] A. Menzies,[1] R. Turner,[2] J. Allen,[1] R. Saw,[1] O. Nieweg,[1] J. Thompson,[1] R. Morton.[2] *1. Melanoma Institute Australia, Utrecht, Netherlands; 2. University of Sydney, Sydney, NSW, Australia.*

Purpose: The use of surveillance imaging in melanoma follow-up is increasing. This study aimed to quantify false-positive and incidental findings from annual surveillance imaging in resected, asymptomatic, stage III patients. Methods: Approval from the local research ethics committee was obtained. This cohort study included patients treated at our institute (2000-2015) with baseline CT or PET/CT imaging and at least two annual surveillance scans. False-positives were defined as findings suspicious for melanoma recurrence that were not melanoma, confirmed by histopathology, subsequent imaging or clinical follow-up. Incidental findings were defined as non-melanoma-related findings requiring further action. The outcomes of incidental findings were classified into three categories: 'benign', if they resolved spontaneously or were not seriously harmful; 'malignant' if a second malignancy was found; or 'other' if they were otherwise potentially harmful. Results: Among 154 patients, 1022 scans were performed (154 baseline staging, 868 surveillance) during a median follow-up of 85 months (IQR 64-115). On surveillance imaging, 77 false-positive results and incidental findings were identified in 61 of 154 patients (40%) (Figure 1). An additional 181 investigations, procedures and referrals were performed to investigate these findings. The findings proved to be benign in 64 of 77 (88%). Ten patients with a benign finding (6% of the cohort) underwent an unnecessary invasive procedure. Conclusion: False-positive results and incidental findings are reported in almost half of all asymptomatic stage III melanoma patients undergoing annual surveillance imaging and the additional healthcare use is substantial. The risk of these findings persists over time. Clinicians need to be aware of the potential for false-positive and incidental findings resulting from surveillance imaging and discuss these risks with their patients.

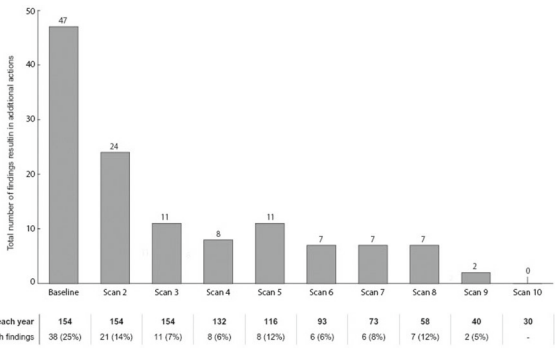


Figure 1 - findings resulting in additional actions in surveillance scans

93

Treatment Matters: Examining the Relationship Between Treatment Adequacy and Survival in Melanoma N.J. Look Hong,[1]* S. Cheng,[2] N. Baxter,[3] F. Wright.[1] *1. Surgical Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 2. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada; 3. St. Michael's Hospital, Toronto, ON, Canada.*

Background: Variability in melanoma management has prompted concerns about equitable and timely treatment. We investigated patterns of melanoma survival associated with treatment adequacy using population-level data within a universal health care system. Methods: Patients with invasive cutaneous melanoma were identified retrospectively from the Ontario Cancer Registry (2007–2015) and deterministically linked with administrative databases to identify patient/disease characteristics, geographic origin, stage at diagnosis, and multimodal treatment patterns within a year of diagnosis. Melanoma treatment was categorized as inadequate or adequate based on multidisciplinary clinical algorithms. Inadequately treated patients were then propensity-score matched with an adequately treated control cohort. Patients were followed until December 2016 to determine overall survival. Uni and multivariable logistic regression was used to model key factors associated with survival. Results: 12,768 patients were diagnosed with cutaneous melanoma from 2007 – 2015 and 704 were inadequately treated. 540 patients were propensity-matched with both groups well-balanced for patient/disease factors. Mean age was 66.4 years and 59.8% were male. The majority of patients (63.3%) were stage I at diagnosis. After median follow-up of 4 years, the inadequately treated cohort had a worse death rate compared with matched adequately treated controls (35.4% vs. 29.1%, p=0.03), with median time to death of 2 years in both groups. Primary cause of death was melanoma in both groups. In multivariable analysis, inadequate treatment (HR 1.67, 95% CI 1.31, 2.13), increasing stage (stage IV; HR 17.72, 95% CI 11.73, 26.79), and cancer centre visit with stage III (HR 3.60, 95% CI 1.49, 8.70) and IV (HR 1.72, 95% CI 1.07, 2.77) disease were associated with worse survival. Visit to a dermatologist within 1 year after diagnosis was associated with improved survival (HR 0.41, 95% CI 0.26, 0.65). Conclusions: Achieving adequate treatment within a year after diagnosis is critical for survival. Systematic efforts should be made to ensure timely access to comprehensive melanoma care, particularly access to a dermatologist.

94

Intratumoral Injection of Anti-PD-1 Generates Peripheral Memory CD4+/CD8+ Lymphocytes R.J. Hendrix,* J. Chuprin, N. Condron, M. Brehm, G. Whalen. *University of Massachusetts Medical School, Worcester, MA.*

Background: Immune checkpoints function to limit peripheral T lymphocyte activity and prevent autoimmunity. Tumors however, are able to exploit these physiologic adaptations to evade detection and facilitate growth. Blockade of programmed cell death protein 1 (PD-1) with targeted systemic immunotherapy has emerged as an effective mechanism for activation of anti-tumor immunity and may contribute to immunologic memory. We aim to evaluate if intratumoral (IT) injection could produce this same effect. Methods: NOD-scid IL2rg^{null}(NSG) mice engrafted with human hematopoietic stem cells (HSCs) had patient derived xenograft (PDX) melanoma tumors implanted subcutaneously. Mice received a single injection of IT anti-PD-1 at 10mg/kg (n=5) or IT PBS solution (n=5). Mice were sacrificed on post-injection day six, and their spleens harvested. Characterization of specific T lymphocyte populations was achieved using flow cytometry to identify surface markers. Analysis was performed using FlowJo software (version 10.0, FlowJo LLC). Results: IT injection of anti-PD-1 significantly reduced expression of PD-1 in CD4+ (0.09% v 19.3%) and CD8+ (1.4% v 17.6%) lymphocytes. There was also increased expression of human leukocyte antigen (HLA) DR (CD4+: 67.8% v 44.4% ; CD8+: 52.1% v 37.4%). Analyzing the subpopulations of CD4+/CD8+ lymphocytes, IT injection of anti-PD-1 resulted in a proportionally distinct group of effector memory (CD4+: 87.8% v 74.1% ; CD8+: 14.0% v 13.6%) and central memory (CD4+: 10.6% v 21.9% ; CD8+: 71.9% v 57.6%) T cell lineages (Table 1). The proportion of naïve undifferentiated lymphocytes was reduced after IT injection of anti-PD-1 (CD4+: 1.2% v 3.3% ; CD8+: 12.5% v 27.4%). Conclusion: Effector memory, central memory and naïve CD4+/CD8+ lymphocyte subpopulations are significantly altered following a single intratumoral injection of anti-PD-1. The increased prevalence of memory CD4+/CD8+ lymphocytes could facilitate defense against micrometastatic disease that remains following surgical resection of an injected primary tumor.

Table 1. CD4+/CD8+ Lymphocyte Subpopulations

	Effector	Central	Naïve	HLA DR	PD-1
CD4+ Lymphocytes					
IT anti-PD-1	87.8	10.6	1.2	67.8	0.09
IT PBS	74.1	21.9	3.3	44.4	19.3
CD8+ Lymphocytes					
IT anti-PD-1	14.0	71.9	12.5	52.1	1.4
IT PBS	13.6	57.6	27.4	37.4	17.6

*All values recorded as % of lymphocytes

95

Biomarker Status and Response of In-Transit Melanoma Metastases to Topical Diphencyprone S. Haywood,[2] J. Garioch,[1] A. Ramaiya,[1] F. Kwong,[1] M. Wilkinson,[1] M. Moncrieff.[1]* *1. Plastic & Reconstructive Surgery, Norfolk & Norwich University Hospital Foundation NHS Trust, Norwich, United Kingdom; 2. University of East Anglia, Norwich, United Kingdom.*

In transit metastases (ITMs) of cutaneous melanoma are challenging to treat and are associated with a poor prognosis. Diphencyprone (DPCP) is a topical immunotherapy agent. It is a simple treatment to administer and has been shown to have a tumour response rate of over 60% in previous studies. To date, no biomarkers have been identified to predict response of ITMs to immunotherapy. We aimed to correlate clinical response to DPCP with tumour BRAF V600 mutation status and PD-L1 expression, in addition to CD8 and PD-1 expression on tumour infiltrating lymphocytes (TILs). 40 patients with complete clinical history and tumour samples were included. BRAF mutation status and PD-L1 expression, with TILs CD8/PD-1 expression were determined by immunohistochemistry techniques. All patients were treated with topical DPCP for a minimum of 12 weeks and assessed clinically for response at 3 and 6 months. Treatment with DPCP was continued until disease progression. The results of the biomarker analysis were correlated against response to DPCP and overall survival. 10 patients (25%) had complete response (CR); 12 patients (30%) had a partial response (PR); 18 patients (45%) had no response. Response to DPCP was significantly associated with increased overall survival (p=0.002). The biomarkers did not predict disease-specific or overall survival. There was a near-significant association with overall response (CR+PR) to diphencyprone and PD-1 status (p=0.07). Only 2 cases were PD-L1 positive but both had a CR to DPCP (p=0.043). Ten (25%) tumours were were found to have a BRAF V600 mutation. BRAF wild-type tumours were significantly more likely to have a CR to DPCP (p=0.025). There was no association of CD8 expression and CR to DPCP. We have previously shown that DPCP is an effective therapy for ITMs. In our latest study, we found that the BRAF wild-type genotype predominated and was significantly associated with a CR to DPCP. Both tumour PD-1 and TILs PD-L1 expression were independently predictive of response to DPCP therapy. These simple biomarkers may help clinicians to target patients suitable for topical immunotherapy for the management of melanoma ITMs. Validation studies are required.

Biomarker status and response to diphencyprone

Variable	Category	Complete response, n	Partial response, n	No response, n	p value ($\chi 2$)
BRAF V600 mutation status	Wild-type	10	6	14	0.025
	Positive	0	6	4	
CD8 expression *	0	1	3	2	0.165
	1	3	2	9	
	2	2	6	5	
	3	4	1	2	
PD-1 expression *	0	1	5	9	0.042
	1	3	4	8	
	2	2	2	1	
	3	4	1	0	
PD-L1 expression **	Negative	8	12	18	0.043
	Positive	2	0	0	

* 0=0cells/mm2, 1=1-10 cells/mm2, 2=11-100 cells/mm2 and 3= ≥101 cells/mm2

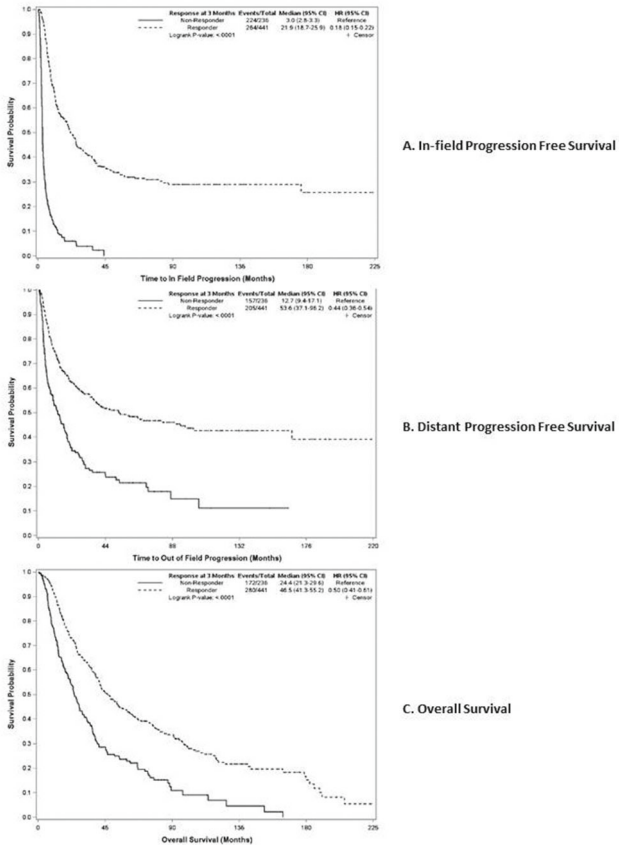
** >5% expression = positive

96

Long-term Oncologic Outcomes Following Isolated Limb Infusion for Locoregional Metastatic Melanoma: An International Multi-Center Analysis J.T. Miura,[1]* H.M. Kroon,[2] G. Beasley,[3] N.E. Farrow,[3] P.J. Mosca,[3] M. Lowe,[4] C. Farley,[4] Y. Kim,[1] S. Naqvi,[1] A. Potdar,[1] H. Daou,[1] J. Sun,[1] D. Mullen,[2] J. Farma,[5] M. Henderson,[6] J. Serpell,[7] K.A. Delman,[4] M. Smithers,[8] B. Coventry,[2] D.S. Tyler,[9] J. Thompson,[10] J. Zager.[1] *1. Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL; 2. Royal Adelaide Hospital, Adelaide, SA, Australia; 3. Duke University School of Medicine, Durham, NC; 4. Emory University School of Medicine, Atlanta, GA; 5. Fox Chase Cancer Center, Philadelphia, PA; 6. Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; 7. The Alfred Hospital, Melbourne, VIC, Australia; 8. University of Queensland, Brisbane, QLD, Australia; 9. University of Texas Medical Branch, Galveston, TX; 10. Melanoma Institute Australia, The University of Sydney, Sydney, NSW, Australia.*

Background: Management of locoregionally metastatic melanoma continues to evolve. Isolated limb infusion (ILI) provides a minimally invasive approach for delivering regional chemotherapy to patients with locally advanced or metastatic melanoma limited to a limb. The present international multicenter study evaluated the perioperative and long-term oncologic outcomes of patients who underwent ILI for stage IIIB/IIIC melanoma. Methods: Patients undergoing first-time ILI for stage IIIB/IIIC (AJCC 7th Ed) melanoma between 1992 and 2018 were identified from 5 Australian and 4 USA tertiary referral centers. ILI was performed using a cytotoxic drug combination consisting of melphalan and actinomycin-D. Toxicity was assessed using the Wieberdink Limb Toxicity Scale. Outcomes measured included treatment response, in-field (IPFS) and distant progression free survival (DPFS), and overall survival (OS). Results: 687 first-time ILI were performed (Stage IIIB: n=383, 56%; Stage IIIC; n=304, 44%). Median age was 71 (Interquartile Range [IQR] : 62-79), with the majority being female (n=412, 60%). Wieberdink toxicity grade IV developed in 27 patients (3.9%); there were no grade V toxicities. Peak creatine kinase levels occurred at a median of 4 days (IQR: 3-5 days) post procedure with median length of stay of 7 days (IQR: 5-9). Overall response rate was 64.1% (Complete Response [CR]: 28.9%, Partial Response [PR]: 35.2%). Stable disease (SD) and progressive disease (PD) occurred in 14.5% and 19.8%, respectively. Median OS was 38.2 months. Stratified by treatment response, responders (CR +PR) had a significantly longer median IPFS (21.9 vs 3.0 months, p<0.0001, Figure 1A), DPFS (53.6 vs 12.7 months, p<0.0001, Figure 1B), and OS (46.5 vs 24.4 months, p<0.0001, Figure 1C) compared to nonresponders (SD+PD). Conclusion: To date, this is the largest series reporting long-term outcomes of ILI for locoregionally metastatic melanoma. Responders to ILI are associated with significantly longer regional and systemic progression-free survival. ILI is a safe and effective treatment modality for patients with stage IIIB/IIIC melanoma limited to a limb.

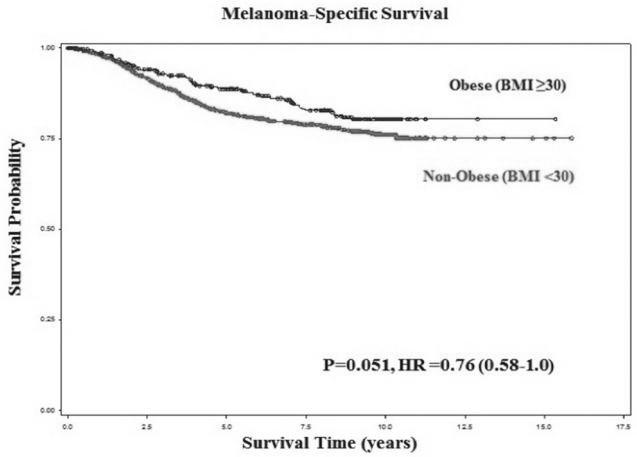
Figure 1: Survival analysis of patients with stage IIIB/IIIC melanoma treated by isolated limb infusion, stratified by treatment response



97

Obesity Paradox in Early Stage Melanoma: Long-Term Follow-up in MSLT-I J.G. Rand,[1]* D. Kirchoff,[2] G. Deutsch,[3] S. Stern,[4] J. Thompson,[5] A. Cochran,[6] N. Mozzillo,[7] O. Nieweg,[8] D. Roses,[9] H. Hoekstra,[10] V. Sondak,[11] B. Coventry,[12] M. Kashani-Sabet,[13] M. Smithers,[14] E. Paul,[15] W. Kraybill,[16] R. Elashoff,[6] D. Lee,[18] M.B. Faries.[17] *1. Cedars Sinai Medical Center, Los Angeles, CA; 2. Charleston Surgical Associates, Roper-St. Francis Hospital, Charleston, SC; 3. Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY; 4. John Wayne Cancer Institute at Providence St. John's Health Center, Santa Monica, CA; 5. The Sydney Melanoma Unit, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; 6. University of California at Los Angeles, Los Angeles, CA; 7. National Cancer Institute, Naples, Italy; 8. Netherlands Cancer Institute, Amsterdam, Netherlands; 9. New York University School of Medicine, New York, NY; 10. University Medical Center of Groningen, Groningen, Netherlands; 11. H. Lee Moffitt Cancer Center, Tampa, FL; 12. Royal Adelaide Hospital, Adelaide, SA, Australia; 13. Sutter Pacific Medical Foundation, San Francisco, CA; 14. Princess Alexandra Hospital, Brisbane, QLD, Australia; 15. The Klinikum Nord, Nuremberg, Germany; 16. Roswell Park Cancer Institute, Buffalo, NY; 17. The Angeles Clinic and Research Institute, Cedars Sinai Medical Center, Los Angeles, CA; 18. Harbor-UCLA Medical Center, Torrance, CA.*

Introduction: Obesity rates are rising throughout the world. In many cancers, obese patients suffer worse outcomes than non-obese. In melanoma, data are mixed with a paradoxical protective effect of obesity reported for patients with metastatic melanoma receiving immune or targeted therapies. In earlier stage melanoma, however, an adverse effect was reported in a single institution series. We examined the outcomes of obese and non-obese patients in an international, multicenter prospective clinical trial. Methods: The first Multicenter Selective Lymphadenectomy Trial (MSLT-I) randomized patients with clinically-localized melanoma to wide excision alone or wide excision with sentinel node biopsy. For this analysis, patients with available BMI at enrollment were evaluated and stratified by obese (BMI ≥30) or non-obese (BMI <30). Disease-free survival (DFS), melanoma-specific survival (MSS) and perioperative morbidity were assessed with regard to BMI status. Results: Among 1839 eligible patients, 376 (20%) were obese and 1463 (80%) were not. BMI was similar in the two trial arms. Age, gender and pathologic characteristics were similar between obese and non-obese. No differences were seen in the degree of intra-tumoral or peri-tumoral immune infiltrates. Overall morbidity rates were also similar (obese 24.5% vs non-obese 21.8%, p=0.27), though obese patients had a significantly increased rate of surgical site infections (11.2 vs 7.4%, p = 0.013). 5-year DFS was significantly better in obese patients (multivariable HR 0.79, 95% CI 0.63-0.98, p=0.036). DFS was also related to age, Breslow thickness, ulceration and nodal status. 5-year MSS was significantly improved in the obese (HR 0.69, 95% CI 0.52-0.91, p=0.01). MSS was similar over the first two years of follow up after which differences emerged and persisted through 10 years of follow up. Conclusions: The obesity paradox appears to apply to earlier stage melanoma patients as well as those being treated for more advanced disease. Immune parameters measured in MSLT-I and analyzed to date do not suggest an immune etiology of the difference, but additional studies of tumor and immune parameters are needed to identify mechanisms of protection.



98

Predictors of Acute Surgical Complications Following Wide Local Excision and Sentinel Lymph Node Biopsy for Melanoma – Analysis from a Prospective Clinical Trial D.E. Gyorki,[1]* M. Moncrieff,[2] R. Saw,[3] A. Spillane,[3] J. Thompson,[3] H. Peach,[4] D. Oudit,[5] J. Geh,[6] P. Dziewulski,[7] E. Wilson,[8] P. Matteucci,[9] R. Pritchard-Jones,[10] R. Olofsson Bagge,[11] F. Wright,[12] N. Crampton,[13] O. Cassell,[14] N. Jallali,[15] A.C. Berger,[16] J. Kelly,[17] S. Hamilton,[18] A. Durrani,[19] S. Lo,[3] E. Paton,[20] M. Henderson.[1] *1. Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; 2. Norfolk & Norwich University Hospital, Norwich, United Kingdom; 3. Melanoma Institute Australia, Sydney, NSW, Australia; 4. Leeds Teaching Hospitals, Leeds, United Kingdom; 5. Christie NHS Trust, Manchester, United Kingdom; 6. Guy's & St Thomas's NHS Trust, London, United Kingdom; 7. St Andrew's Centre for Burns & Plastic Surgery, Chelmsford, United Kingdom; 8. North Bristol NHS Trust, Bristol, United Kingdom; 9. Hull & East Yorkshire NHS Trust, Hull, United Kingdom; 10. Mersey Centre for Burns & Plastic Surgery, Liverpool, United Kingdom; 11. Sahlgrenska University Hospital, Goteborg, Sweden; 12. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 13. Gold Coast Melanoma Clinic, Gold Coast, QLD, Australia; 14. Oxford University Hospitals NHS Trust, London, United Kingdom; 15. Imperial Hospital NHS Trust, London, United Kingdom; 16. Jefferson University Hospital, Philadelphia, PA; 17. The Alfred Hospital, Melbourne, VIC, Australia; 18. Royal Free Hospital NHS Trust, London, United Kingdom; 19. Cambridge University Hospitals, Cambridge, United Kingdom; 20. Australia & New Zealand Melanoma Trials Group, Sydney, NSW, Australia.*

Introduction Wide local excision (WLE) and sentinel lymph node biopsy (SLNB) is standard of care for patients with intermediate thickness cutaneous melanoma. Discussing a patient's risk of perioperative complications is an

important part of the consent process. We utilised the prospective dataset from the MelMarT feasibility study[1]to identify variables associated with surgical adverse events (SurgAE) within 30 days of surgery. Methods The MelMarT study is a phase III multicentre trial [NCT02385214] administered by the Australian & New Zealand Melanoma Trials Group which randomised patients with primary cutaneous melanoma >1mm in Breslow thickness to a WLE with 1cm vs 2cm clinical margin. All patients had SLNB. Neuropathic pain was measured at baseline then at 3, 6 and 12 months. Univariable and multivariable regression analysis was performed to predict factors associated with acute SurgAE. Results There were 400 patients from 17 centres recruited between January 2015 and June 2016. 377 patients with complete data were included in this analysis. Primary melanomas were located on the trunk (56.9%), extremities (35.6%) and head & neck (7.4%). SurgAE were noted in 96 patients (25.5%). 96% of SurgAE were Clavien Dindo Grade I-II and 4% were grade III. The most common SurgAEs were seroma (10.6%), wound infection (8.5%) and wound dehiscence (4.2%). There was a significant increase in neuropathic pain after 3 months, which returned to baseline at 6 months. Patients with an inguinal SLNB were more likely to have SurgAE than those with SLNB at other sites (HR 2.78, p<0.001). Younger age was also associated with a higher incidence of SurgAE (p=0.04). There was no association between margin width (1cm vs 2cm margin), method of wound closure (primary versus skin graft or local flap) or obesity with SurgAE. Conclusion This contemporary series of WLE and SLNB for melanoma demonstrates a low rate of acute surgical complications with 1.3% of patients having serious surgAE. Patients with inguinal SLNB have the highest rates of surgAE irrespective of width of excision. [1]Moncrieff et al Ann Surg Oncol 2018

99

Efficacy of Talimogene Laherparepvec (T-VEC) Therapy in Patients with In-Transit Melanoma Metastasis Decreases with Increasing Lesion Size S.J. Masoud,[2]* J.B. Hu,[2] G. Beasley,[1] J.H. Stewart,[3] P.J. Mosca.[1] *1. Department of Surgery, Duke University Medical Center, Durham, NC; 2. School of Medicine, Duke University Medical Center, Durham, NC; 3. College of Medicine, University of Illinois, Chicago, IL.*

Background: Approximately 4-10% of patients with melanoma develop in-transit (IT) recurrence. Talimogene Laherparepvec (T-VEC) is the first injectable oncolytic viral therapy approved for IT disease and has a reported overall response rate of 25% and complete response (CR) rate of 10%. In order to better understand the impact of patient selection, we aimed to determine the impact of lesion size on probability of a clinical response. Methods: Medical records were extracted for patients with recurrent Stage II, III or IV melanoma who completed T-VEC at Duke University Medical Center between January 1, 2016 and September 1, 2018. Kaplan-Meier analysis was used to assess time to CR. Bivariate logistic regression evaluated the impact of primary and IT lesion characteristics, mean T-VEC treatment dose, and receipt of either PD-1 inhibitor, other adjuvant therapy, or no additional treatment on therapeutic response. Results: Of 32 patients who underwent T-VEC therapy, 12/26 (46.2%) achieved CR at a median of 18 weeks (95% CI 16.9-19.1 weeks) (Table 1). Of patients experiencing CR, 6 (50%) developed transient increases in lesion diameter upon treatment initiation. Four patients (12.5%) experienced treatment-limiting complications, including infection, skin necrosis, herpes simplex virus infection, and high fevers. Logistic regression demonstrated that the odds of CR decrease 59% (95% CI 2.5%-83%) for each 1 cm increase in maximal IT lesion diameter ($\chi^2(1)=7.0$, p=.008). Conclusions: Complete response rates to T-VEC therapy may be higher than suggested by clinical trials, even when excluding patients with smaller lesions. Though our analysis is limited by a small sample size, the only factor associated with clinical response to T-VEC was IT lesion diameter. Nearly half of patients who eventually responded experienced initial growth in their lesions, suggestive of pseudoprogression. Therefore, IT lesion diameter is a readily assessed clinical predictor of successful T-VEC therapy and may constitute an important factor in patient selection for T-VEC treatment.

Table 1. Clinicopathologic and treatment features of melanoma patients who underwent T-VEC therapy.

Characteristics	N	%
Median age (years)	62.5	
Sex		
Male	15	47
Female	17	53
Location of primary tumor		
Extremities	20	63
Abdomen/trunk	5	16
Head/Neck	7	22
Stage at treatment		
IIB	1	3
IIC	1	3
IIIA	2	6
IIIB	8	25
IIIC	13	41
IV	7	22
BRAF status		
Wild-type	11	34
Mutant	8	25
unknown	13	41
Adjuvant treatment		
None	13	41
PD-1	11	34
Other	8	25
Median time to response (weeks)	16	
Mean number of treatments	7.2	
Median diameter largest lesion (mm)	12	
Treatment Response		
Complete response	14	44
Lesion growth prior to response	*6*	*43 (out of 14)*
Partial response	1	3
Stable disease	3	9
Progressive disease	11	34
Undetermined	3	9

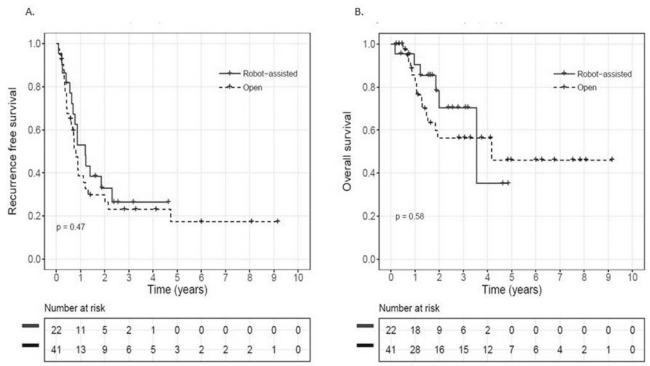
100

Robotic-Assisted Pelvic Lymphadenectomy for Metastatic Melanoma Results in Durable Oncologic Outcomes J.T. Miura,[1]* L.A. Dossett,[2] S. Naqvi,[1] Y. Kim,[1] A. Potdar,[1] H. Daou,[1] J. Sun,[1] A.A. Sarniak,[1] J. Zager.[1] *1. Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL; 2. University of Michigan, Ann Arbor, MI.*

Background: Robotic pelvic lymphadenectomy (rPLND) has been demonstrated to be a safe and effective minimally invasive approach for patients with metastatic melanoma to the iliac nodes. However, the long term oncologic benefits of this procedure remain poorly defined. Methods: A single institutional study comparing perioperative outcomes and survival (recurrence free [RFS] and overall survival [OS]) between rPLND and open PLND (oPLND) for metastatic melanoma was conducted. Relative indications for PLND included > 3 involved inguinal nodes, a large (≥3cm) inguinal metastasis, or pelvic sentinel node identified (but not sampled) on lymphoscintigraphy in the setting of a positive node in the superficial groin. Biopsy positive pelvic nodes without evidence of distant disease was an absolute indication, with or without neoadjuvant therapy. Results: From 2006 to 2018, a total of 63 PLND cases that met inclusion criteria were identified: 22 rPLND and 41 oPLND. Evidence of isolated pelvic metastasis was the most common indication for PLND in both groups (rPLND: 64%, oPLND: 85%). There was no difference in median operative time (210 vs 205 minutes, p=0.78) or median pelvic lymph node yield (10 vs 10 nodes) between rPLND and oPLND. Neither treatment group experienced a ≥3 Clavien Dindo complication. rPLND was associated with a shorter length of stay when compared to oPLND (2.3 vs 4.5 days, p<0.001). With a median follow up of 37.2 months, there was no difference in RFS (14.4 vs 9.6 months, p=0.47, Figure 1A) and OS (42.6 vs 50 months, p=0.58, Figure 1B) between rPLND and oPLND respectively. In multivariate models, rPLND was not independently associated with worse survival when

compared to oPLND (RFS: HR 0.87; p=0.69, OS: HR 0.82; p=0.69). In basin recurrence was low with only 1 (4.5%) and 3 (7.3%) patients in the rPLND and oPLND cohorts respectively experiencing an event(p=0.9). Conclusion: rPLND for metastatic melanoma remains a safe treatment strategy that results in similar recurrence and survival rates as oPLND but shorter hospital stays.

Figure 1: Survival Analysis



101

Age and Lymphovascular Invasion Accurately Predict Sentinel Lymph Node Metastasis for T2 Melanoma Patients in a Validated Prediction Model M.E. Egger,* M. Stevenson, N. Bhutiani, C.R. Scoggins, P. Philips, R. Martin, K.M. McMasters. *Surgery, University of Louisville, Louisville, KY.*

Introduction: The risk of sentinel lymph node (SLN) metastasis for melanoma is directly related to tumor thickness and inversely to age. A common clinical problem is to weigh the risks and benefits of SLN biopsy for elderly patients with T2 melanomas. We hypothesized that for T2 (thickness 1.1-2.0 mm) melanoma, age and other factors may be able to identify a cohort of patients with low risk of SLN metastases. Methods: We developed logistic regression models to predict positive SLNs in patients undergoing SLN biopsy for T2 melanoma using the National Cancer Database (NCDB) 2015 Melanoma Public Use File 2010-2015. Classification and regression tree (CART) analysis was used to identify groups of patients with high and low risk of SLN metastases. The prediction model was then validated with a separate dataset of 1,531 T2 melanoma patients from a multicenter randomized clinical trial. Results: We identified 12,918 patients with T2 melanoma undergoing SLN biopsy with clinically node negative melanoma using NCDB. On multivariable analysis, increasing thickness, younger age, LVI, mitotic rate ≥1/mm^2, axial location, and Clark level IV/V were independent risk factors for SLN metastases. Age ≤56 was a significant cut point for discrimination of SLN metastases, in addition to LVI. A cohort based on age (>56) and no LVI was identified with a relatively low (7.8%, 95% CI 7.2-8.4%) risk of SLN metastases. The validation dataset confirmed these findings (Figure). This relatively lower risk cohort represents a significant proportion of patients with T2 melanoma undergoing SLN biopsy (60%). In elderly patients (age >75) with melanoma ≤ 1.2 mm and without LVI, the risk of a positive SLN was 4.9% (3.3-7.1%). Conclusion: Younger age and LVI are powerful predictors of SLN metastases in patients with T2 melanoma. Patients age >56 and no LVI have a low (7.8%) risk of SLN metastasis; those age >75 have an even lower risk. This prediction model can inform shared decision-making regarding whether to perform SLN biopsy in older patients with otherwise low risk T2 melanoma.

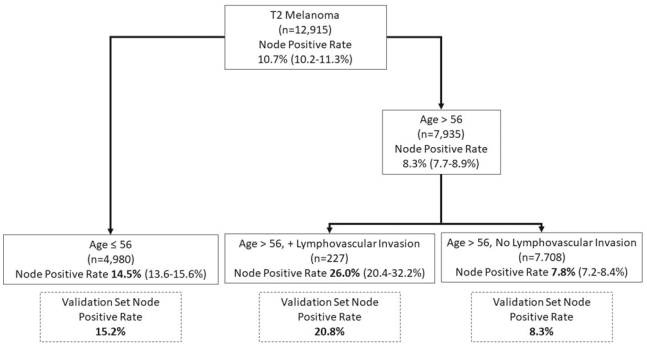


Figure. Rates of positive SLN in T2 melanoma patients based on age and lymphovascular invasion.

102

Extent of Lymphadenectomy in Patients with Melanoma and Clinical Node Disease M. Kwak,[1]* Y. Song,[2] P.A. Gimotty,[2] N.E. Farrow,[3] A.D. Tieniber,[2] J.G. Davick,[1] G.N. Tortorello,[2] G. Beasley,[3] C.L. Slingluff,[1] G. Karakousis.[2] *1. Surgery, University of Virginia, Charlottesville, VA; 2. Hospital of the University of Pennsylvania, Philedelphia, PA; 3. Duke University Hospital, Durham, NC.*

Introduction: Randomized controlled trials confirmed the safety of close observation for patients with microscopic nodal disease at time of sentinel lymph node (SLN) biopsy. The standard approach for macroscopic nodal disease is complete lymph node dissection (CLND), although improved survival data over selective LND are lacking. We sought to identify factors to predict additional non-clinical nodal disease in this patient population in an effort to limit the extent of lymphadenectomy and subsequent morbidity. Methods: A retrospective study was performed with pooled data from three academic melanoma centers. Patients who underwent CLND for clinically-detected LN metastases of melanoma were selected, excluding LN disease found on SLNB only. Patients with prior CLND were also excluded. To identify subgroups most likely to have just one pathologic node, univariate and multivariate classification and regression tree (CART) analyses were performed. Results: 185 patients met study criteria. Based on imaging, 102 (55%) had one, 35 (19%) had two, and 48 (26%) had three or more suspicious LN. On pathologic evaluation of CLND specimens, 1+ LN was found in 87 (47%), 2+ LN in 31 (17%), and 3 or more positive LN in 67 (36%). The CART analysis showed the number of suspicious LN on imaging was associated with finding additional LN at the time of CLND for all LN groups, and largest LN size if ≧2 LN predicted. Preop imaging accurately predicted LNs in 109 (59%) patients while 76 (41%) had at least one additional LN than suspected. In patients with 1 clinically suspicious LN, the rate of finding additional LN was 29% (95% CI 21%-39%). In patients with 2 or more suspicious LNs, only 10% (95% CI 0.2%-45%) had additional LN when largest LN size on imaging was ≤1.25 cm, in contrast to 62% (95% CI 50%-73%) had additional LN when >1.25 cm. Conclusions: Of patients presenting with LN recurrence and only 1 LN involved by imaging, 71% had only 1 positive LN at CLND. While preop imaging may help risk stratify patients, further effort should be made to better predict additional non-clinical disease and study the impact of more extended lymphadenectomy in this population, especially in the era of novel therapeutics

103

The Devil's in the Details: Discrepancy Between Biopsy Thickness and Final Pathology in Acral Melanoma A.Y. Lee,[1]* E. Friedman,[1] J. Sun,[2] A. Potdar,[2] H. Daou,[2] N.E. Farrow,[3] C. Farley,[5] J. Vetto,[4] D. Han,[4] M. Tariq,[5] R. Shapiro,[1] G. Beasley,[3] C. Contreras,[6] I. Osman,[1] M. Lowe,[5] J. Zager,[2] R. Berman.[1] *1. Surgery, New York University, Mount Kisco, NY; 2. Moffitt Cancer Center, Tampa, FL; 3. Duke University, Durham, NC; 4. Oregon Health and Science University, Portland, OR; 5. Emory University, Atlanta, GA; 6. University of Alabama, Birmingham, AL.*

Introduction: We hypothesized that initial biopsy may understage acral lentiginous melanoma (ALM) due to overlying callous, sampling error in large lesions, and lack of familiarity with nail matrix biopsies. Understanding this possibility can potentially aid surgical planning and improve primary tumor

staging. Methods: The US Melanoma Consortium is a newly founded collaboration of 6 academic centers. A retrospective review of this large prospectively-collected melanoma database was performed. Primary ALMs treated between 2000 and 2017 were included. We reviewed pathology characteristics of initial biopsy, final excision specimens, surgical margins, and sentinel lymph node biopsy (SLNB). Results: We identified 416 primary ALMs, including 321 plantar, 34 palmar, and 61 subunguals for whom both initial biopsy and final pathology T category were available. Median final thickness was 1.9mm (range, 0.0-19.0). There was a discrepancy in thickness between the initial biopsy and final pathology in 177 patients with a median difference of 1.6mm (range 0.1-16.4). Final T category was greater in 132 patients (32%), including 44% of initially in situ, 34% of T1, 40% of T2, and 25% of T3 lesions ($p<0.001$, Table 1). T category was more likely to be increased in subungual (46%) and palmar (41%) melanomas than plantar (28%) melanomas ($p<0.01$). Patients initially Tis or T1 (n=163) were more likely to be upstaged; however, site-specific differences were less pronounced ($p=0.08$) with 54% of subungual, 46% of palmar, and 32% of plantar melanomas upstaged. SLNB was performed in 74 patients (45%) initially Tis or T1, of whom 10 (14%) were positive (6 plantar and 4 subungual). Among the 51 patients upstaged from initial Tis/T1 to T2 or higher, 24 (47%) had ≤1cm margins taken and 12 (24%) did not have a SLNB performed, resulting in incomplete staging. Conclusions: In this large cohort of ALMs, final T category was frequently increased from the initial biopsy. A high index of suspicion for understaging is necessary for lesions in situ or T1 on biopsy and consideration should be given to performing additional punch biopsies, wider margin excisions, and/or SLNB.

		Final Pathology T Category				
		Tis	T1	T2	T3	T4
Initial biopsy T Category	Tis (n=36)	20 (55%)	8 (22%)	2 (6%)	4 (11%)	2 (6%)
	T1 (n=127)	--	84 (66%)	21 (17%)	10 (8%)	12 (9%)
	T2 (n=139)	--	--	83 (60%)	29 (21%)	27 (19%)
	T3 (n=66)	--	--	--	49 (75%)	17 (25%)
	T4 (n=48)	--	--	--	--	48 (100%)

Correlation of T category between initial biopsy and final pathology

104

Sentinel Node Biopsy in Melanoma Patients with a Local Recurrence or In-Transit Metastasis A. Nijhuis,[1]* I. D. de A.O. Santos,[2] L. Holtkamp,[3] R. Uren,[4] J. Thompson,[1] O. Nieweg.[1] *1. Melanoma Institute Australia, Utrecht, Netherlands; 2. A.C. Camargo Cancer Center, Sao Paulo, Brazil; 3. University of Groningen, Groningen, Netherlands; 4. Alfred Nuclear Medicine and Ultrasound, Sydney, NSW, Australia.*

Background - Sentinel node biopsy (SNB) is not routinely performed in melanoma patients with a local recurrence or in-transit metastasis (ITM). The purposes of the study were to assess the injection sites of the tracers, sentinel node (SN) identification and involvement, false negative rate, SN influence on disease stage, and survival outcome. Methods – Approval from the local research ethics committee was obtained. The institute's prospectively collected database was queried for the period between 1992 and 2015. Patient and primary tumor characteristics, lymphoscintigrams, SNB results, and follow-up data were analyzed. Results – A total of 7999 patients underwent SNB, of whom 128 met the selection criteria (1.6%). Eighty-five of them had a local recurrence, seventeen an ITM from a known primary tumor and 26 an ITM from an unknown primary. The median follow-up duration from SNB to last visit was four years. Information about the injection site of the radiopharmaceutical and/or blue dye could be retrieved in 24 of the 43 patients with an ITM (56%). Injection was around the ITM in 21 patients (88%), around the primary tumor site in one (4%) and at both locations in two (8%). SNs were successfully retrieved in all 128 patients with a median of 2 nodes per patient. The SNs revealed metastatic disease in sixteen patients (13%). Thirteen of the 102 patients with a known primary (13%) were upstaged due to the positive SN. Follow-up data were available for 114 patients. The false negative rate was 27%. Five-year overall survival was 54% for SN positive patients and 81% for SN negative patients ($P=0.01$; Figure 1). Conclusion – SNB can be performed in patients with a local recurrence or an ITM with a high identification rate, although the false negative rate was considerable with 27%. A tumor positive SN was found in 13% of the patients and was associated with a worse overall survival rate. SNB can improve staging of patients with a local recurrence or ITM, which may aid in further management decisions.

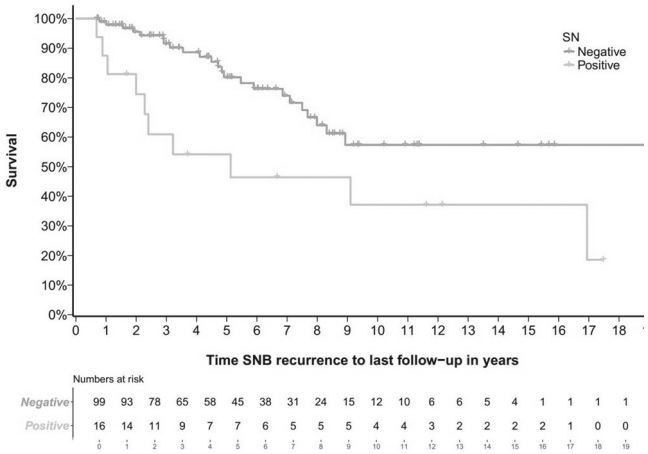


Figure 1 - Kaplan Meier curve: overall survival SN negative and positive patients

105

Clinical Outcomes of Melanoma Patients with Low Sentinel Lymph Node Tumor Burden W.R. Burns,* A. Durham, L.A. Dossett, T.B. Hughes, A.E. Chang, C.K. Bichakjian, M.S. Sabel. *University of Michigan, Ann Arbor, MI.*

Introduction: The prognosis of individuals with Stage III melanoma is difficult to predict, given a wide range of outcomes for this diverse population. However, these patients face important care decisions regarding additional surgery and adjuvant therapy. To better understand a subset of Stage III melanoma patients with low lymph node tumor burden, we explored clinical outcomes of these patients following sentinel lymph node (SLN) biopsy. Methods: Using an institutional dataset, we identified patients with melanoma and a SLN tumor burden < 1%. This included patients with isolated tumor cell(s), small clusters of tumor, or maximum tumor dimension < 1 mm. Patients found to have distant metastatic disease on initial staging were excluded. Primary outcome measures were overall survival (OS) and melanoma-specific survival (MSS). We also evaluated patterns of recurrence and pathological features associated with tumor recurrence. Results: We identified 370 patients with SLN tumor burden < 1% treated between 1998 – 2017. Median follow-up was 5.3 years. A majority of patients (75%, n=279) underwent completion node dissection, where non-sentinel lymph node metastasis was identified in only 14 patients (5%). For the entire cohort, OS was 78% and MSS was 87%. In terms of recurrence, 21 patients (6%) developed local/regional recurrence and 60 patients (16%) developed distant metastasis; 71% of patients (15/21) with local/regional recurrence also developed distant metastasis. Features associated with development of distant metastasis were primary tumor thickness (3.1 vs 2.3, $P<0.01$), mitotic rate (8.0 vs 4.2, $P<0.0001$), ulceration (32% vs 12%, $P=0.00001$), satellitosis (50% vs 15%, $P<0.001$), and angiolymphatic invasion (38% vs 15%, $P<0.01$); having more than one positive SLN was not associated with distant metastasis (26% vs 15%, $P=0.12$). In a subset of 261 patients without these high-risk features, OS was 87% and MSS was 92%. Conclusions: Patients with Stage III melanoma and low (< 1%) SLN tumor burden have a favorable prognosis, especially in the absence of adverse pathological features of the primary tumor. These data may aid in tailoring treatment and surveillance plans for this low-risk group.

106

Patterns of Failure After Immunotherapy with Checkpoint Inhibitors Predict Durability of Curative-Intent Surgery for Patients with Metastatic Melanoma N.D. Klemen,[1]* M. Wang,[1] P.L. Feingold,[1] S. Pavri,[3] K. Olino,[1] S. Khan,[1] D. Han,[2] F. Detterbeck,[1] D. Boffa,[1] D. Narayan,[1] J. Clune,[1] S. Ariyan,[1] R.S. Salem,[1] H. Kluger,[1] M. Sznol,[1] C. Cha.[1] *1. Yale University, New Haven, CT; 2. Oregon Health & Sciences University, Portland, OR; 3. Orlando Health, Aesthetic & Reconstructive Surgery Institute, Orlando, FL.*

Introduction: Checkpoint inhibitors (CPI) including antibodies against CTLA-4, PD-1 and PD-L1 have revolutionized treatment of metastatic melanoma. Despite excellent response rates associated with CPI, many patients relapse following an initial response. Surgery is playing an increasing role in the management of selected patients with oligoprogressive disease (OPD) after CPI, but the application of this strategy is not well established. Methods: We performed a retrospective review of 485 patients with metastatic melanoma treated with CPI at a single institution. Patients with OPD in 1-2 sites underwent complete metastasectomy to remove all disease or selective metastasectomy to remove discordant lesions in the setting of responding or stable lesions elsewhere. We excluded procedures performed for diagnosis, palliation, or CNS disease. Results: Forty patients had surgery a median of 19 months after the first CPI dose (interquartile range, 10 - 31 mo). At a median follow-up of 25 months, the five-year disease specific survival (DSS) was 69%, versus 42% for patients who didn't have surgery. Patients who had selective metastasectomy (n = 13) had similar DSS and PFS as patients who had complete metastasectomy (n = 27; P = 0.44, 0.80 respectively). Regardless of whether complete or selective metastasectomy was performed, 5-year survival was greater than 90% following resection of established metastases that were evident before CPI, while patients who had resection of new metastases had comparatively worse outcomes (P = 0.025) (Figure 1). Conclusions: Surgical resection of OPD following CPI therapy was associated with favorable long-term survival, especially after resection of established lesions. Selective metastasectomy of discordant lesions may be a useful strategy to manage immunorefractory tumors. Improvements in systemic therapy may lead to an expanded role for surgery in this metastatic patient population.

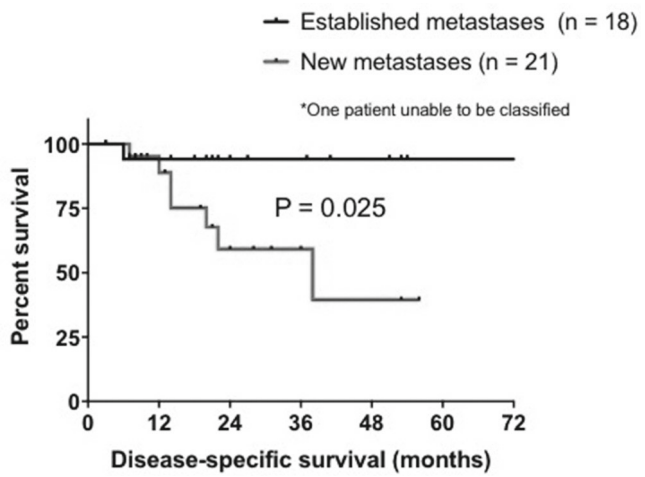


Figure 1: Disease-specific survival after surgery. Established metastases were evident before the first cycle of CPI; new metastases appeared after. One patient was unable to be classified.

107

Institutional Variation in Recovery After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: An Opportunity for Enhanced Recovery Pathways O.S. Eng,[1]* A.M. Blakely,[2] K.J. Lafaro,[2] K. Fournier,[3] N. Fackche,[4] F.M. Johnston,[4] S. Dineen,[5] B. Powers,[5] R.J. Hendrix,[6] L.A. Lambert,[7] D. Abbott,[8] K. Vande Walle,[8] T.E. Grotz,[9] J.L. Leiting,[9] S.H. Patel,[10] V.K. Dhar,[10] J.M. Baumgartner,[11] A.M. Lowy,[11] C.N. Clarke,[12] H. Mogal,[12] M.Y. Zaidi,[13] C. Staley,[13] C. Kimbrough,[14] J. Cloyd,[14] B. Lee,[2] M. Raoof.[2] *1. Surgery, University of Chicago, Chicago, IL; 2. City of Hope National Medical Center, Duarte, CA; 3. MD Anderson Cancer Center, Houston, TX; 4. Johns Hopkins University, Baltimore, MD; 5. Moffitt Cancer Center, Tampa, FL; 6. University of Massachusetts, Worcester, MA; 7. University of Utah, Salt Lake City, UT; 8. University of Wisconsin, Madison, WI; 9. Mayo Clinic, Rochester, MN; 10. University of Cincinnati, Cincinnati, OH; 11. University of California at San Diego, San Diego, CA; 12. Medical College of Wisconsin, Milwaukee, WI; 13. Emory University, Atlanta, GA; 14. Ohio State University, Columbus, OH.*

Introduction Enhanced recovery after surgery (ERAS) pathways reduce variation by standardizing peri-operative care. For moderate complexity operations, ERAS pathways reduce healthcare costs and post-operative morbidity. However, their role in cytoreductive surgery with heated intraperitoneal chemotherapy (CRS/HIPEC) is less clear. To determine if ERAS pathways would be beneficial, we sought to characterize institutional variation in peri-operative care of patients undergoing CRS/HIPEC among experienced US academic institutions. Methods This is a retrospective multi-institutional cohort study of CRS/HIPEC patients from 1999-2018. We characterized institutional variation in: baseline demographics; clinicopathologic variables; and peri-operative processes and outcomes. Process measures included: Intra-operative fluid administration; number of abdominal drains; length of ICU stay; days to nasogastric tube removal; and days to diet initiation. Outcome measures included length of hospital stay, 30-day complications and readmissions. Institutional variation was analyzed using hierarchical mixed-effects linear or logistic regression models. Results A total of 2372 operations from 12 major academic institutions (range 49 – 456 per institution) were included. CRS/HIPEC was performed most commonly for appendiceal adenocarcinoma (32.6%) and low-grade appendiceal mucinous neoplasm (23.3%). Median PCI was 13 (IQR 7-21). Institutional variation in process and outcome measures is summarized in the Table. In every process or outcome variable category, institutional practices were significantly different (p<0.001). These variations persisted after adjusting for age, sex, performance status, BMI and PCI. Rate of complications (56.3%, range 31.8-70.9), and readmissions (20.6%, range 8.9-33.3) also varied by institution (Adjusted p<0.001, both). Conclusions This study demonstrates significant variation in peri-operative care of patients undergoing CRS/HIPEC at major US academic institutions. These findings provide a strong rationale for the investigation of best practices and the development ERAS pathways in CRS/HIPEC patients.

Table. Institutional Variation in Process and Outcome Measures after CRS/ HIPEC

Parameter	Drains	Intraop Fluids	Duration NG	Duration NPO	ICU stay	Hospital stay
(N=2372, 12 institutions)	no.	liters	days	days	days	days
Median - All patients	1	6.5	3	4	2	9
Range of Institutional Medians	0 - 3	4.2 - 8.4	0 - 6	1 - 6	0 - 3	7 - 12
Unadjusted p-value (Random-effects)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Adjusted* p-value (Random-effects)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Variation Attributable to Institutional Practices	38.90%	23.50%	14.60%	9.50%	8.60%	3.20%

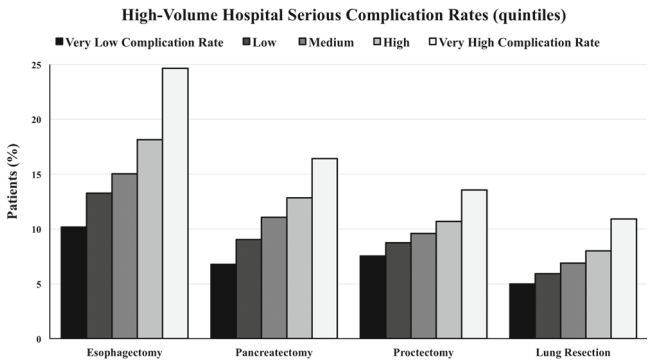
*Model Adjusted for age, sex, ECOG performance status, Peritoneal Carcinomatosis Index and Body Mass Index. A sig p-value denotes that a hierarchial model including institutional-level (random) effects is superior to a model with patient-level (fixed) effects alone.

108

Are Volume Standards for Cancer Resections Enough?

M.E. Smith,* U. Nuliyalu, J.B. Dimick, H. Nathan. *General Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: Based on a strong volume-mortality relationship, payer organizations such as the Leapfrog Group advocate that complex operations should occur only at hospitals meeting minimum volume thresholds. However, even high-volume, low-mortality hospitals may exhibit variation in postoperative complications, which have significant repercussions even if they do not result in mortality. In cancer pts, postoperative complications are associated with decreased long-term survival. As such, volume-based referral alone may be insufficient to achieve optimal long-term outcomes. We assessed variation in non-mortality outcomes following cancer resections among high-volume hospitals. Methods: We identified pts aged. >65 years undergoing esophagectomy (esoph), pancreatectomy (panc), proctectomy (rectal) and lung resection (lung) in 2012-2014 Medicare claims data. Hospital volume was based on all-payer claims. High-volume hospitals (HVH) were defined as those that met 2018 Leapfrog Group volume standards. Postoperative outcomes were ascertained from inpatient and outpatient Medicare claims. HVHs were stratified into quintiles of serious complication rates to assess variation. Results: Only 1/5 of hospitals performing these procedures were HVH (esoph n=81 (9%); panc n=177 (17%); rectal n=586 (22%); lung n=375 (20%). HVH cared for only 2/3 of pts (54% esoph, 75% panc, 66% rectal, 63% lung). As expected, HVH had significantly lower mortality rates than low-volume hospitals for each procedure. There was wide variation in serious complication rates among HVH (Fig). Esoph complications ranged from 10% in the lowest complication quintile of HVH to 25% in the highest quintile, 7à16% for panc, 8à14% for rectal, and 5à11% for lung (all p<0.001). Variation in serious complications among HVH remained after accounting for HVH individual volume. Conclusion: Avoidance of low-volume surgery is critical to prevent postoperative mortality but is insufficient to prevent morbidity. Even when patients are rescued from complications, they may suffer from inferior long-term outcomes. Efforts to improve quality of complex surgery should focus not just on identifying low-mortality hospitals but also consider occurrence of complications.



Rates of Serious Complications Among High-Volume Hospitals According to Hospital Quintiles of Serious Complications.

109

Quality Improvement for Surgical Resection of Pancreatic Head Adenocarcinoma: Hospital and Surgeon Predictors of Higher than Expected R1 Resection Using the National Cancer Data Base

B. Nuckles,* K. Lam, J. Dove, M. Hunsinger, M. Shabahang, T. Arora, J. Blansfield. *General Surgery, Geisinger Medical Center, Danville, PA.*

INTRODUCTION The mainstay of treatment for pancreatic cancer is surgical resection, however positive surgical margins remain commonplace with significant implications on patient survival. We identified hospitals with higher than predicted rates of positive margins and isolated factors that contributed to this discordance. METHODS This is a retrospective review of patients with head of the pancreas adenocarcinoma in the National Cancer Database (NCDB, 2004-2015). A previously developed nomogram from our group, based on tumor and patient variables, was used to calculate the observed to expected positive margin rates (O/E) for facilities in the database. For this study, the probability that a hospital had exactly the number of observed events (compared to expected) was calculated. If the O/E differed significantly (p<0.05) it was considered an outlier. RESULTS Our group previously reported that in a group of 19,968 patients, 24.3% had positive margins. A total of 136 hospitals among 852 and were assigned outlier status (83 higher than expected rates of positive margin and 53 lower than expected positive margin outliers). Hospitals identified as high margin positive outliers had an O/E ratio of 2.11 compared to 0.57 for hospitals designated as low outliers. Among hospitals with lower than expected positive margin rates, 73.6% were academic or research programs, 17% were comprehensive community cancer programs and none were community cancer programs (p=0.0002). Within the group with higher than expected positive margin rates, 47% were comprehensive community cancer programs and 38.6% were academic or research programs (p=0.0002). The mean hospital volume (total cases from 2004-2015) was higher in the low positive margin group compared to high outliers (110.4 vs 48.8, p<0.0001). CONCLUSIONS Facility type and hospital volume can predict improvement in the observed to expected ratio for margin positivity in pancreatic adenocarcinoma resection. Surgeons should consider referral to academic or research facilities with higher case volumes for improved complete surgical resection.

Table 1: Facility Metrics of Low and High Outliers

Variable	Low Margin Positive Outlier Hospitals = 53	High Margin Positive Outlier Hospitals = 83
Observed/Expected Ratio of Positive Margins after Resection		
mean ± standard deviation	0.57 ± 0.23	2.11 ± 0.88
median	0.59 (0.49, 0.75)	1.86 (1.53, 2.30)
range	[0, 0.96]	[1.01, 5.45]
Facility Type		
Community Cancer Program	0 (0%)	3 (3.6%)
Comprehensive Community Cancer Program	9 (17%)	39 (47%)
Academic/Research Program	39 (73.6%)	32 (38.6%)
Integrated Network Cancer Program	5 (9.4%)	9 (10.8%)
Total Hospital Volume (cases)		
mean ± standard deviation	110.43 ± 90.44	48.80 ± 75.28
median	97 (51, 121)	26 (11, 54)
Yearly Hospital Volume (cases)		
mean ± standard deviation	9.86 ± 7.44	4.78 ± 6.21
median	8.17 (4.73, 11.11)	2.57 (1.57, 5.42)

110

Analysis of Surgical Trends for Axillary Lymph Node Management in Patients with Ductal Carcinoma In Situ Using the NSQIP Database: Are We Following National Guidelines?

B. Pyfer,[1]* M. Jonczyk,[2] J. Jean,[3] R. Graham,[2] L. Chen,[2] A. Chatterjee.[2] *1. Surgery, Duke University Hospital, Durham, NC; 2. Tufts Medical Center, Boston, MA; 3. Tufts University Medical School, Boston, MA.*

Introduction: For patients with ductal carcinoma in situ (DCIS), multiple national cancer organizations recommend that sentinel lymph node biopsy (SLNB) should be offered when treated with mastectomy (MAST) and should not be offered when treated with breast-conserving surgery (BCS). This study analyzes national surgical trends of axillary lymph node (ALN) management in DCIS patients undergoing breast surgery with the aim to quantify the deviation of practice management from national guidelines. Methods: A retrospective cohort analysis of the ACS NSQIP database from 2005-2016 used International Classification of Disease codes to identify patients with DCIS. Patients were categorized by their primary method of breast surgery as indicated by current procedural terminology codes: MAST or BCS. They were further categorized by their ALN management: no intervention, or ALN surgery (SLNB or ALN dissection (ALND)). Data analysis was conducted via linear regression and a non-parametric Mann-Kendall test to assess a temporal trend and Sen's slope. Results: 36,636 patients with DCIS met inclusion criteria: 17,883 underwent MAST and 18,753 underwent BCS. Analysis of 2005-2016 trends revealed the following changes in ALN management in DCIS patients: SLNB or ALND increased in MAST patients from 53.6% to 69.5% (Sen's slope 1.5%, R^2 0.69, $p < 0.01$), while it changed little in the BCS population: 22.5% to 26.4% (Sen's slope 0.4%, R^2 0.18, $p = 0.09$). MAST patients undergoing immediate reconstruction tended to undergo ALN surgery more frequently than when undergoing MAST alone. However, the MAST alone group saw the most dramatic trend towards current guidelines, where ALN surgery rates increased from 48.6% to 65.1% (Sen's slope 1.5%, R^2 0.79, $p < 0.01$). Conclusions: Despite national guideline recommendations for the management of ALNs in patients undergoing breast surgery for DCIS, nearly 30% of cases continue to not follow these guidelines. Further investigation is needed as to why such a high rate of cases are not following guidelines, as well as future education endeavors to promote guideline adherence.

TABLE 1 Axillary Lymph Node Surgery Trend Analysis in DCIS Patients

Surgery Method	Mastectomy		Breast-conserving Surgery	
2005-2016 Trends in ALNSx	Mastectomy Alone	Mastetomy with Immediate Reconstruction	Lumpectomy	Oncoplastic Surgery
2005 Rate of ALNSx	46.8%	61.9%	22.8%	0.0%
2016 Rate of ALNSx	65.1%	72.8%	25.9%	31.8%
R^2	0.76	0.60	0.11	0.28
Sen's Slope	1.5%	1.0%	0.3%	1.1%
p value	<0.01	<0.01	0.45	0.24

ALNSx, *axillary lymph node surgery*

111

Outpatient Mastectomy Outcomes: Breast Cancer Surgery in the Era of ERAS® K. Jogerst,* O. Thomas, H. Kosiorek, R. Gray, P. Cronin, W. Casey, A. Rebecca, R. Craner, T. Young-Fadok, B. Pockaj. *General Surgery, Mayo Clinic Arizona, Phoenix, AZ.*

Background: Enhanced recovery after surgery (ERAS®) principles have been beneficial in major abdominal surgery. ERAS® was instituted in our breast surgery practice in 2017. The goal of this study was to evaluate the feasibility of outpatient mastectomies before and after ERAS® protocol. Methods: A retrospective review of all mastectomies between 1/2013- 6/2018 was performed. Exclusion criteria: patients receiving autologous flap reconstruction. The institution-specific ERAS® pathway began February 1, 2017. Patient characteristics, operative intervention, and postop outcomes were compared between pre-ERAS® and post-ERAS® groups and between outpatient and inpatient subgroups. Continuous and categorical variables were compared using Wilcoxon rank sum and Chi-Square analysis, respectively. Results: 470 patients were analyzed. 348 (74%) were prior to ERAS®, 122 after (26%). Same day discharge occurred in 53.3% of post-ERAS® patients vs. 6.9% of pre-ERAS® patients. The two groups were not significantly different in background characteristics except the post-ERAS® group was less likely to have had prior breast surgery, 11.6% vs 21.3%. Liposomal bupivacaine intercostal block was used for pain-control more in post-ERAS® patients, 58.2% vs. 6.6%. Reconstruction type differed with 100% of post-ERAS® group undergoing direct-to-implant reconstruction vs 92% of pre-ERAS® patients. The implant was submuscular in 84.5% of pre-ERAS® vs. 30.3% of post-ERAS® group. Acellular dermal matrix was used more often in the pre-ERAS® group 76.3%, vs the post-ERAS® group (30.3%). In the post-ERAS® era neoadjuvant therapy was more common, 48.4% vs 34.5%, and patients were more likely to receive radiation, 29.5% vs 19.5%. Complications rates, including hematomas, were lower in the post-ERAS® group vs the pre-ERAS® group, 34.4% vs 52.9%, p<0.001. Overall complication rates did not differ between outpatient and admitted subgroups, except for lower hematoma rates in the outpatient group. Post-ERAS® outpatient vs admitted mastectomies are compared in the table below. Conclusion ERAS® principles can be applied to breast cancer patients and allow for outpatient mastectomies with no increase in postoperative morbidity.

Table I: Post-ERAS Outpatient Mastectomy Outcomes

Characteristics	Post-ERAS® Admission Status		Total	P-Value
	Outpatient	Post-Operative Admission		
Age, Mean (SD)	58.2 (12.3)	54.3 (14.4)	56.4 (13.4)	0.085 [1]
Body Mass Index, Mean (SD)	26.1 (5.1)	27 (5.6)	26.5 (5.3)	0.342 [1]
Final Cancer Stage 0, n (%)	9 (14.1)	5 (9.6)	14 (12.1)	0.224 [2]
Final Cancer Stage I, n (%)	21 (32.8)	12 (23.1)	33 (28.4)	
Final Cancer Stage II, n (%)	20 (31.3)	22 (42.3)	42 (36.2)	
Final Cancer Stage III, n (%)	11 (17.2)	13 (25)	24 (20.7)	
Final Cancer Stage IV, n (%)	3 (4.7)	0 (0)	3 (2.6)	
Neoadjuvant Treatment, n (%)	32 (49.2)	27 (47.4)	59 (48.4)	0.837 [2]
Reconstruction, n (%)	27 (41.5)	39 (68.4)	66 (54.1)	0.003 [2]
Bilateral + Reconstruction, n (%)	22 (64.7)	30 (75)	52 (70.3)	0.334 [2]
Axillary Lymph Node Dissection, n (%)	57 (87.7)	53 (93)	110 (90.2)	0.328 [2]
Liposomal Bupivacaine Used, n (%)	46 (70.8)	25 (43.9)	71 (58.2)	0.003 [2]
Pertinent Comorbidities, n (%)	20 (30.8)	17 (29.8)	37 (30.3)	0.910 [2]
Complications, n (%)	19 (29.2)	23 (40.4)	42 (34.4)	0.425 [2]
Hematoma, n (%) [3]	0 (0)	6 (10.5)	6 (4.9)	0.007 [2]

1Wilcoxon rank sum p-value; 2Chi-Square p-value; 3Of the six hematomas: two were subclinical and did not require surgical intervention. Three were noted in the PACU or shortly after transfer to the floor and taken back to surgery immediately. The sixth one was surgically evacuated at OSH after patient sustained chest trauma while on therapeutic anticoagulation for atrial fibrillation.

112

What Factors Influence Clinical Trial Implementation? Results from an NAPBC Survey A. Weiss,[1]* N. Lopez,[2] A. Caudle,[3] K. Lee,[1] D. Dickson-Witmer,[4] K.J. Kelly,[2] L. Jacobs,[5] L. Williams Martin,[6] C. Chang,[7] K. Hunt,[3] K. Yao,[7] S. Blair.[2] *1. Surgery, Brigham and Women's Hospital, Boston, MA; 2. UC San Diego, San Diego, CA; 3. UT MD Anderson Cancer Center, Houston, TX; 4. Christiana Care, Newark, DE; 5. Johns Hopkins Medical Institute, Baltimore, MD; 6. University of Virginia, Charlottesville, VA; 7. Northshore University Health System, Evanston, IL.*

Background: It can be two decades before clinical trial results are implemented after publication. Provider-reported barriers to clinical trial implementation have never been reported. Methods: We report a cross sectional survey of physicians who work at breast centers accredited by the National Accreditation Program for Breast Centers (NAPBC). Survey questions were developed by the American College of Surgeons Clinical Research Program Dissemination and Implementation committee. Participants were asked about factors that prevent clinical trial implementation. Results: There were 1226 providers at 382 institutions, a 68% provider response rate. Most institutions (75%) were hospital-based practices; 23% were in the Northeast, 32% in the Midwest, 32% in the South, 13% in the West. 46% were 0-200 bed hospitals and 13% were affiliated with a medical school. Providers identified national guidelines and meetings as the most compelling way to receive practice changing information (Table). 47% reported that patient preferences were the largest barrier to clinical trial implementation, 39% reported strongly held beliefs by partners/colleagues, 31% added time to discuss new practices, and 26% lack of access to new trial information. Fear of legal repercussions, outdated trial findings, or difficulty interpreting published results were each reported as barriers by <20% of respondents. Providers felt the following at least sometimes prevent clinical trial implementation: lack of agreement from multidisciplinary tumor board (33%), fear of reimbursement loss (24%), resistance from clinical staff (20%), risk of losing referrals (19%), and reprimand from institutional quality committee (11%). There were no significant differences in reported barriers by practice type, location, hospital size. Non-affiliated providers reported a lack of access to new trial information more often than medical school-affiliated (P=.05). Conclusions: Providers consider national guidelines and conferences their most important source of practice changing information. However, there is opportunity to address significant barriers with tumor board interventions, or novel patient-facing materials like video education.

Route of information	Percent that considers this route the most compelling way to obtain practice changing information*
National guidelines	40%
National meetings	33%
Journal articles	20%
Local tumor board	7%
UpToDate Inc.	5%
Email blasts from specialty organization	3%
Email blasts from journals	2%
Online video/streaming	1%
Social Media	1%

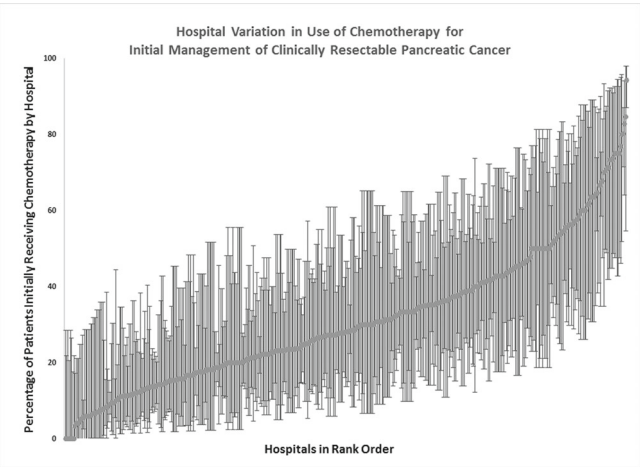
*could report more than 1 option as the most compelling, added values >100%

113

National Use of Chemotherapy in Initial Management of Stage I Pancreatic Cancer and Failure to Perform Subsequent Resection R.J. Ellis,* C.R. Schlick, R.P. Merkow, D.J. Bentrem, K.Y. Bilimoria, A.D. Yang. *Surgical Outcomes and Quality Improvement Center, Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL.*

INTRODUCTION: Neoadjuvant therapy is increasingly used in select patients with early stage, resectable disease. The national prevalence and outcomes of this practice are poorly understood. Our objectives were to (1) describe utilization of chemotherapy in initial management of Stage I pancreatic cancer and (2) define hospital variability in subsequent surgical resection. METHODS: The National Cancer Database was used to identify patients from 2006-2015 treated for clinical Stage I pancreatic adenocarcinoma. Patients were classified as receiving surgery or chemotherapy as initial treatment. In those initially managed with chemotherapy, rates of subsequent surgical resection were calculated. Associations between patient/hospital factors and both initial management and subsequent resection were assessed by hierarchical

multivariable logistic regression. RESULTS: A total of 19,561 patients at 1,204 hospitals were included in the study. Overall, 69.6% had surgery and 30.4% underwent chemotherapy as initial treatment. Initial management with chemotherapy was more likely in patients who were ≥80 years old (OR 2.10, 95%CI 1.73-2.55), had T2 tumors (OR 2.14 vs T1, 95%CI 1.98-2.31) or were treated at a low volume center (OR 1.84, 95%CI 1.30-2.60). Significant hospital variation was observed in use of upfront chemotherapy (range 0% to 94.3%; Figure). Among patients receiving initial chemotherapy, only 27.6% subsequently underwent attempted resection. Subsequent resection was more likely in patients with T1 tumors (OR 1.21 vs T2, 95%CI 1.05-1.41) and in those treated at academic centers (OR 1.74, 95%CI 1.41-2.14) or high-volume centers (OR 2.55, 95%CI 1.40-4.64). Only 15% of hospitals attempted resection in >50% of patients after initial management with chemotherapy. CONCLUSION: Early stage pancreatic cancer is still often managed initially without surgery. The proportion of patients that eventually undergo resection varies considerably between hospitals. Underuse of surgery after initial chemotherapy remains a significant problem and should be considered as an internal quality of cancer care measure to encourage appropriate surgical referrals.



Measured hospital-level rates of utilization of chemotherapy as initial management of Stage I pancreatic cancer (blue dots) with 95% confidence intervals (bars) demonstrating both low and high outliers in initial use of chemotherapy.

114

How We Define Volume in Complex Surgical Oncology Impacts Its Association with Outcomes R. Williams,[1]* J. Levy,[2] N. Hanna,[1] B. Lal,[1] C. Mullins.[1] *1. University of Maryland, Baltimore, MD; 2. Johns Hopkins, Baltimore, MD.*

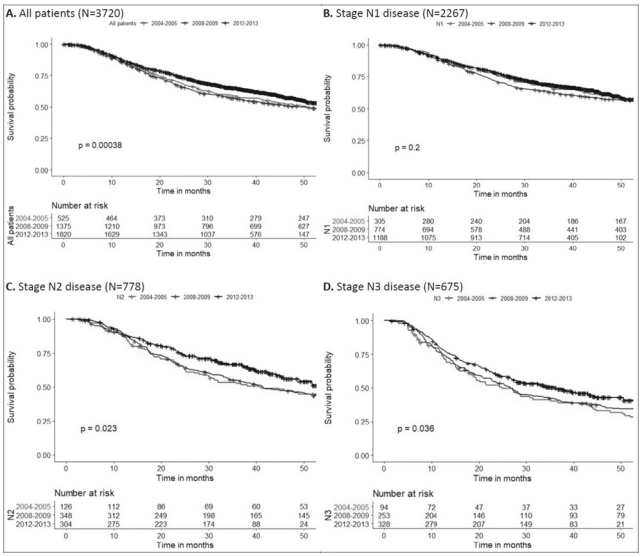
There is an inverse relationship between surgical volume and outcome. This led to initiatives advocating referral of patients undergoing high-risk procedures like esophagectomy and pancreatectomy to high volume hospitals/surgeons. However, surgical volume is inconsistently defined in the literature. This study examines the impact of different definitions of surgical volume on the volume-outcome relationship. We analyzed 1991 esophagectomy and 8295 pancreatectomy patients in New York State Inpatient Database, 2009-2014. High volume hospitals/surgeons were defined using annual volume thresholds (hospital 20, surgeon 5) from "Take the Volume Pledge" (NEJM 2015; 373:1388) and varying whether all procedures counted toward volume or only procedures done for cancer. Generalized linear models were used to assess the independent effect of volume on length of stay, cost, mortality, readmission. 43% of esophagectomies (848) and 47% of pancreatectomies (3891) were done for cancer. When all procedures were used to derive volume, 6% of hospitals were high volume for esophagectomy and 13% for pancreatectomy. When only cancer procedures were used, high volume hospitals dropped to 3% and 9% for esophagectomy and pancreatectomy respectively. With all procedures 7% of surgeons were high volume for esophagectomy, which dropped to 3% with only cancer procedures. For pancreatectomy, high volume surgeons decreased from 9% to 5%. High volume surgeon was an independent predictor of reduced surgical mortality with all esophagectomies (OR 0.31, $p<0.001$) but not for cancer esophagectomies. For pancreatectomy, high volume hospital predicted reduced mortality (OR 0.34, $p<0.01$) for all procedures but not cancer procedures. This effect was reversed for high volume surgeons, with a significant effect for cancer procedures (OR 0.4, $p<0.001$) but no effect for all pancreatectomies. High volume hospital reduced readmission in cancer patients (OR 0.74, $p<0.001$) but had no effect for all pancreatectomies. How we define volume impacts conclusions about the effect of volume on short-term outcomes. Volume must be consistently defined to facilitate fair comparisons across studies and to be used for selective referral.

115

Clinical Stage III Melanoma in the Contemporary Therapeutic Era Y. Song,* A.D. Tieniber, T.C. Mitchell, R.K. Amaravadi, L.M. Schuchter, D. Fraker, G. Karakousis. *Hospital of the University of Pennsylvania, Philadelphia, PA.*

Introduction: Immune checkpoint inhibition and targeted therapies have demonstrated significant impact on outcomes in patients diagnosed with advanced melanoma within the context of clinical trials. We sought to determine the overall survival (OS) in clinical stage III melanoma patients at a population level in the contemporary therapeutic era. Methods: Patients newly diagnosed with clinical stage III melanoma who underwent regional lymph node (LN) surgery were identified using the National Cancer Database. Patients were categorized by diagnosis year into historic (P1 2004-05, P2 2008-09) and contemporary (P3 2012-13) cohorts. The primary outcome was OS estimated using the Kaplan-Meier method. Factors associated with OS were identified using multivariate Cox proportional hazards model. Results: Of 3720 patients, 525 (14%) were diagnosed in P1, 1375 (37%) in P2, and 1820 (49%) in P3. Median age (58, 59, 61 years in P1, P2, P3, respectively, P=0.004) and the use of adjuvant radiation (15%, 18%, 21% in P1, P2, P3, respectively, P<0.001) increased over time. The number of positive LN, number of LN removed, and use of adjuvant immunotherapy and chemotherapy did not differ by diagnosis period. OS was significantly longer in P3 (median 58.2 months) than both P1 (50.5 months, log-rank P=0.035) and P2 (49.3 months, log-rank P<0.001), but did not differ between P1 and P2 (log-rank P=0.91). In the multivariate Cox model, diagnosis in P3 was associated with reduced hazard ratio (HR) compared to P1 (HR 0.75, P<0.001), and the difference was most pronounced for N3 disease (HR 0.66, P=0.005). Extent of LN surgery was associated with OS only for N3 disease (≥10 vs. <5 LN removed, log-rank P=0.02), but was not significant in the multivariate Cox model (P=0.18). Conclusions: OS has significantly improved for clinical stage III melanoma patients diagnosed in the contemporary therapeutic era and will likely continue to do so as these therapies are increasingly used in the adjuvant setting. Extent of LN surgery in this population does not appear to impact survival. Increased awareness of these changing outcomes is important when counseling patients with newly diagnosed locally advanced melanoma.

Figure 1. Overall survival of patients newly diagnosed with clinical stage III melanoma by period of diagnosis



OS: overall survival.
A. OS for all clinical stage III patients by diagnosis year. OS was significantly longer for patients diagnosed in 2012-2013 compared to 2004-2005 (P=0.035) and 2008-2009 (P<0.001). There was no difference in OS between the 2004-2005 and 2008-2009 cohorts (P=0.91).
B. OS for patients with clinical N1 disease. There was no significant difference in OS by diagnosis year.
C. OS for patients with clinical N2 disease. OS was significantly longer for the 2012-2013 compared to the 2008-2009 cohort (P=0.013), but did not reach statistical significance compared to the 2004-2005 cohort (P=0.056). There was no difference in OS between the 2004-2005 and 2008-2009 cohorts (P=0.79).
D. OS for patients with N3 disease. OS was significantly longer for patients diagnosed in 2012-2013 compared to 2004-2005 (P= 0.043), but did not reach statistical significance compared to 2008-2009 (P= 0.061). There was no difference in OS between the 2004-2005 and 2008-2009 cohorts (P= 0.23).

116

Prognostic Significance of Acellular Mucin in Patients Undergoing Cytoreductive Surgery and HIPEC (CRS/HIPEC) for Appendiceal Neoplasm C.P. Scally,* K. Robinson, K. Beaty, S. Rafeeq, K. Raghav, C. Eng, M. Overman, W. Foo, M. Taggart, P. Mansfield, R. Royal, K. Fournier. *MD Anderson Cancer Center, Houston, TX.*

Introduction: Appendiceal cancers are rare tumors with propensity for peritoneal dissemination. The standard of care for select individuals is CRS/HIPEC. The behavior of these tumors after surgical resection is difficult to predict; peritoneal recurrence is common. In the current 8th AJCC Staging system, a finding of only intraperitoneal acellular mucin (M1a) during CRS/HIPEC is classified as Stage IVA. There is concern that the current AJCC classification system may over-stage patients. Methods: We conducted a single-institution retrospective review of patients with mucinous appendiceal adenocarcinoma (MAA) from 1993-2016. Patients undergoing CRS/HIPEC for whom final pathology demonstrated only intraperitoneal acellular mucin (M1a disease) were included for analysis. Overall and recurrence-free survival were assessed and compared to patients with peritoneal mucinous deposits containing tumor cells and well-differentiated MAA (M1b, G1). We also investigated the yield of postoperative surveillance protocols. Results A total of 68 patients had M1a disease at the time of surgery. Median follow-up was 5.9 yrs (IQR 3.3-9.2). 5 year overall survival was 98% (95% CI 88-100%); 5 year recurrence free survival was 100%. In comparison, patients with M1b G1 disease (also considered Stage IVA) had 88% overall (80-94%) and 74% 5 year RFS (64-82%). During postoperative surveillance, 65 patients had tumor markers (CEA, CA-125, CA 19-9) checked regularly; 23 (35%) patients had increased markers, with a median time to marker increase of 8.3 years. In 17 cases these were transient or low-level elevations. None of the patients with elevated markers had evidence of disease recurrence. Conclusions: A finding of only acellular mucin after CRS/HIPEC for MAA is associated with extremely high rates of overall and recurrence-free survival. The presence of acellular mucin in the peritoneal cavity should not be perceived as a metastatic equivalent. Current AJCC staging does not accurately reflect this prognostic finding. Our analysis indicates that high-intensity surveillance may have limited benefit in this patient population.

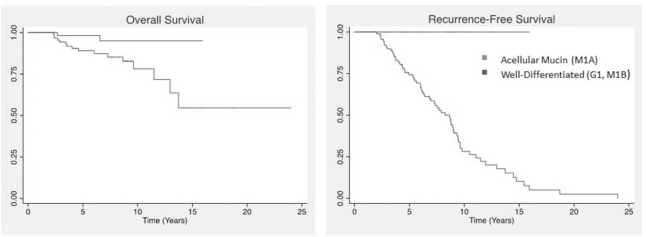


Figure. Overall and Recurrence-Free survival for patients with appendiceal adenocarcinoma and acellular mucin within the peritoneal cavity (M1A disease) compared to patients with well-differentiated adenocarcinoma and epithelial neoplastic cells in the peritoneal cavity (G1, M1B disease)

117

Variation in Inadequate Lymphadenectomy for Gastric, Lung, and Bladder Cancer: Attributable to the Surgeon, Pathologist, or Hospital? C.T. Aquina,* R. Kaur, Z. Xu, C.F. Justiniano, M. Truong, A.Z. Becerra. *Surgery, University of Rochester, Rochester, NY.*

Introduction: The Commission on Cancer recently released quality of care measures regarding adequate lymph node yield for colon, gastric, lung, and bladder cancer. Previous studies have evaluated variation in inadequate lymphadenectomy for colon cancer. However, there is currently little information regarding variation in lymph node yield for gastric, lung, and bladder cancer. Methods: The New York State Cancer Registry and Statewide Planning & Research Cooperative System were queried for stage I-III gastric, stage I-II lung, and stage I-III bladder cancer resections from 2004-2014. Multilevel logistic regression analyses assessed factors associated with inadequate lymphadenectomy (gastric <15; lung <10; bladder <2 for patients <80 years old). Additionally, the proportion of variation attributable to the surgeon, pathologist, and hospital was estimated among a subset of Medicare patients. Results: Among 3,822 gastric, 18,766 lung, and 2,276 bladder cancer resections, there were high rates of inadequate lymphadenectomy (gastric=48.4%, lung=64.4%, bladder=37.8%). In comparing 2004-2006 and 2012-2014, there was significant improvement in inadequate lymphadenectomy for gastric cancer (61.7% vs 34.4%, p<0.0001) but more modest improvement for lung (67.2% vs 62.4%) and bladder (39.9% vs 36.4%) cancer. Large variation existed across surgeons, pathologists, and hospitals for each organ system. For gastric and lung cancer, the majority of variation was attributable to hospitals (gastric: surgeon=9%, pathologist=8%, hospital=83%; lung: surgeon=37%, pathologist=7%, hospital=56%). For bladder cancer, nearly all of the variation was attributable to pathologists (surgeon=0.001%, pathologist=99.991%, hospital=0.008%). Conclusions: Inadequate lymphadenectomy rates are high for gastric, lung, and bladder cancer with only modest improvement over time for lung and bladder cancer. Given that the proportion of variation attributable to the surgeon, pathologist, and hospital is different for each organ system, future quality improvement initiatives should appropriately target the underlying causes, which likely vary by individual organ system.

Table: Variation in Inadequate Lymphadenectomy Rates Across Surgeons, Pathologists, and Hospitals

	Gastric Cancer (Median Rate [Range])	Lung Cancer (Median Rate [Range])	Bladder Cancer (Median Rate [Range])
Surgeon	76.4% (16.8–87.4%)	79.2% (31.0–95.2%)	38.8% (35.2–46.1%)
Pathologist	75.5% (21.8–89.6%)	77.5% (36.2–92.0%)	40.7% (27.2–50.0%)
Hospital	79.2% (21.3–90.4%)	81.2% (43.5–93.2%)	40.6% (27.6–49.2%)

118

Association Between Preoperative Patient-Reported Symptoms and Postoperative Outcomes in Rectal Cancer Patients: A Retrospective Cohort Study L. Bubis,[1]* N. Coburn,[1] R. Sutradhar,[2] V. Gupta,[1] Y. Jeong,[1] L. Davis,[3] Q. Li,[2] A. Mahar,[4] P. Karanicolas.[1] *1. University of Toronto, Toronto, ON, Canada; 2. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada; 3. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 4. University of Manitoba, Winnipeg, MB, Canada.*

Background:Rectal cancer patients undergoing preoperative radiotherapy experience significant symptom burden. However, it is unknown whether symptoms reported during radiotherapy may portend adverse postoperative outcomes and healthcare utilization following proctectomy. Methods:A retrospective cohort study was performed of rectal cancer patients undergoing neoadjuvant radiotherapy and proctectomy in Ontario from 2007-2014. The primary outcome was a complicated postoperative course – a dichotomous variable created as a composite of postoperative mortality, major morbidity, and hospital readmission. Patient-reported Edmonton Symptom Assessment System scores were linked to administrative healthcare databases. Receiver-operating characteristic analysis was used to compare ESAS scoring approaches and to stratify patients into low vs. high symptom score groups. Multivariable regression models were constructed to evaluate the association between preoperative symptom scores and postoperative outcomes. Results:1455 rectal cancer patients underwent sequential radiotherapy and proctectomy during the study period and recorded symptom assessments. Patients with worse preoperative symptom scores were significantly more likely to experience a complicated postoperative course (OR 1.55, 95%CI 1.23-1.95). High preoperative ESAS scores were also associated with secondary outcomes of emergency department visits (OR 1.34, 95%CI 1.08-1.66), and prolonged length of stay (IRR 1.23, 95%CI 1.04-1.45). Conclusions:Rectal cancer patients reporting elevated symptom scores during neoadjuvant radiotherapy are at increased odds of experiencing a complicated postoperative course. Preoperative patient-reported outcome screening may be a useful tool to identify at-risk patients and to efficiently direct perioperative supportive care.

119

A Telehealth Prehabilitation-to-Rehabilitation Intervention for Older Cancer Surgery Patients and Their Family Caregivers V. Sun,* K.J. Lafaro, D. Raz, N. Ruel, S. Hite, J. Kim, G. Varatkar, L. Erhunmwunsee, L.G. Melstrom, B. Lee, G. Singh, A. Hurria, Y. Fong. *City of Hope, Duarte, CA.*

Background: Older adults undergoing cancer surgery are at greater risk for poor postoperative outcomes. Family caregivers (FCGs) also endure significant burden. Prehabilitation/rehabilitation may improve physical/psychological functioning and enhance overall well-being for both patients and FCGs. In this study, we assessed the feasibility of a telehealth prehab-to rehab intervention for older (≥65 years) GI and lung cancer surgery patients/FCGs. Methods: Participants completed four telehealth sessions with PT/OT before surgery and up to 2 weeks post-discharge. Outcomes included pre-op geriatric assessment, functional measures (pedometer steps, 6MWT, TUG, SPPB), and validated PROs (distress, QOL). Data were summarized descriptively over time, and stratified by participant type and diagnosis. Pre/post-intervention trends/trajectories for outcomes were explored. PT/OT notes were qualitatively analyzed to explore facilitators of adherence. Results: 34 patient/caregiver dyads (16 GI, 18 lung) were included. Accrual rate was 76% over 8 months; retention rate was 88% over 2 months. Pre-op ADLs were normal (mean=13; SD=1.5). Median for postop 6MWT exceeded baseline values for GI patients (411m vs. 396m). Mean TUG scores gradually improved from baseline to postop for lung patients (10.0sec to 9.1sec). Improvements in mean SPPB score were observed from pre- to post-discharge (GI: 6.0-7.5; lung 6.4-8.2). Preop adherence to pedometer was 79%, and 68% postop. Preop median number of steps was 6324; this decreased to 1050 during hospitalization and gradually increased to 2927 in the first 2 weeks after discharge. Family caregiver distress levels were higher than patients at all timepoints. Participant satisfaction scores were high (4/5). Social support, coping strategies, goal setting, and reminders facilitated adherence to the intervention. Conclusion: Conceptually-based, multimodal, telehealth prehab-to-rehab intervention for older patient/caregiver dyads is feasible and acceptable. It offers an opportunity to improve post-operative outcomes by promoting perioperative physical activity through telehealth and telemonitoring approaches.

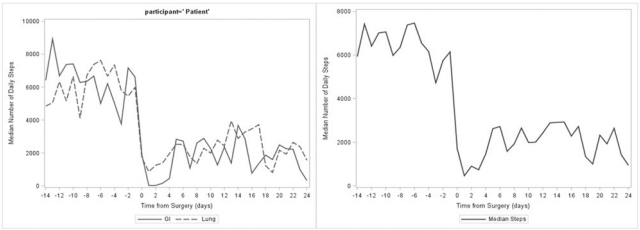


Figure 1. Daily Steps Trajectory and Trends Before Surgery, During Hospitalization, and Up to 2 weeks Post-Discharge, by Diagnosis (Lung, GI) and Entire Cohort

120

Disproportionate K-Grant Conversion Rates for Surgical Oncologists T. Nguyen,* A. Uppal, A. Teng, T.D. Fischer, A. Bilchik. *Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA.*

Background: NIH funding has been increasingly difficult to obtain, particularly for surgeon scientists. Career development K grants were designed as mentored awards to facilitate early and mid-career scientists on the path to pursue research independently and to receive major NIH grant support. We sought to determine whether there was a disparity in K award grant conversion rates to independent NIH research project grants (R level grants) between surgical oncologists and medicine departments. Methods: The NIH Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER), a publicly available database of NIH funded projects, was queried for fiscal years 2006-2017 for K level and R level grants awarded to surgery and medicine departments. Grant awardee information including fellowship training data was obtained from the faculty webpages. Results: Between 2006-2017, 41 surgical oncologists were awarded career development K grants. During that time period, 10 obtained R level grants for a K award conversion rate of 24.4%. The mean number of publications per award for those who converted was significantly higher than those who did not obtain R level grants (22.9 v. 13.1 publications, p=0.04). During the same time period 167 oncology related K grants were awarded to physicians in medicine departments with a K grant conversion rate of 49.7% (83/167 grants). The mean number of publications per K award in medicine for those who converted to R level grants was 16.8 compared to 9.3 for those who did not. Conclusion: Surgical oncologists had a lower K grant conversion rate to R level grants compared to their medicine counterparts despite having a trend towards a higher publication rate per awarded K grant.

121

The Effect of Palliative Care on Symptom Burden in Patients with Gastrointestinal Cancer S. Merchant,[1]* S. Brogly,[1] C. Booth,[1] C. Goldie,[1] S. Nanji,[1] S. Patel,[1] K. Lajkosz,[1] N. Baxter.[2] *1. Surgery, Queen's University, Kingston, ON, Canada; 2. University of Toronto, Toronto, ON, Canada.*

Introduction: The symptom profile in patients with cancer and the association between palliative care (PC) and symptom burden has not been studied in the general population. We addressed this knowledge gap in patients with gastrointestinal (GI) cancer in the final year of life. Methods: Patients who died of esophageal, gastric, colon and anorectal cancers during 2003-2015 were identified from the Ontario Cancer Registry. Health information was derived from administrative data. Symptom severity scores were recorded in the year before death with the Edmonton Symptom Assessment System (ESAS) which includes scores from 0-10 in nine domains. ESAS scores were categorized as none-mild (≤3) or moderate-severe (≥4-10). Adjusted associations between outpatient PC and moderate-severe ESAS scores were determined in a cross-sectional cohort using logistic regression. The effect of PC initiation on ESAS scores was estimated in a prospective cohort of patients using generalized estimating equations. Results: The cohort included 11,242 patients who died of esophageal (17%), gastric (20%), colon (38%), and anorectal (26%) cancers. Mean age was 67.0 years and 63% were male. Fifty percent of patients experienced moderate-severe scores in tiredness, lack of well-being and lack of appetite earlier (weeks 18-12 before death), whereas 50% experienced moderate-severe scores in drowsiness, pain and shortness of breath later (weeks 5-2 before death) in the disease course. Most patients (78%)

received outpatient PC after cancer diagnosis. In the cross-sectional cohort, outpatient PC was associated with increased likelihood of having moderate-severe scores in all symptom domains, with highest symptom burden in pain (OR 1.86, 95% CI 1.68, 2.05). In PC-naïve patients with moderate-severe scores, initiation of outpatient PC was associated with a one to three point decrease in subsequent scores, with greatest reductions in the pain (-1.91, 95% CI -2.11, -1.70) and nausea (-3.01, 95% CI -3.31, -2.71) domains. Conclusions: Patients with GI cancer experience high symptom burden in the final year of life. Outpatient PC initiation is associated with a clinically meaningful decrease in patient-reported symptoms.

122

Educating Providers on Perioperative Opioids in Surgical Oncology: Results of a Departmental Survey on Perceptions of Opioid Needs and Prescribing Habits H.A. Lillemoe,* T.J. Vreeland, T.E. Newhook, E.M. Arvide, W.L. Dewhurst, E.G. Grubbs, T. Aloia, J.E. Lee, C.D. Tzeng. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: Patients undergoing oncologic surgery are at an increased risk for persistent postoperative opioid use. As part of a quality improvement initiative, we sought to quantify provider perceptions regarding acceptable opioid prescribing habits after oncologic procedures. Methods: Attending surgeons, clinical fellows, and advanced practice providers (APPs) in the Department of Surgical Oncology at a high-volume institution were surveyed before and after education sessions on perioperative opioid use. The sessions included literature review and retrospective analyses of departmental prescribing patterns. Results: The response rate for the pre-education survey was 72/103 (70%): 22/34 (65%) attendings, 19/21 (90%) fellows, 31/48 (65%) APPs. For all 5 index operations (port, colectomy, thyroidectomy, wide local excision, open abdominal cancer resection), fellows answered that patients should be off opioids at shorter postoperative intervals than attendings and APPs. For all cases except open abdominal resection, APPs recommended greater numbers of opioid pills than attendings and fellows. 45% (46/103) completed both pre-/post-surveys. The matched post-education cohort recommended lower numbers of opioid pills for all procedures and thought that patients should be off opioids sooner (Table 1). There was 95% median agreement (IQR 69-100) regarding plans to prescribe less opioids following the education session. Compared to pre-education, more providers agreed that discharge opioid prescriptions should be based on a patient's last 24 hours of inpatient opioid use (83% vs. 91% median agreement, p=0.006). Conclusions: There is wide variation in perceived perioperative opioid prescribing habits among provider types with those most involved in the daily care and discharge process tending to recommend more opioids. After education, providers significantly lowered their recommended discharge opioid amounts and felt that patients should be off opioids sooner. Next steps include assessing for quantitative changes in actual opioid prescribing habits and implementing a standardized opioid prescribing algorithm.

Table 1. Perceptions of Opioid Needs and Prescribing Habits, Pre- vs. Post-Educational Intervention*

	Pre-Education	Post-Education	P value
Open Abdominal Cancer Resection			
Pain Score at Discharge	3 (3, 4)	3 (3, 4)	0.959
# Opioid Pills at Discharge	28 (20, 30)	20 (10, 22)	<0.001
Postop Day off Opioids	10 (7, 14)	7 (5, 10)	<0.001
Laparoscopic Colectomy			
Pain Score at Discharge	3 (2, 3)	2 (2, 3)	0.235
# Opioid Pills at Discharge	20 (11, 27)	10 (5, 20)	<0.001
Postop Day off Opioids	5 (4, 7)	5 (3, 7)	0.008
Wide Local Excision with Sentinel Lymph Node Biopsy			
Pain Score at Discharge	2 (2, 3)	2 (1, 3)	0.569
# Opioid Pills at Discharge	10 (10, 20)	10 (5, 10)	0.005
Postop Day off Opioids	5 (3, 7)	3 (2, 5)	<0.001
Total Thyroidectomy			
Pain Score at Discharge	2 (2, 3)	2 (2, 3)	0.266
# Opioid Pills at Discharge	10 (7, 20)	6 (0, 10)	<0.001
Postop Day off Opioids	3 (2, 6)	3 (1, 4)	0.005
Port Placement			
Pain Score at Discharge	2 (1, 3)	2 (1, 2)	0.726
# Opioid Pills at Discharge	6 (0, 10)	0 (0, 8)	<0.001
Postop Day off Opioids	2 (0, 3)	1 (0, 2)	0.022

*Values listed as median (interquartile range, IQR); Wilcoxon Signed Rank test; numerical score in 0-10 pain scale; pills with 1 standard pill=5mg hydrocodone=50mg tramadol; days post-operation

123

Variation in Contemporary Perioperative Opioid Prescribing Practices in Surgical Oncology T. Newhook,[1]* T.J. Vreeland,[1] W.L. Dewhurst,[1] E.M. Arvide,[1] M. Bruno,[1] K. Robinson,[1] N.F. Rajkot,[1] H.A. Lillemoe,[1] N. Kuete,[2] E.G. Grubbs,[1] T. Aloia,[1] M.H.G. Katz,[1] J. Vauthey,[1] J.E. Lee,[1] C.D. Tzeng.[1] *1. MD Anderson Cancer Center, Houston, TX; 2. Morehouse School of Medicine, Atlanta, GA.*

Background: Characterization of current perioperative opioid prescribing practices is imperative to inform prospective opioid reduction strategies after cancer surgery. The primary aim of this study was to enumerate and compare opioid prescriptions among a range of index cancer operations. Methods: Data were abstracted for a convenience sample of gastric, peritoneal surface, pancreas, sarcoma, and hepatic surgery at a high-volume cancer center from 2016 to 2018. Inpatient and discharge opioid use (in oral morphine equivalents [OME]) were summarized and compared. Results: A total of 904 patients who underwent gastric (n=111, 12%), peritoneal surface (n=132, 14.6%), pancreas (n=158, 17.5%), sarcoma (n=192, 21.2%), and liver (n=311, 34%) operations. Median total inpatient OME was 165mg (range 0-7,308mg): highest after pancreatectomy (median 423mg, range 0-4,362mg) and lowest after liver resection (median 95mg, range 0-1,657mg; Fig 1A). Median discharge prescription OME was 300mg (range 0-8,360mg): highest after peritoneal surface operations (median 600mg, range 0-5,430mg) and lowest after liver resection (median 200mg, range 0-3,600mg; Fig 1B). 23% (n=208) of patients used zero opioids in the last 24 hours of their inpatient stay, yet the majority of these patients (n=172/208, 82.7%) received opioids at discharge (median 218mg, range 8-1000mg). Overall, 211 patients (23%) did not receive any discharge opioids. Discharge OME had weak correlation with total inpatient (Pearson r=0.48, p<0.001; Fig. 1C) and final 24 hour OME (Pearson r=0.59, p<0.001). A hypothetical multiplier of 5 times a patient's last 24 hours inpatient OME would decrease overall discharge OME volume by 66%, which in this cohort of 904 patients would equal 275,445mg of morphine, which can be visualized as over 36,000 oxycodone 5mg tabs or over 55,000 tramadol 50mg pills. Conclusion: Wide variation in opioid administration occurs following cancer surgery, providing a salient opportunity for quality improvement. Coordinated prospective efforts to decrease opioid use in the hospital and standardize discharge prescriptions can limit opioid dissemination among cancer survivors, their families, and communities.

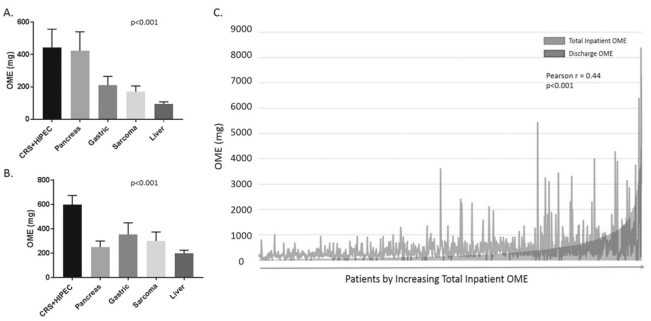


Figure 1. Opioid use following oncologic surgery. **A.** Median total inpatient OME following oncologic surgery by disease site, 95% CI. **B.** Median discharge prescription OME following oncologic surgery by disease site, 95% CI. **C.** Graph of all patients following oncologic surgery in study by total inpatient OME with superimposed corresponding discharge prescription OME.

124

Maintaining Functional Status in Elderly Cancer Patients Using Comprehensive Geriatric Assessments to Guide Interventions E.C. Sturm,[1]* J.C. Hardaway,[1] T. Liu,[2] N.J. Espat,[3] P. Somasundar.[3] *1. Surgical Oncology, Roger Williams Medical Center, Providence, RI; 2. Brown University, Providence, RI; 3. Roger Williams Medical Center affiliate of Boston University, Providence, RI.*

Introduction: The population globally is experiencing a silver tsunami resulting in increasing cancer incidence in the elderly. Chronological age alone is not sufficient to guide intervention. Proper stratification of individuals by geriatric assessment can guide subsequent interventions. We hypothesized that using a structured comprehensive geriatric assessment (CGA) to guide supportive interventions in elderly patients undergoing cancer treatment would result in maintenance of functional status. Methods: From 2012 to 2018, a

cancer center at a single institution performed CGA's on 311 cancer patients aged 65 or older. The CGA included scoring of activities of daily living (ADL), independent activities of daily living (IADL), timed up and go (TUG), mini mental status exam (MMSE), nutrition screen, patient health questionnaire-9 depression screen (PHQ-9), and polypharmacy evaluation. Interventions were implemented according to needs identified. Data was prospectively collected regarding patient demographics, clinical characteristics, CGA results, and interventions applied. A CGA was performed pre-treatment and at 30, 90, and 180 days after treatment was initiated. A retrospective review was then performed, and the CGA scores of the elderly (ages 65-75) and very elderly (age >75) were compared. Trends in patient CGA scores over time were also evaluated. Results: Compared with elderly patients (ages 65-75), the very elderly (age >76) had poorer TUG scores ($\Delta = 2.1$; $p<0.001$), and MMSE scores ($\Delta = -1.3$; $p=0.016$). ADL, IADL, nutrition screen, and polypharmacy scores did not differ significantly between the two age groups. Over time, both age groups showed improved mini mental status exam scores (increasing trend; p=0.006), and less severe depression scores (decreasing trend; p=0.001). Patients had worse polypharmacy over time (increasing trend; p=0.002). IADL, nutrition screens and TUG scores were maintained over time. Conclusion: In elderly cancer patients undergoing treatment, comprehensive geriatric assessments that guide interventions can improve cognitive and psychiatric well-being and can overall maintain functional status.

125

Identifying Factors Predicting Long-Term Narcotic Use After Mastectomy M.R. Woeste,* N. Bhutiani, A. Geller, H. Eldredge-Hindy, K.M. McMasters, N. Ajkay. *Department of Surgery, University of Louisville, Louisville, KY.*

Background: Women who undergo mastectomy for breast cancer are at risk of developing chronic pain and, as a result, may be prone to prolonged opioid use. However, risk factors for long-term narcotic use after mastectomy remain unclear. This study sought to identify risk factors for prolonged opioid use (POU) after mastectomy. Methods: A single-institution database was queried for women who underwent mastectomy for breast cancer between January 2016 and December 2017. Patients were stratified based on opioid use <90 or ≥ 90 days after mastectomy (POU). The Kentucky All-Schedule Prescription Electronic Reporting system was used to confirm all opioid discharge doses. Patients who underwent partial mastectomy and non-Kentucky residents were excluded. Discharge doses were converted into daily oral morphine equivalents (OMEs) using standard ratios provided by the Centers for Disease Control and Prevention. Clinicopathologic and operative parameters as well as preoperative and postoperative narcotic usage were compared. Results: On univariate analysis, younger age (50.6 years POU vs. 59.3 years no POU, p<0.001), concomitant psychiatric illness (46.6% POU vs. 23.3% no POU, p=0.01), preoperative opioid use (22.7% POU vs. 7.0% no POU, p=0.03), breast reconstruction (71.6% POU vs. 46.5% no POU, p=0.007), and higher daily OME dosage at discharge (342.6±310.8 mg POU vs. 240.2±126.7 no POU, p=0.04) were associated with POU. On multivariable analysis, greater daily OME at discharge (odds ratio (OR)=1.02, 95% confidence interval (CI)=1.001-1.04, p=0.03) and preoperative opioid use (OR=6.43, 95% CI=1.46-28.27, p = 0.01) were independently associated with prolonged opioid use. Meanwhile, older age at surgery was independently associated with decreased likelihood of prolonged opioid use (OR 0.94, 95% CI 0.90-0.98, p=0.008). Conclusions: Age at surgery, preoperative opioid use, and daily OME at discharge, but not tumor stage or extent of surgery, may predict POU after mastectomy. These factors should prompt both preoperative discussions about realistic pain management expectations and aggressive multi-modal pain control regimens in the postoperative period.

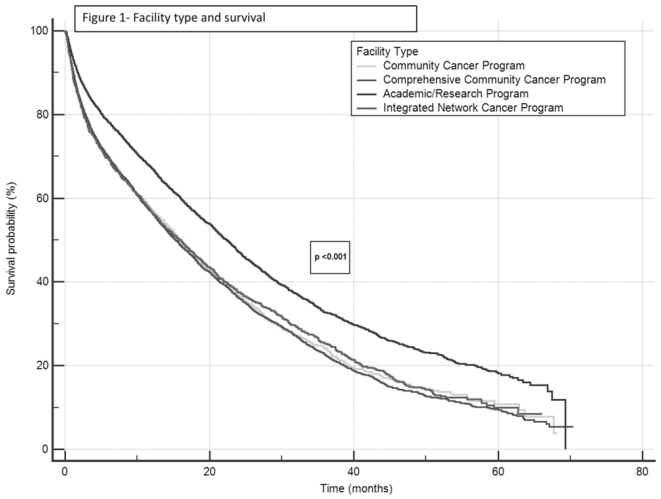
Demographic, tumor and treatment characteristics

	≥90 Days Opioid Use N = 88	<90 Days Opioid Use N = 43	p value
Age (years)	50.6±11.7	59.3±12.1	<0.001
Preoperative opioid use	20 (22.7%)	3 (7.0%)	0.03
Psychiatric illness	41 (46.6%)	10 (23.3%)	0.01
Illicit drug use	10 (11.4%)	1 (2.3%)	0.10
Private Insurance	38 (43.2%)	21 (48.8%)	0.71
Government Insurance	49 (55.7%)	23 (53.5%)	
AJCC Staging			
0	20 (22.7%)	14 (32.6%)	0.36
I	27 (30.7%)	13 (30.2%)	
II	26 (29.5%)	9 (20.9%)	
III	7 (8.0%)	8 (18.6%)	
IV	3 (3.4%)	0 (0.0%)	
Estrogen Receptor (ER) +	63 (71.6%)	37 (86.0%)	0.08
HER2+	14 (15.9%)	9 (20.9%)	0.47
Bilateral mastectomy	49 (55.7%)	17 (39.5%)	0.10
Unilateral mastectomy	39 (44.3%)	26 (60.5%)	
Reconstruction	63 (71.6%)	20 (46.5%)	0.007
Tissue expander/implant	56 (88.9%)	17 (85.0%)	0.76
Axillary dissection	24 (27.3%)	15 (34.9%)	0.42
Regional anesthesia	30 (34.1%)	10 (23.2%)	0.23
Preoperative chemotherapy	23 (26.1%)	11 (25.6%)	1.00
Postoperative chemotherapy	32 (36.4%)	11 (25.6%)	0.24
Radiation therapy	17 (19.3%)	5 (11.6%)	0.33
Daily oral morphine equivalent dose at discharge (mg)	342.6±310.8	240.2±126.7	0.04

126

Disparities in Treatment of Stage IVA Colorectal Cancer with Liver Metastasis: Is it Time to Consider Regionalization of Care? S. Kang,[4]* S. Kerlakian,[4] L. Hussain,[3] H. Guend,[2] E. Dunki-Jacobs,[1] D.Y. Lee.[1] *1. Surgical Oncology, Trihealth Cancer Institute, Cincinnati, OH; 2. Trihealth Surgical Institute, Cincinnati, OH; 3. Hatton Research Institute, Trihealth, Cincinnati, OH; 4. Good Samaritan Hospital General Surgery Residency Program, Trihealth, Cincinnati, OH.*

Introduction We aimed to examine treatment patterns of Stage IVA colorectal cancer (CRC) with liver metastasis (LM) using a national database. Methods The NCDB database was queried from 2010-2014 for patients ≥ 18 years with clinical stage IVA CRC with LM. Demographics, tumor characteristics, treatment pattern, as well as the facility type were noted. Results Of the 18,201 patients who met our study criteria, 53.7% of the patients were male and 79.1% were Caucasians. The average primary tumor size was 5.5 ± 4.8 cm and 18.9% were high grade tumors. Overall, 12.3% of the patients were treated at community cancer programs, 43.7% at comprehensive community cancer programs, 33.2% at academic/research programs (ARP), and 10.9% of the patients at integrated network cancer programs (INP). The rate of surgery at the primary site was higher at non-academic/research programs (NAP) (54.1% vs 45.9%, p <0.001) compared to ARP. However, the rate of metastectomy at the distant site was significantly higher at ARP compared to NAP (23.6% vs 12.2%, p<0.001). On multivariable analysis, treatment at ARP increased the likelihood of metastectectomy (OR 2.05, 95% CI 1.78-2.36, p<0.001). Other factors associated with increased metastectomy include treatment at INP, receipt of chemotherapy and higher income status. Black and Hispanic race, increased age, and higher tumor grade were associated with less likelihood metastectomy. In this database, treatment at ARP was associated with better survival compared to NAP (Figure 1). On multivariable analysis, receipt of chemotherapy (HR 0.33, 95% CI 0.32-0.35, p<0.001), surgery to metastatic site (HR 0.54, 95%CI 0.51-0.57, p<0.001) and treatment at ARP (HR 0.93, 95% CI, 0.87-0.99) improved survival. Right sided primary tumor, higher Charlson/Deyo score, no insurance and Black race were all significantly associated with worse survival. Conclusion Metastectomy, chemotherapy and treatment at APR were associated with improved survival in patients with stage IVA colorectal cancer with liver metastasis. Black race, lower income status, no insurance, and right sided primary tumor were associated with worse survival.



127

Association Between Neighborhood Socioeconomic Status and Utilization of Surgery for Resectable Gastrointestinal Cancers

D.S. Swords,* C.L. Scaife. *Surgery, University of Utah, Salt Lake City, UT.*

Introduction: Surgery is the backbone of curative-intent treatment for resectable gastrointestinal (GI) cancers. Despite this, surgery is underutilized for some GI cancers, particularly among individuals with low socioeconomic status (SES). Previous studies examining the association between SES and utilization of surgery measured SES at large, non-granular geographic areas. We hypothesized that disparities in utilization of surgery according to SES are larger than previously appreciated for some cancers, and that the magnitude of this disparity varies widely among different GI cancers. Methods: This is a retrospective cohort study of the 2010-2015 Surveillance, Epidemiology, and End Results (SEER) Census Tract-level database, which includes a composite neighborhood-level SES score not available in standard SEER data. We examined the association between quintiles of this score and utilization of surgery among patients with resectable stages of 7 different GI adenocarcinoma types. Patients with contraindications to or refusal of surgery, death before planned surgery, or unknown surgical status were excluded. Adjusted rates of surgery were obtained by calculating after fitting multivariable logit models. Results: The Table shows that surgery rates ranged from 61.2% for pancreatic cancer to 96.8% for colorectal cancer. Esophageal, extrahepatic bile duct, and pancreatic adenocarcinoma had the lowest surgery rates and a significant, graded association between higher SES and use of surgery was observed in these cancers. There were smaller but still clinically significant disparities in surgery rates for gastric and small bowel cancers. SES-based disparities in use of surgery in ampullary and colorectal cancer were clinically insignificant. Conclusions: SES is a powerful determinant of whether patients receive guideline-recommended surgery for some cancers, but it appears to play a minimal role in others. Importantly, the GI cancers with the lowest rates of surgery tended to be those with worse prognoses. National quality improvement efforts are needed to increase utilization of appropriate surgery in some poor prognosis GI cancers.

Association Between Neighborhood Level Socioeconomic Status and Utilization of Surgery in Seven Gastrointestinal Cancers

			Adjusted Rates of Surgery by Quintiles of Neighborhood Socioeconomic Status (95% CI)				
Adenocarcinoma type	Overall Rate of Surgery	ARD in Q1 vs. Q5 (95% CI)	Quintile 1 (Lowest SES)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (Highest SES)
Stage I-III esophageal (N=5,321)	61.3%	-14.7 (-19.2, -10.1)*	52.9 (49.4, 56.5)*	57.8 (54.8, 60.7)*	62.5 (59.7, 65.2)*	62.7 (60.1, 65.4)*	67.6 (64.9, 70.3)
Stage I-III gastric (N=10,838)	78.2%	-4.9 (-7.5, -2.4)*	76.9 (75.1, 78.8)*	75.6 (73.8, 77.4)*	77.0 (76.0, 79.4)*	78.8 (77.0, 80.5)*	81.9 (80.2, 83.5)
Stage I-III extrahepatic bile duct (N=755)	71.7%	-19.7 (-31.0, -8.4)*	58.7 (49.4, 68.1)*	66.8 (59.1, 74.5)*	74.0 (66.8, 81.1)	74.7 (68.2, 81.1)	78.4 (72.5, 84.3)
Stage I-III ampullary (N=1,628)	91.8%	-3.6 (-7.8, 0.7)	90.5 (87.1, 93.8)	91.1 (88.0, 94.3)	91.7 (88.9, 94.6)	91.3 (88.3, 94.4)	94.0 (91.6, 96.5)
Stage I-II pancreatic (N=12,434)	61.2%	-13.9 (-16.7, -11.0)*	53.5 (51.3, 55.8)*	57.5 (55.4, 59.5)*	61.0 (59.1, 62.9)*	63.6 (61.8, 65.4)*	67.4 (65.7, 69.1)
Stage I-III small bowel (N= 1,661)	86.5%	-8.2 (-13.4, -3.0)*	83.2 (79.1, 87.3)*	86.7 (82.9, 90.5)*	82.8 (78.6, 86.9)*	87.7 (84.3, 81.2)*	91.4 (88.4, 94.3)
Stage I-III colorectal (N=105,808)	96.8%	-1.0 (-1.3, -0.6)*	96.2 (95.9, 96.5)*	96.7 (96.4, 96.9)*	97.0 (96.7, 97.2)	97.1 (96.9, 97.4)	97.2 (96.9, 97.4)

Abbreviations: SES, socioeconomic status; ARD, adjusted rate difference. NOTES: These models adjusted for sex, age, race/ethnicity, personal cancer history, and marital status. Insurance status was considered an intermediate variable and was not adjusted for. Highest SES patients (Quintile 5) were considered the referent group, and ARDs and predicted rates with a star next to them indicate statistical significance at P < 0.05 compared to Quintile 5 SES patients.

128

Postoperative Aspiration Risk in Major Abdominal Cancer Surgery: A Prevention Strategy Using the Model for Improvement Framework R. Jrearz,* M. Sadeghi, A. Nadler, S. Michaelson, B. Haas, E. Avila, J. Zhou, K. Baldock, A. Van Osch, E. Tran, A. Nathens, J. Hallet. *Surgical Oncology, University of Toronto, Toronto, ON, Canada.*

Introduction: Post-operative aspiration accounts for one third of re-intubations after abdominal surgery, and carries a 50% mortality risk. Over 2014-17, 13% of post-operative deaths in our cancer program were due to aspiration. Data on prevention of aspiration in major abdominal cancer surgery is scarce. We aimed to develop an aspiration prevention strategy using the model for improvement framework. Methods: A multidisciplinary working group was assembled. A root-cause analysis was conducted using an Ishikawa diagram. Practice patterns were reviewed using the Canadian Incident Analysis Framework and environmental audits. Change ideas were developed for priority root causes, and implementation planned using Plan-Do-Study-Act (PDSA) cycles. The primary outcome was aspiration mortality. Process measures aligned with change ideas. Results: The following root causes were identified: aspiration risk-assessment (lacking in 100%), nasogastric tube (NGT; routine clamping as per institutional policy), and patient position during meal (24% in chair). Change ideas are: perioperative aspiration risk-assessment tool, new institutional NGT policy, initiative to have patients sitting in chair during meals by optimizing patients' access to bedside chairs, educating patients and families, and delivery of meal trays away from the bedside. With the initial PDSA cycles aimed at bedside chair access and increased education, 37% of meal-eligible patients were up in chair at meals (from 24%). From 12/2017 to 07/2018, there was no aspiration-related mortality among 8 post-operative deaths after abdominal surgery. Conclusion: Developing an institutional aspiration prevention strategy using structured quality improvement methodology is crucial in measuring and implementing change. We have developed a systematic and structured assessment for post-operative aspiration; a common, yet modifiable, cause of morbidity and mortality in major abdominal cancer surgery. Changes have led to early improvements in aspiration mortality and in institutional policies. This study provides a framework that can be used by others for quality improvement in cancer surgery.

129

Has the Outcome of Primary Retroperitoneal Sarcoma Changed Over the Past 15-Years? D. Callegaro,[1]* C.P. Raut,[2] D. Ng,[1] D. Strauss,[3] C. Honoré,[4] E. Stoeckle,[5] S. Bonvalot,[6] R. Haas,[7] N. Vassos,[3] L. Conti,[8] R. Gladdy,[1] M. Fairweather,[2] W.J. van Houdt,[7] Y. Schrage,[9] P. Hohenberger,[10] F. van Coevorden,[7] P. Rutkowsky,[11] A. Gronchi,[8] C. Swallow.[1] *1. Surgery, University of Toronto, Toronto, ON, Canada; 2. Brigham and Women's Hospital, Boston, MA; 3. Royal Marsden Hospital, London, United Kingdom; 4. Institut Gustave Roussy, Villejuif, France; 5. Institut Bergonie, Bordeaux, France; 6. Institut Marie Curie, Paris, France; 7. Netherlands Cancer Institute, Amsterdam, Netherlands; 8. Istituto Nazionale Tumori, Milan, Italy; 9. Leids Universitair Medisch Centrum, Leiden, Netherlands; 10. Mannheim University Hospital, Mannheim, Germany; 11. Maria Sklodowska-Curie Institute, Warsaw, Poland.*

RATIONALE: Recent advances in surgical technique, radiotherapy (RT) administration and systemic therapies may have influenced the oncologic outcome in retroperitoneal sarcoma (RPS) patients. AIM: The purpose of this study was to determine temporal trends in treatment strategy and oncologic outcomes in patients managed in high volume sarcoma centers over a 15-year time span. METHODS: Consecutive patients who underwent resection of primary non-metastatic RPS at 10 sarcoma referral centers between 2002 and 2017 were included. Patients enrolled in the STRASS trial from 2012-2017 were excluded from analysis. Five-year overall survival (OS) and crude cumulative incidence (CCI) of local recurrence (LR) and distant metastases (DM) were calculated. RESULTS: In total, 1771 patients are included in the study cohort. At 5 years post resection, OS was 67.6% (95% CI 65.0-70.4), CCI of LR was 25.3% (22.8-27.8), and CCI of DM was 21.6% (19.4-23.8). Patients were grouped into three time intervals (t): 2002-2006 (t1, n=399), 2007-2011 (t2, n=608) and 2012-2017 (t3, n=764) (Table). We noted an increase in the number of resected organs from t1 (median=2, IQR 1-3) to t3 (median=2, IQR 2-4) (p<0.001) and a drop in the rate of R2 resection (6.3% in t1, 3.6% in t2, 2.9% in t3, p=0.016). Receipt of preoperative RT increased over time (13.8% in t1, 24.7% in t2, 17.7% in t3, p<0.001), while receipt of perioperative chemotherapy did not change (18.8% in t1, 17.8% in t2 and 14.7% in t3, p=0.13). OS at 5 yr post-resection increased between t1 and t2 (p=0.002), and remained stable in t3. For the total cohort, there were no consistent temporal changes in CCI of LR or DM. Dedifferentiated Liposarcoma was the most common histology (n=712), and differences in management and outcome were most salient in this subgroup: increased use of preoperative RT (p=0.008), decreased R2 rate (p=0.056), and improved 5 yr OS (p=0.03) were seen between t1 and t2. CONCLUSIONS: The observed improvement in 5 yr OS coincided with increased use of preoperative RT and improved surgical decision making. Increased OS without a drop in recurrence rate may reflect refinement in patient selection and/or better survival after recurrence.

	t1 2002-206	t2 2007-2011	t3 2012-2017	
n	399	608	764	
Follow Up Time, mo, median (IQR)	96 (84-117)	43 (29-57)	35 (21-55)	
Age, median (IQR)	57 (48-67)	59 (49-68)	63 (53-70.5)	<0.001 ANOVA
Gender Male Female	 210 (52.6%) 189 (47.4%)	 314 (51.6%) 294 (48.4%)	 405 (53.0%) 359 (47.0%)	 0.86 Chi square
Tumor size, cm, median (IQR)	20 (13-30)	20 (12.7-30)	20 (12-29.3)	0.79 KW rank sum
Histologic Subtype WDLPS DDLPS LMS MPNST SFT UPS Other	 101 (25.3%) 150 (37.6%) 69 (17.3%) 22 (5.5%) 24 (6.0%) 6 (1.5%) 27 (6.8%)	 162 (26.6%) 220 (36.1%) 125 (20.6%) 11 (1.8%) 35 (5.8%) 16 (2.6%) 39 (6.4%)	 157 (20.6%) 342 (44.7%) 137 (17.9%) 13 (1.7%) 45 (5.9%) 36 (4.7%) 34 (4.5%)	 <0.02 Chi square
Resected organs, no, median (IQR)	2 (1-3)	2 (1-4)	2 (2-4)	<0.001 KW rank sum
R2 resection	25 (6.3%)	22 (3.6%)	22 (2.9%)	0.016 Chi square
Preoperative RT	55 (13.8%)	150 (24.7%)	135 (17.7%)	<0.001 Chi square
Perioperative CT	75 (18.8%)	108 (17.8%)	112 (14.7%)	0.13 Chi square
OS, 5 yr	61.1% (95% CI 56.3, 66.2)	72.7% (95% CI 68.5, 77.1)	70.2% (95% CI 65.7, 75.0)	0.002 Log rank
CCI of LR, 5 yr	26.6% (95% CI 22.1, 31.2)	22.6% (95% CI 18.3, 26.9)	26.8% (95% CI 22.8, 30.8)	0.57 Grays
CCi of DM, 5 yr	18.9% (95% CI 15.0, 22.8)	23.0% (95% CI 19.2, 26.8)	22.6% (95% CI 18.7, 26.5)	0.36 Grays

IQR, inter quartile range; Tumor size = maximum dimension; WDLPS, well-differentiated liposarcoma; DDLPS, dedifferentiated liposarcoma; LMS, leiomyosarcoma; MPNST, malignant peripheral nerve sheath tumor; SFT, solitary fibrous tumor; UPS, undifferentiated pleomorphic sarcoma; RT, radiation therapy; CT, chemotherapy; OS, overall survival; CCI, crude cumulative incidence; LR, local recurrence; DM, distant metastasis.

130

Integrin α-10 Gene Expression is Prognostic for Metastasis and Survival in Mxyofibrosarcoma and Undifferentiated Pleomorphic Sarcoma R.W. Cass,* T. Okada, L. Qin, N. Socci, Y. Shen, S. Singer. *Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Myxofibrosarcoma (MFS) and undifferentiated pleomorphic sarcoma (UPS) are two common and aggressive types of genetically complex sarcomas. The complexity of alterations has made it difficult to find the drivers of oncogenesis. Previous work has shown integrin α-10 (ITGA10) is a key driver of cell growth and viability in a subset of MFS. We aim to study the pro-metastatic role of ITGA10 in MFS/UPS, to determine its value as a prognostic marker and target for therapy in metastatic disease. Methods: Primary, high grade MFS(n=64) and UPS (30) of the extremity/trunk were analyzed by U133A gene expression arrays and Agilent CGH arrays for copy number alterations. A panel of MFS and UPS cell lines were characterized by array CGH and ITGA10 mRNA expression. Knockdown was by lentiviral shRNA. Proliferation was assessed by CyQUANT and apoptosis by annexin V staining. A genetically engineered mouse model of UPS with conditional $KRAS^{G12D}$ and p53 mutations was used (KP-mice). Results: High ITGA10 expression in the group of 94 MFS/UPS tumors associates with decreased DSS (HR: 3.7, p<0.001) and DRFS (HR: 3.1, p<0.001). In a multivariate analysis, ITGA10 significantly associates with DSS and DRFS when adjusting for tumor type (MFS vs UPS) and for tumor size (>8 cm vs. <8 cm). Knockdown of ITGA10 decreased proliferation and induced apoptosis of MFH 4746 cells with high ITGA10 expression. In the KP-mouse model, ITGA10 mRNA in metastasis was 5.2-fold higher compared to primary tumors (p=0.02). In matched metastasis and primary tumors from the same animal, ITGA10 mRNA was 0.5-fold to 89-fold higher in metastasis than in the primary (mean: 10.7-fold, p<0.01). Comparing a panel of cell lines derived from KP-mouse primary tumors and metastasis, the metastasis-derived UPS cells had a 1.8-fold higher ITGA10 mRNA expression. Conclusions: ITGA10 mRNA expression, tumor size, and tumor type are independent predictors of DSS and DRFS in MFS and UPS. ITGA10 gene expression associates with metastasis in a transgenic mouse model of UPS. These data suggest that ITGA10 drives metastasis, and thus mortality, in UPS and is a potential target for therapy.

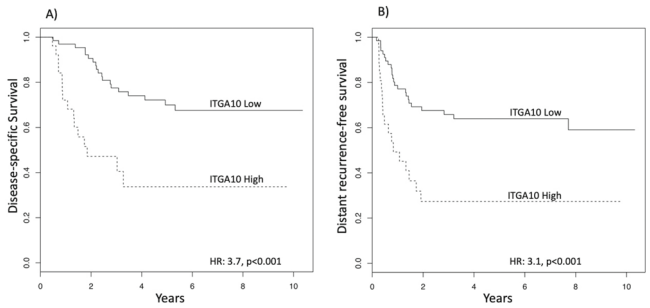


Figure 1. A) Disease-specific survival (DSS) of MFS/UPS patients with low ITGA10 mRNA (n = 68) and high ITGA10 mRNA (n = 27) by Affymetrix U133A microarray B) Distant recurrence-free survival (DRFS) of the same two groups of patients

131

A Nomogram to Predict Postoperative Morbidity After Resection of Retroperitoneal Sarcoma E.E. Burke,* D.C. Boulware, R.J. Gonzalez, J.E. Mullinax. *Surgical Oncology, Moffitt Cancer Center, Tampa, FL.*

Introduction: No model for predicting postoperative morbidity following retroperitoneal sarcoma (RPS) resection has been developed and established models do not apply. The aim of this study was to create a nomogram predictive of postoperative morbidity after RPS resection based on preoperative patient characteristics. Methods: The National Surgical Quality Improvement Program (NSQIP) was used to identify patients with RPS that underwent resection from 2011-2016. Patients were randomly assigned to a training group and test group in a 2:1 fashion. Thirty-day mortality and morbidity (including 21 complications), discharge to facility other than home and length of stay (LOS) >14 days were combined into a composite endpoint named "Postoperative Morbidity". Nineteen preoperative variables consistently reported in NSQIP were identified. Using univariate and multivariate regression analysis those variables associated with postoperative morbidity were identified and a nomogram developed. The nomogram was validated using the test group. Results: A total of 1,084 patients were identified. The median age was 61 years and 52.4% were women. The vast majority of patients (98.0%) were functionally independent prior to surgery and were classified as ASA 2 (32.3%) or 3 (60.2%). Thirty-day mortality and morbidity was 0.8% and 19.6% respectively. The minority of patients (9.1%) had LOS >14 days and 15.5% were discharged to a facility. After univariate and multivariate analysis only age, creatinine and albumin remained associated with postoperative morbidity (Figure 1). The nomogram created using these 3 variables was predictive with a c-statistic of 0.66 when patients with missing data for any of the 3 variables were excluded and 0.65 when missing values were imputed and all patients included. Conclusion: This study provides the first validated nomogram to predict outcomes after RPS resection based on preoperative patient characteristics that allows for individualized preoperative counseling of patients about risks of postoperative morbidity. The addition of disease-specific factors from a prospective multicenter database may allow for refinement of this model moving forward.

Preoperative Variable	Univariate Analysis (OR, CI)	Multivariate Analysis (OR, CI)
Gender	Male (1.5, 1.1-2.0)	NS
Age	Increasing age (1.02, 1.0-1.03)	Increasing age (1.02, 1.0-1.03)
BMI	NS	..
Year of Operation	NS	..
Diabetes	NS	..
Current Smoker	NS	..
Dyspena	NS	..
Functional Status	Partially dependent (8.4, 1.7-40.8)	NS
Severe COPD	NS	..
Congestive heart failure	NS	..
Hypertension	NS	..
Dialysis dependent	NS	..
Steroid use	NS	..
>10% body weight lost	Yes (2.0, 1.1-3.6)	NS
ASA Classification	NS	..
Hematocrit (HCT)	Increasing HCT (0.9, 0.92-0.98)	NS
BUN	Increasing BUN (1.03, 1.0-1.1)	NS
Creatinine (Cr)	Increasing Cr (1.8, 1.2-2.7)	Increasing Cr (1.7, 1.1-2.5)
Albumin (Alb)	Increasing Alb (0.57, 0.43-0.74)	Increasing Alb (0.58, 0.44-0.77)

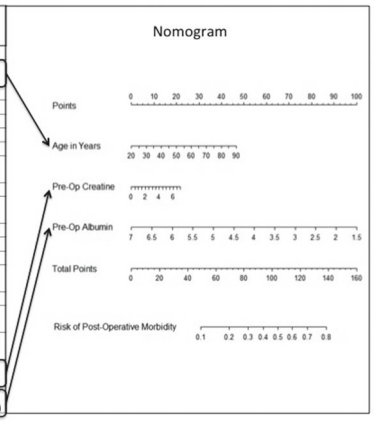


Figure 1. Univariate and multivariate analysis of preoperative variables associated with postoperative morbidity and predictive nomogram for postoperative morbidity after resection of retroperitoneal sarcoma.

132

TAB2 Amplification on 6q23-25 Drives Cell Proliferation and Inhibits Senescence in Well-differentiated Liposarcoma via JNK Activation and Upregulation of MDM2 A. Lofthus,[1]* J. Hu,[1] A. Craig,[2] C. Antonescu,[1] N. Socci,[1] S. Singer,[1] A. Crago.[1] *1. Gastric and Mixed Tumors, Memorial Sloan Kettering Cancer Center, New York City, NY; 2. Icahn School of Medicine at Mount Sinai, New York City, NY.*

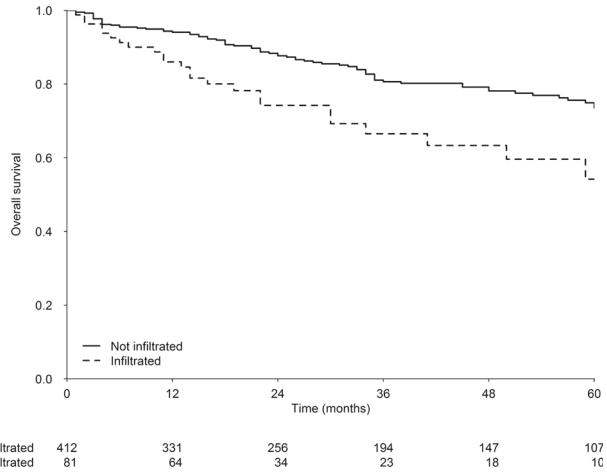
Background: 12q13-15 amplification results in overexpression of oncogenes CDK4 and MDM2 in the majority of well-differentiated and de-differentiated liposarcoma (WD/DDLS). Amplification of 6q23-25 is found in 18% of WDLS and associates with local recurrence. This study aimed to identify oncogenes encoded by 6q23-25. Methods: WDLS (n=49) were analyzed by array comparative genomic hybridization (aCGH) and U133A gene expression arrays. Fisher's exact test was used to compare gene expression in tumor with versus without 6q23-25 amplification. Cell lines derived from surgically resected specimens were characterized by aCGH. Proliferation was analyzed using CyQuant, senescence with β-galactosidase staining (β-gal) and protein expression with immunoblot. Results: The 6q23-25 encoded TAB2 gene, a positive regulator of JNK and NFκB activity, is specifically overexpressed in 6q23-25 amplified WDLS compared to non-amplified tumors (FC=2.14, FDR 0.0025). shRNA knockdown of TAB2 in the 6q23-25 amplified cell line, WD4847, decreases proliferation by >90% as compared to scramble control ($p<0.05$) and decreases protein levels of p-JNK, NF-kB, and MDM2. Consistent with MDM2's known role in senescence, TAB2 shRNA also increased β-gal staining (69% vs. 8% in scramble controls; $p<0.01$). The JNK inhibitor SP600125 similarly decreased MDM2 expression and increased β-gal (58% vs. 9% in control vehicle; $p<0.01$), but the NFκB inhibitor BAY11-7082 did not. To examine whether this effect was specifically dependent on 6q23-25 amplification, two cell lines without 6q23-25 amplification underwent shRNA knockdown of TAB2. No significant increase in β-gal staining, or changes in protein levels of p-JNK or MDM2 were observed in WDLS cells lacking TAB2 amplification. Conclusions: Inhibition of the 6q23-25-encoded TAB2 gene downregulates MDM2 and leads to senescence in TAB2 amplified WDLS cells but not in WDLS cell lines lacking TAB2 amplification. TAB2 regulates a senescence program modulated by JNK. The TAB2-JNK-MDM2 axis may represent a therapeutic target and may mediate the worse outcomes associated with 6q23-25 amplified WDLS.

133

Intraperitoneal Penetration of Retroperitoneal Sarcomas: A Novel Risk Factor for Dismal Prognosis E. Nizri,[1]* M. Fiore,[2] C. Colombo,[2] S. Radaelli,[2] D. Callegaro,[2] R. Sanfillipo,[2] C. Sangalli,[2] P. Collini,[2] R. Micelli,[2] S. Stacchiotti,[2] P. Casalli,[2] A. Gronchi.[2] *1. Surgery, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; 2. Istituto Nazionale dei Tumori, Milano, Italy.*

Introduction: Retroperitoneal sarcomas (RPS), as their name implies, lie in the retroperitoneal space, displacing adjacent organs and are usually covered by a thin peritoneal layer. However, some of these tumors have an intraperitoneal

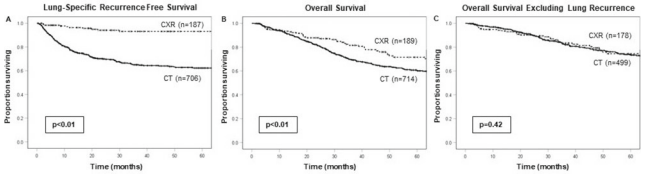
penetration (IP), a component connected to the main tumoral mass and not covered by peritoneum. The significance of such a clinical presentation is unknown. Methods: We retrospectively analyzed our prospectively institutional database of RPS, retrieving in addition intraoperative photos taken to document the primary tumor extent at laparotomy. 493 patients operated between January 2012 and December 2017 were analyzed. The effects of IP on overall survival (OS), local recurrence (LR) and distant metastasis (DM) were evaluated. Results: IP was present in 81 patients (16.5%). It was significantly associated with older age (median: 64 vs. 59, p=0.008), gender (67% males vs. 33%, p=0.005) and multifocality (9/11 of multifocal RPS had IP; p<0.0001). IP was not associated with size (median size 20 vs. 21 cm) or any specific histology, while a trend for an association with high malignancy grade was observed (41% of IP occurred in grade 3 tumors; p=0.07). At a median follow up of 32 months IP was associated with worse 5-yrs overall survival (OS) (54% vs. 74%, p<0.001) and crude cumulative incidence (CCI) of local recurrence (LR) (5-Yrs CCI of LR: 27% vs. 19%, p=0.001), but not to CCI of distant metastases. However at multivariable analysis age (HR=1.55, p=0.03), tumor grade (HR=5.62, p<0.001) and macroscopic complete resection (HR=6.7, p<0.001) were the predominant predictor for OS, whereas size (HR=1.33, p=0.02) and grade (HR=0.42, p=0.003) were the ones for LR. Conclusions: IP is associated to increased LR and decreased survival. However, the effect of IP on prognosis is related to other tumor characteristics and can be also accurately predicted by other factors previously validated in published nomograms.



134

Lung Surveillance Strategy for High-Grade Soft Tissue Sarcomas: CT Scan or Chest X-ray? A.C. Gamboa,[2]* C. Ethun,[2] M.Y. Zaidi,[2] T. Tran,[5] G. Poultsides,[5] V. Grignol,[4] J.H. Howard,[4] M. Bedi,[3] T. Gamblin,[3] K. Roggin,[6] J. Tseng,[6] K. Chouliaras,[7] K.I. Votanopoulos,[7] D. Cullinan,[8] R. Fields,[8] S. Oskouei,[1] D. Monson,[1] N. Reimer,[1] S. Maithel,[2] K.A. Delman,[2] K. Cardona.[2] *1. Winship Cancer Institute, Emory University, Atlanta, Georgia; 2. Winship Cancer Institute, Emory University, Atlanta, GA; 3. Medical College of Wisconsin, Milwaukee, WI; 4. The Ohio State University, Columbus, OH; 5. Stanford University, Palo Alto, CA; 6. University of Chicago, Chicago, IL; 7. Wake Forest University, Winston-Salem, NC; 8. Washington University School of Medicine, St. Louis, MO.*

Background Given the propensity for lung metastases (LM), NCCN guidelines recommend lung surveillance with either computed tomography (CT) or chest x-ray (CXR) in pts with high-grade soft tissue sarcoma (STS). Considering survival, diagnostic sensitivity and cost, the optimal modality is unknown. Methods The US Sarcoma Collaborative database (2000-2016) was reviewed for pts who underwent resection of a primary high-grade STS. Primary outcomes were lung recurrence-free survival (L-RFS) and overall survival (OS). Cost analysis for each modality based on 2017 Medicare Physician Fee Schedule was performed. Results Of 968pts identified, 83% had truncal/extremity and 17% had retroperitoneal (RPS) tumors. Recurrence at any site occurred in 48% of which 52% were in the lung. Lung surveillance was performed with CT in 80% and CXR in 20%. Both groups were similar for baseline demographics although CT pts had more RPS and recurrences. Regardless of imaging modality, 85-90% of LM were detected within the first 2yrs of surveillance and both groups had a similar reintervention rate (p=0.77). LM was associated with decreased OS (HR:3.91; 95%CI 3.11-4.92; p<0.01). CT patients had a decreased 5yr L-RFS (62 vs 93%, p<0.01; Fig1A) and 5yr OS (60 vs 71%, p<0.01; Fig1B). However, when considering age, tumor size, location, margin status, receipt of radiation, and presence of LM, CXR was not associated with worse OS (HR:1.01; 95%CI 0.71-1.4; p=0.97). Furthermore, when analyzing pts in whom no LM was detected, both imaging cohorts had a similar OS (73 vs 74%, p=0.42; Fig1C), suggesting equivalent diagnostic sensitivity. When adhering to a guideline-specified surveillance protocol for a projected 4,406 cases in 2018, lung surveillance for initial 5yrs would cost $314/pt in a CXR vs $2,579/pt in a CT protocol, with a potential savings of $6M/yr to the US healthcare system. Conclusion In this large multicenter study, when considering adverse clinicopathologic factors, utilizing CXR for lung surveillance of high-grade STS was not associated with decreased OS. Considering a potential cost savings of 88%/pt, a CXR-based protocol may optimize resource utilization for lung surveillance in pts with high-grade STS.



135

Targeting SFRP2 as Novel Immunotherapy for Sarcoma

N. DeMore,[1]* P. Nasarre,[1] I. Bonilla,[1] Y. Peterson,[1] P. Chakraborty,[1] L. Spruill,[1] A. Broome,[1] E. Hill,[1] E. Hilliard,[1] J. Yustein,[2] S. Mehrotra.[1] *1. Surgery, Medical University of South Carolina, Charleston, SC; 2. Baylor College of Medicine, Houston, TX.*

Introduction: Secreted frizzled related protein 2 (SFRP2) promotes angiogenesis via activation of calcineurin/NFAT signaling in endothelial cells. In T-cells, activation of NFAT increases expression of CD38, which is a mechanism of resistance to PD-1 inhibition. We hypothesized that SFRP2 activates NFAT and increases CD38 in T-cells, and SFRP2 antagonism combined with a PD-1 inhibitor (nivolumab) would have additive inhibitory effects on tumor growth. Methods: In vitro: T-cells were treated with control or recombinant SFRP2 protein (30nM) for 1 hour, cells were lysed and nuclear and cytoplasmic fractions were collected and subjected to Western blot. T-cells were co-cultured with tumor cells with our without a humanized SFRP2 monoclonal antibody (hSFRP2 mAb) and subjected to flow cytometry to assess tumor proliferation. In vivo: SVR angiosarcoma or Hs578T breast carcinoma-sarcoma cells were injected into nude mice, mice were treated with hSFRP2mAb 4 mg/kg iv q3 days, and tumor volumes were measured. In C57BL6 mice, R420 osteosarcoma cells were injected via tail vein and mice were treated with control, hSFRP2 mAb, nivolumab, or hSFRP2 mAb + nivolumab for 21 days. Lung metastases were quantitated, and splenocytes were processed for flow cytometry. Results: Western blot analysis of T-cells treated with SFRP2 showed an increase in nuclear NFATc3 and surface CD38. Co-culture of T-cells with Hs578T or RF420 cells significantly reduced T-cell proliferation, which was restored by hSFRP2 mAb (n=3, p<0.01). Importantly, hSFRP2 mAb treatment reduced SVR angiosarcoma (n=10, p<0.05), Hs578T breast (n=11, p<0.05), and metastatic RF420 osteosarcoma (n=12, p<0.0001) growth in vivo. The combination of hSFRP2 mAb and nivolumab had additive inhibitory effect on metastatic osteosarcoma growth (n=12, p<0.01). Splenocytes and tumor infiltrating lymphocytes from mice treated with hSFRP2 mAb displayed decreased CD38 levels compared to control (n=4, p<0.001). Conclusion: SFRP2 activates the calcineurin/NFAT pathway in T-cells and upregulates CD38, while hSFRP2 mAb reduces CD38 levels in vivo. The hSFRP2 mAb inhibits both primary and metastatic tumor models, and has additive efficacy when combined with nivolumab in osteosarcoma.

136

Combined Regional and Systemic Immunotherapy Inhibits Tumor Growth of Extremity Melanoma and Sarcomas and Improves Survival J.H. Terhune,* M. Kim, A. Gudkov, J.J. Skitzki. *Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Advanced extremity melanomas and sarcomas can be treated with isolated limb perfusion(ILP) with melphalan; complete response rates are up to 63%, however ILPs are resource demanding and can incur significant toxicity. CBL0137, an anti-cancer agent from the curaxin family, is ideal for regional treatments due to its minimal impact on healthy cells, rapid accumulation in tumor, and potential stimulation of immune reactivity. We have demonstrated the safety and efficacy of CBL0137 as an intra-arterial(IA) infusion in murine models. Combined with the clinical standard PD-1 blockade, we hypothesize that the anti-tumor effects of CBL0137 IA infusion may be augmented in extremity melanoma and sarcomas. C57BL/6 mice were inoculated in the extremity(B16 melanoma or MCA205 sarcoma). 7-10 days later an IA infusion was performed via the superficial femoral artery for 15 minutes with vehicle(D5W) or CBL0137. Experimental groups included vehicle, anti-PD-1 mAb, CBL0137, and combination(anti-PD-1 & CBL0137) groups. Anti-PD-1 mAb(5 mg/kg) was injected 3 times a week intraperitoneally, and tumor volume was measured. Toxicity was monitored daily and mice sacrificed per protocol. In the B16 model, the combination therapy prolonged survival(p=0.01), while both the combination and CBL0137 treatment impacted tumor growth(p<.0001 for both) compared to vehicle(Fig 1A,B). In the MCA205 model, CBL0137 and the combination groups had an impact on survival(p=0.01, p=0.02 respectively) and tumor growth(p<.0001 for both) compared to vehicle(Fig 1C); one MCA205 mouse treated with the combination maintained a complete response >50 days after infusion. Tumors harvested 7 days after IA infusion had a higher number of $CD8^+$ T cells in anti-PD-1 mAb injected groups(anti-PD-1 alone p=0.01 and combination p=.002)(Fig 1D). Combined regional and immune therapy effectively controlled growth of extremity melanoma and sarcomas. The combination of agents prolonged survival in B16 tumor bearing mice and induced durable complete responses in a portion of MCA205 bearing mice. Combining CBL0137 IA infusion with immunotherapy may enhance responses by synergistic immune-mediated mechanisms.

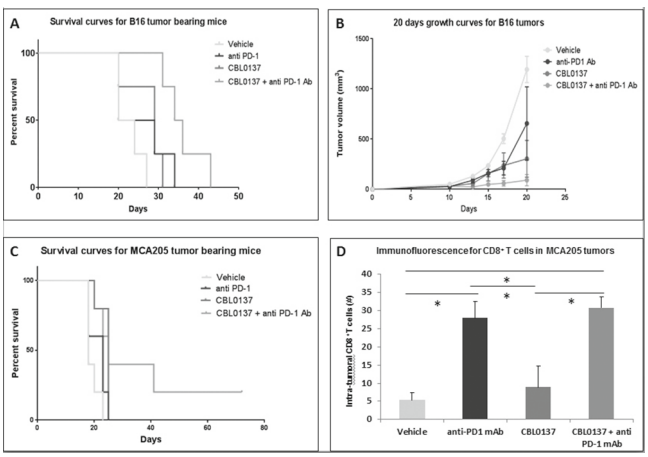


Figure 1. All experiments were perfomed in C57BL/6 mice and each graph is a single experiment with 4 or 5 mice per group, representative of repeated experiments. The four experimental conditions are the same for each experiment: vehicle, anti PD-1 mAb alone, CBL0137 alone, and CBL0137 combined with anti PD-1 mAb. (A) Survival of the B16 tumor bearing mice, days represents the number of days after intra-arterial (IA) infusion. (B) Tumor growth curve of B16 tumors for 20 days after IA infusion. (C) Survival of the MCA205 tumor bearing mice, days represents the number of days after IA infusion. (D) MCA205 tumors were collected 7 days after IA infusion and immunoflourescence staining was performed for intratumoral CD8+ T cells.

137

Low-dose Sorafenib Enriches for Cancer Stem Cells and Accelerates Tumor Progression in Sarcomas and Other Solid Tumors S. Judge,* I.R. Sturgill, J.I. Luna, M. Chen, J.S. Park, A.M. Monjazeb, M.A. Darrow, W.J. Murphy, R.J. Canter. *Surgery, University of California, Davis, Sacramento, CA.*

Introduction: Numerous studies demonstrate that cancer stem cells (CSCs) influence tumor heterogeneity and repopulation in multiple cancer types. We sought to evaluate the impact of drug dosing on CSC phenotype after exposure to multi-kinase inhibitor sorafenib. Methods: In vitro, human cancer cell lines and primary sarcomas were exposed to escalating doses of sorafenib to determine cell viability and expression of CSC marker ALDH. In vivo, $ALDH^{bright}$ CSCs were isolated, exposed to sorafenib, and xenograft growth and survival were evaluated. Patient specimens were analyzed for ALDH expression and outcome after neoadjuvant sorafenib and/or RT. Parametric and non-parametric statistical analyses were used. Results: In vitro, low-dose sorafenib lead to expansion in $ALDH^{bright}$ CSCs in 3 sarcoma lines and 3 non-sarcoma lines (range fold increase 0.5-4X, P<0.05). We observed a 9X increase in $ALDH^{bright}$ CSCs in human primary sarcomas (P<0.001). Sorafenib pretreated A673 cells implanted into NSG mice lead to decreased survival when compared to untreated A673 cells (median survival 35 vs. 50 days, P=0.05). IHC analysis of specimens from sarcoma patients treated with neoadjuvant sorafenib and RT (NCT#00805727) demonstrated a significant increase in the ALDH H-score among patients who developed metastases vs. those who did not. We observed a significant inverse correlation (Pearson's r = -0.746, P=0.03) between ALDH H-score and metastasis-free survival (MFS) with a trend toward worse MFS by Kaplan-Meier (KM) analysis (P=0.09). Mechanistically, we detected increased epidermal growth factor receptor expression in sorafenib treated sarcoma cells. Human NK cells demonstrated preferential killing of $ALDH^{bright}$ A673 cells at multiple effector:target ratios. Conclusions: Low-dose sorafenib expands CSCs, increases tumor growth, and is associated with higher rates of metastasis formation in sarcoma patients. Increased tumor expression of EGFR may underlie these observations. NK killing of CSCs is an attractive strategy, though paradoxical CSC effects of anti-proliferative agents like sorafenib may impact these efforts.

138

Novel Diagnostic Approach for Gastrointestinal Stromal Tumor Using an anti-KIT DNA Aptamer S. Banerjee,[1]* P. Ray,[2] M. Yebra,[2] C. Tang,[2] R. White,[2] J.K. Sicklick.[2] *1. UC Los Angeles/UC San Diego, La Jolla, CA; 2. UC San Diego, La Jolla, CA.*

Introduction: Gastrointestinal stromal tumor (GIST) is the most common sarcoma. At present, GIST diagnosis is cumbersome relying on invasive tissue biopsy. Aptamers are an emerging class of detection molecules and are short, single-stranded oligonucleotides that selectively bind protein targets with high affinity and specificity. We hypothesized that a KIT-specific aptamer can label GIST cells and can serve as an accurate GIST diagnostic. Methods: We investigated the capacity of a KIT DNA aptamer (Zhao et al., Biomaterials 2015) to bind GIST cells. Aptamer binding was assessed by flow cytometry in human GIST cell lines, primary human GISTs and transgenic murine GISTs. Cell killing was assessed by in vitro viability assay, and confocal immunofluorescence (IF) microscopy was performed on human GIST cell lines. Results: KIT aptamer bound human GIST-T1 cells (Geometric Mean, GM 250) with similar avidity to anti-KIT antibody (GM 226), but not scrambled control aptamer (GM 4.5) (Fig. 1A). Similar findings were observed in the GIST882 line (GM 145, 124 and 9.4, respectively), but not Panc1, a low KIT expression pancreatic cancer cell line (GM 9.9, 3.0 and 7.1, respectively). Treatment of GIST cells with KIT aptamer or scrambled control had minimal effect on cell viability suggesting that the aptamers are non-toxic. Primary human GIST cell preparations had high KIT aptamer binding compared to scrambled control (GM 403, 98.6, respectively) and was 2.3-fold higher than anti-KIT antibody (GM 172) (Fig. 1B). Similarly, KIT aptamer bound primary KIT^{K641E} murine GIST cells 3-fold higher than scrambled control (GM 35.2, 11.9, respectively). Using GIST lines, confirmatory confocal IF demonstrated plasma membrane and cytosolic binding of the KIT aptamer, which colocalized with the anti-KIT antibody (Fig. 1C). Conclusion: For the first time, we report aptamer labeling of human and murine GIST cells, including primary human tumor cells. KIT aptamer labeling was equivalent or superior to anti-KIT antibody and bound a similar distribution of KIT molecules. Taken together, these studies provide proof-of-principle for investigating the utility of KIT aptamers for developing novel GIST diagnostics.

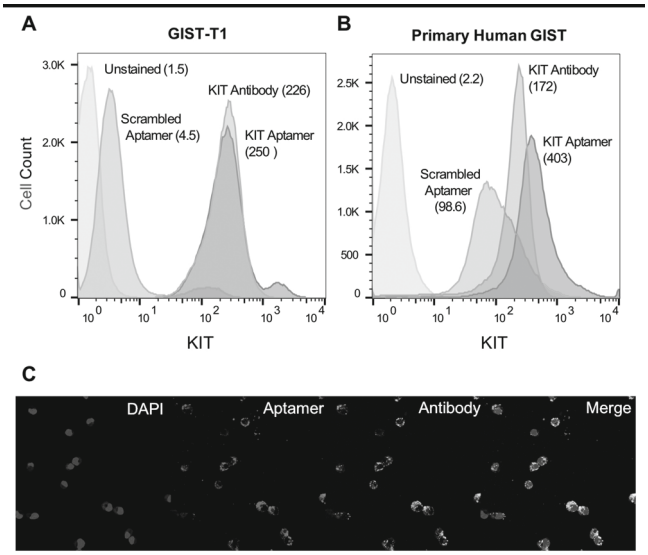


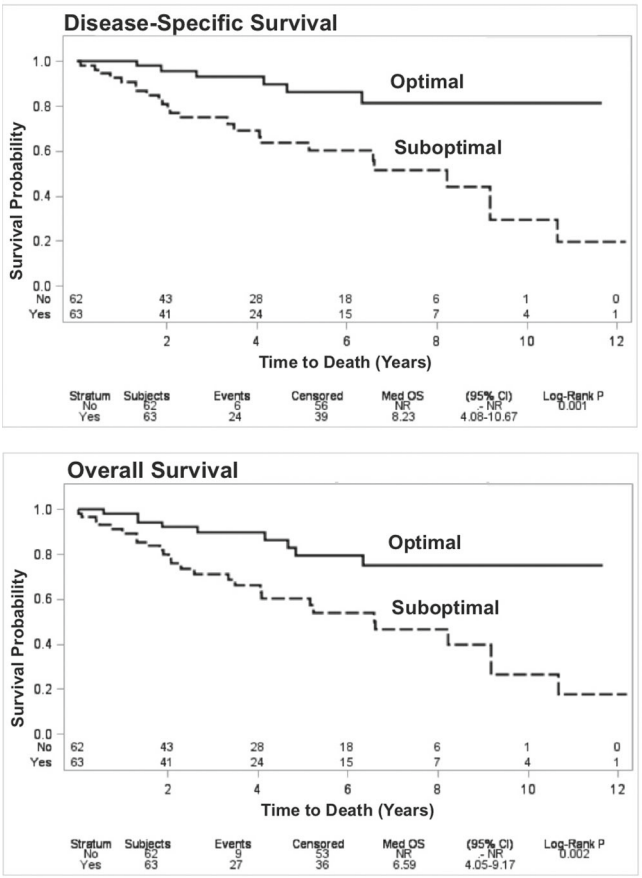
Figure 1: Anti-KIT aptamer specifically binds human KIT in (A) gastrointestinal stromal tumor (GIST) cell lines, (B) primary human GIST, and (C) colocalizes with human KIT antibody.

139

Tumor Mitotic Rate After Neoadjuvant Imatinib is Associated with Outcome in Primary Gastrointestinal Stromal Tumor (GIST)

M.J. Cavnar,* K. Seier, G. Mithat, V.P. Balachandran, C. Curtin, M. Keohan, W. Tap, C. Antonescu, S. Singer, R.P. DeMatteo. *Memorial Sloan Kettering Cancer Center, New York, NY.*

INTRODUCTION: Neoadjuvant imatinib (Neo-IM) may facilitate R0 resection in GISTs that are large or arising in difficult locations, such as the gastroesophageal junction, duodenum, or rectum. While response to preoperative tyrosine kinase inhibitors is associated with better outcome in metastatic GIST, little is known about factors related to outcome after Neo-IM in primary GIST. METHODS: Using a prospective institutional sarcoma database spanning 1982-2016, we identified 150 patients with primary GIST treated with Neo-IM. Patients were excluded if they lacked complete data for Response Evaluation Criteria in Solid Tumors (RECIST) assessment, tumor viability (%), and mitotic rate on pathology (# of mitoses in the most viable portion of the tumor per 50 high-powered fields [HPF]). Disease-specific and overall survival (DSS, OS) were estimated by Kaplan-Meier and compared with the log rank test. Cox proportionate hazard models were used for univariate and multivariate analysis. RESULTS: There were 125 patients treated for a median of 7.5 months (range 0.2-112). By RECIST, partial response, stable disease, and progressive disease were seen in 38%, 51%, and 11%, respectively. By pathologic analysis, ≤50% of the tumor was viable in 69%, and the mitotic rate was ≤5/50HPF in 73%. We defined optimal response as either partial response or stable disease by RECIST, AND ≤50% viable tumor, AND ≤5 mitoses/50 high-powered fields; suboptimal response was defined as absence of any of these factors. Optimal response occurred in 62 (50%) patients and was associated with a 5yr DSS and OS of 86 and 80% vs. 64 and 61% (p=0.002, 0.001; Figure). On multivariate analysis, mitotic rate was associated with outcome, with a hazard ratio for DSS and OS of 4.9 (CI 2.0-11.9, p=0.0004) and 4.2 (CI 1.9-9.5, p=0.0004). By multivariate analysis, incomplete gross resection was significant (p<0.05), but presence of synchronous metastases, RECIST response, and tumor viability were not. CONCLUSIONS: Neo-IM achieved a RECIST partial response in a minority of patients with GISTs. A high tumor mitotic rate following imatinib therapy was associated with poor outcome.



DSS (top) and OS (bottom) in primary GIST after neoadjuvant imatinib therapy, stratified by treatment response.

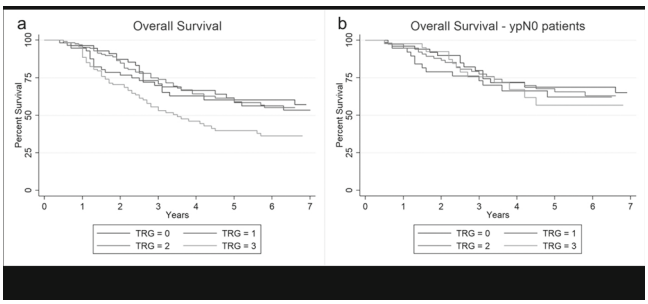
140

Tumor Regression Grade in Gastric Cancer After Preoperative Therapy

N. Ikoma,* J. Estrella, M. Blum, P. Das, B. Minsky, K. Fournier, P. Mansfield, B. Badgwell. *Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX.*

Background The AJCC 8th edition updated ypStage TNM grouping for patients with gastric cancer. We previously reported that nodal status after preoperative therapy (ypN) was most predictive for overall survival (OS). We intended to investigate if tumor regression grade (TRG) of the primary tumor scored by pathologists is helpful to predict survival of gastric cancer patients treated with preoperative therapy. Methods We reviewed an institutional database to identify patients with clinically non-metastatic gastric adenocarcinoma who underwent gastrectomy after preoperative chemo- or chemoradiation therapy. Pathology reports were reviewed, and TRG was classified into following categories: 0 (complete response), 1 (few clusters of viable tumor cells, £1-2%), 2 (significant response, viable cells £ 50%), 3 (minor or no treatment response, viable cells >50%). Associations between TRG and clinicopathological factors were examined. Univariable and multivariable Cox regressions were performed to determine associations with OS. Results We identified 356 patients who met study criteria, including 80 (23%) patients with GEJ tumors; 56% were white and 60% were male. Preoperative chemoradiation therapy was given to 268 (75%). Fifty-six (16%) had TRG 0, 57 (16%) had TRG 1, 128 (36%) had TRG 2, and 115 (32%) had TRG 3. There were no associations between TRG and pretreatment factors. TRG 2 or 3 was associated with advanced ypT and ypN categories (both p<0.001), ypM1 (p=0.004), and R1 resection (0.052). Of all patients, median OS was 6.6 y, and 5-year OS was 54.1%. TRG 3 was associated with worse OS than other groups (p = 0.015, Figure 1a), while there was no significant OS difference among

TRG 0-2 groups (p = 0.803) in univariate analyses. On multivariable analysis, TRG was not associated with OS after adjustment for ypN status (Figure 1b). Conclusion In patients with gastric cancer who underwent preoperative therapy, TRG 3 was associated with advanced ypStage and R1 resection. Patients with TRG 3 had worse OS, due to associated advanced ypStage, particularly ypN+ status. Further studies are warranted to identify better definitions of treatment response and to identify the optimal modality for obtaining ypN0 status.



141

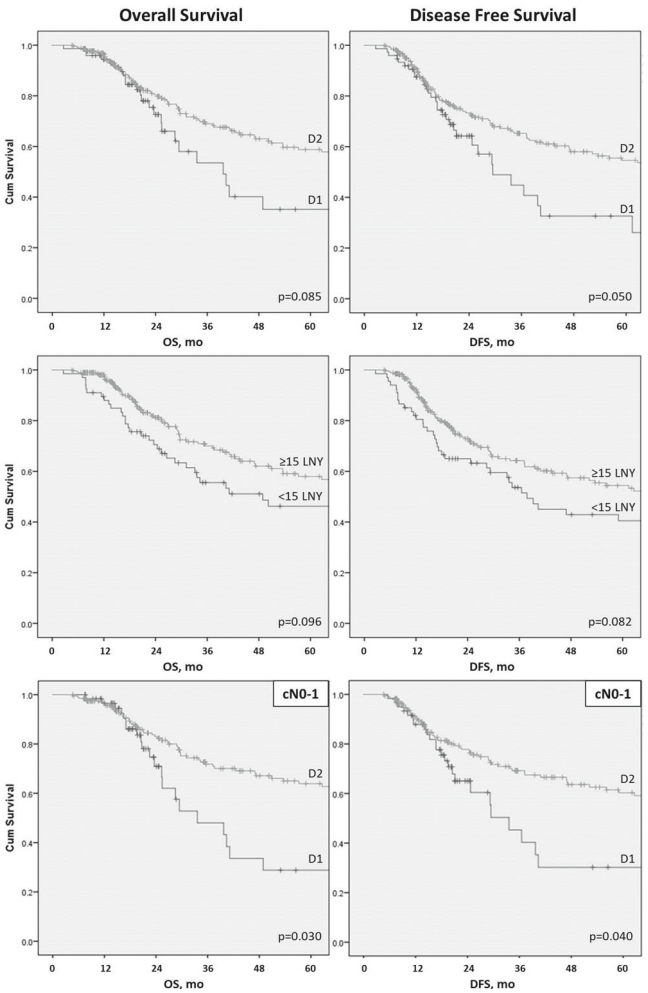
Development and Validation of a Staging System for Gastric Adenocarcinoma Following Neoadjuvant Chemotherapy and Gastrectomy with D2 Lymphadenectomy J. Lin,[2] J. Lu,[2]* C. Yoon,[1] D. Jacopo,[3] B. Yi,[1] P. Li,[2] C. Zheng,[2] A. Parisi,[3] C. Huang,[2] V. Strong,[1] S. Yoon.[1] *1. MSKCC, New York, NY; 2. Fujian Medical University Union Hospital, Fuzhou, China; 3. St. Mary's Hospital, University of Perugia, Terni, Italy.*

Background: Neoadjuvant chemotherapy (NC) followed by gastrectomy with D2 lymphadenectomy LAD is commonly used at referral centers for patients with locally advanced gastric adenocarcinoma GA. However, the 8th American Joint Committee on Cancer (AJCC) ypTNM staging system is based primarily on patients undergoing more limited LAD at non-referral centers. We sought to develop a system for accurate staging of locally advanced GA treated with NC followed by gastrectomy with D2 LAD. Methods: Using the prospectively maintained database from Memorial Sloan Kettering Cancer Center (MSKCC), we developed a modified staging system (m-ypTNM) based on overall survival (OS) of patients receiving NC followed by gastrectomy with D2 LAD. This system was then validated using data from an international cohort of similarly-treated patients. Results: From 2000-2014, 325 MSKCC patients were identified, including 33 (10.2%) with ypT0N0/+ status who are not classified under the current AJCC system. Five-year OS for m-ypTNM stages I, II, IIIA, and IIIB were 89%, 71%, 42%, and 10%, respectively, compared to 82%, 65%, and 29% for AJCC stages I, II, and III, respectively. The concordance index (C-index, 0.730 vs. 0.709), estimated area under the curve (0.765 vs. 0.740), and time-dependent ROC curve throughout the observation period were all superior for m-ypTNM staging. For the international validation cohort of 186 patients, the m-ypTNM system was again better at separating patients into prognostic groups for OS (C-index 0.688 vs. 0.657). Conclusion: The m-ypTNM staging system improves the accuracy of prediction of OS for patients treated with NC followed by gastrectomy with D2 LAD, and may guide decisions regarding adjuvant therapy and surveillance.

142

Prognostic Value of Lymph Node Yield Following Neoadjuvant Chemoradiation for Gastric Adenocarcinoma C.J. Allen,* T. Newhook, T.J. Vreeland, P. Das, B. Minsky, M. Blum, J. Ajani, N. Ikoma, P. Mansfield, B. Badgwell. *Surgery, MD Anderson Cancer Center, Houston, TX.*

Introduction According to current NCCN guidelines, regional lymphatic resection for gastric adenocarcinoma (GA) should include perigastric (D1) and those along the branches of the celiac axis (D2), with a total lymph node yield (LNY) of at least 15. However, the optimal LNY after neoadjuvant chemoradiation (NACXRT) is not defined as these guidelines are based on studies in patients who underwent upfront surgery or received neoadjuvant chemotherapy only. Therefore, we assess the prognostic value of LNY after NACXRT. Methods We analyzed data from a prospectively maintained database of patients who underwent resection following NACXRT for GA at our institution. Survival of those who underwent D1 vs D2 resections or with <15 vs ≥15 LNY were compared. Patients with early clinical nodal disease (cN0-1) were separately analyzed. Kaplan-Meier survival analyses were used to examine effects on overall survival (OS) and disease-free survival (DFS). Results A total of 345 patients underwent resection of GA following NACXRT. Age was age was 61±13y, 217 (63%) were male, 188 (55%) were white, and 203 (59%) underwent total gastrectomy. 269 (78%) received a D2 resection and 277 (80%) had ≥15 total LNY. There were no differences between patient age or AJCC disease stage between the groups based on D1/D2 or total LNY (all p>0.05). Median OS for D1 and D2 was 20.7 vs 25.7 months (p=0.041), respectively. 5y OS was 35% vs 59% for D1 and D2 (p<0.001), and 46% vs 58% for <15 and ≥15 total LNY (p=0.060). In those with early clinical N stage (cN0-1), patients undergoing D2 resections had improved 5y OS and DFS (both p<0.05). The figure depicts 5y OS and DFS based on D1/D2 and total LNY in the entire cohort and in those with early clinic N stage. Conclusions Patients with GA undergoing resection following NACXRT have improved survival after D2 lymphadenectomy, particularly in those with early N stage disease. There is also a survival trend in those who have a total LNY of at least 15. Despite the potential effects of tumor downstaging with preoperative therapy, a thorough locoregional lymphatic resection is recommended.



143

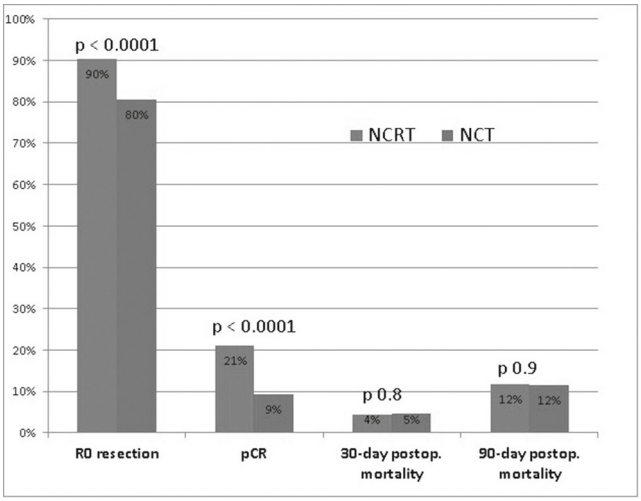
Complete Neoadjuvant Chemotherapy with FLOT (5-Fu/Leucovorin/ Oxaliplatin/Docetaxel) Does Not Increase Perioperative Morbidity and Mortality in Resected Patients with Gastric Cancer: A Pilot Study J.A. Gajardo,* J. Matute, N. Devaud, R. Charles, S. Hoefler, J.M. Butte. *Gastrointestinal Surgery, Fundación Arturo López Pérez, Santiago, Chile.*

Introduction. Perioperative chemotherapy with a FLOT-based regimen has been associated with a higher rate of complete pathological response. However, only 50% of patients complete postoperative cycles. Objectives. To evaluate the perioperative outcomes of patients undergoing complete preoperative chemotherapy with FLOT, and to compare them to those of patients undergoing surgery after perioperative adjuvant therapy with ECF/ DCX (Epirrubicin or Docetaxel plus Cisplatin and 5-Fu). Methods. This study included all patients with histologically confirmed gastric cancer and clinical staging cT1-4N+M0, that where submitted to complete preoperative chemotherapy with FLOT (Group A) and resective surgery with curative intent. The control group (Group B), included a historical cohort of patients submitted to perioperative chemotherapy with ECX/DCX regimen, using 1:2 matching based on age, gender, co-morbidities and clinical stage. Data analysis was obtained with Stata 14. Results. Fifty-one matched patients were included. Thirty-four (67%) men with a median age of 60±9 years. A total of 17 patients received preoperative FLOT and 34 perioperative DCX/ECX. No differences were found in terms of age, gender, co-morbidities and clinical staging. Thirteen patients (77%) completed all 8 cycles of preoperative FLOT. Duration of surgery (220 versus 225 minutes), intraoperative blood loss (180 versus 200 mL), and length of hospital stay (8 days) were similar between both groups. Complete pathological response was achieved in 4 patients of Group A and in 1 patient of Group B (p=0.03). Overall morbidity and 90-day mortality was the same for both groups (5% and 0% respectively). Conclusion. Complete preoperative chemotherapy with FLOT seems to be a reasonable strategy for patients with locally advanced gastric cancer, as it allows a better possibility of receiving the complete treatment without increasing surgical morbidity and mortality.

144

The Impact of Neoadjuvant Chemoradiation versus Chemotherapy on Short and Long-term Outcomes Among Gastric Carcinoma Patients B. Azab,[2]* F. Macedo,[1] O. Picado,[1] D. Franceschi,[1] A.S. Livingstone,[1] D. Yakoub.[1] *1. University of Miami, Yorktown, VA; 2. Sentara Healthcare, Hampton, VA.*

Background: There is little consensus on the use of neoadjuvant chemoradiation (NCRT) vs. neoadjuvant chemotherapy (NCT) in gastric carcinoma (GC) patients. We sought to compare the outcomes of these two approaches in a large national data base. Methods: National Cancer Data Base PUF (2004-2014) of GC patients who underwent NCRT/NCT followed by resection were included. Primary outcome was overall survival (OS), secondary outcomes were pathological complete response (pCR), R0 resection and postoperative mortality. Results: A total of 4204 GC patients with NCT were included, 62% of them had additional neoadjuvant radiotherapy (NRT). NCRT had higher pCR and R0 rates [551/2613 (21%), 2314/2561 (90%)] than NCT group [148/1573 (9%), 1242/1543 (80%)], p <0.0001. Multivariate logistic regression showed similar higher odds of pCR (OR 2.8, 95% CI 1.65-4.60, p <0.0001) and R0 (OR 1.5, 95% CI 1.14-1.99, p=0.004) among NCRT vs. NCT. There was no significant difference in length of hospital stay, 30-day readmission rate, 30- and 90-day postoperative mortality. Median, 3- and 5-year OS for NCRT vs. NCT were: (20.4 months, 24% and 11%) vs. (18.3 months, 19% and 6%), p<0001. Univariate cox regression analysis showed superior OS with NRT (HR 0.9, 95% CI 0.80-0.91, p<0.001). After adjusting for confounding variables, pCR (HR 0.2, 95% CI 0.18-0.24, P<0.001) and R0 (HR 0.7, 95% CI 0.61-0.75, P<0.001) had better OS, while NRT was not Conclusion: NRT improved pCR and R0 rates in GC without increase in surgical morbidity/mortality. The long-term OS benefit of NRT is likely secondary to higher pCR and R0 resection. Further studies are needed to evaluate these findings in randomized control trials.



The pathological complete response (pCR), R0 resection, 30- and 90-day postoperative mortality rates with neoadjuvant chemoradiation (NCRT) and chemotherapy (NCT) among gastric carcinoma patients.

145

Prognostic Significance of Postoperative and Surgery-Induced Sarcopenia in the Long-term Survival of Gastric Cancer Patients Y. Park,* S. Ahn, D. Park, H. Kim. *Surgery, Seoul National University Bundang Hospital, Seongnam-si, Korea (the Republic of).*

Background: It is well known that preoperative sarcopenia is associated with a poor long-term prognosis for patients with gastric cancer (GC). However, most GC patients rapidly lose body weight and muscle mass after gastrectomy. This retrospective cohort study analyzed the effect of postoperative sarcopenia and surgery-induced sarcopenia on long-term outcomes. Methods: The study reviewed 1885 GC patients who underwent curative gastrectomy between January, 2009 and December, 2013 at Seoul National University Bundang Hospital. The patients were categorized into the sarcopenia group or the non-sarcopenia group according to their skeletal muscle index calculated using abdominal computed tomography images. Results: Preoperative sarcopenia was present in 538 (29.0%) patients and postoperative sarcopenia in 904 (48.7%). Among the postoperative sarcopenic patients, 420 (46.5%) showed surgery-induced sarcopenia. The 5-year overall survival (OS) rate was significantly poorer in the preoperative sarcopenic group than in the preoperative non-sarcopenic group (80.0% vs. 90.3%, P<0.001), and the same result was repeated in the postoperative sarcopenia (82.2% vs. 92.1%, P<0.001). However, in the multivariable Cox-regression analyses, preoperative sarcopenia was not the independent risk factor of OS (HR 1.23, 95% CI 0.94-1.59), but postoperative sarcopenia was the independent poor prognostic factor for OS (HR 1.36, 95% CI 1.02-1.81). The multivariable analysis also showed that the preoperative non-sarcopenic and postoperative sarcopenic group (surgery-induced sarcopenia) was associated with significantly higher mortality (HR 1.57, 95% CI 1.10-2.22), but the pre- and postoperative sarcopenic group was not (HR 1.25, 95% CI 0.87-1.79). Conclusion: Postoperative sarcopenia was associated with a poor long-term survival in GC patients who underwent curative gastrectomy. Surgery-induced sarcopenia should be avoided for the favorable long-term outcome.

146

Expression of the Plk4 Inhibitor FAM46C Predicts Better Survival Following Resection of Gastric Adenocarcinoma (GCa) S. Luu,[1]* K. Kazazian,[1] J. Conner,[1] J. Swett-Cosentino,[2] K. Pacholczyk,[2] D. Ng,[1] S. Brar,[1] A. Govindarajan,[1] C. Swallow.[1] *1. University of Toronto, Toronto, ON, Canada; 2. Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada.*

Background: Despite improvements in surgical technique and perioperative adjuvant therapy for GCa, ≈40% of Western patients die of recurrent disease. Novel molecular markers and targets are urgently needed. We are investigating the role of the oncogene Plk4 and a 61-gene panel of BioID-defined Plk4

interactors (Cancer Research 2017; 77:434) in GCa progression. Methods: Patients who underwent curative-intent resection for GCa from 2006-2016 were identified in our institutional database. Banked primary tumor (T) and paired normal mucosa (NM) samples were microdissected, RNA extracted, and the status of the Plk4 interactome interrogated using qPCR. Pattern of recurrence was categorized as locoregional, peritoneal or distant. Survival was estimated by Kaplan-Meier method and comparisons made by log-rank analysis. Results: From 84 consecutive resection specimens, Plk4 interactome expression analysis was informative in 77 cases, and these patients form the study cohort (median age=69 yrs, F:M 30:47). At median follow-up time of 47 mos (IQR 29-75), 33 patients had died of GCa, 5 had died of other causes, and 39 were alive with no evidence of disease. Plk4 was modestly overexpressed in GCa tumor tissue (median T/NM 1.45, IQR 0.59-3.0), but not prognostic of overall survival (OS) or disease-specific survival (DSS). The Plk4 inhibitory interactor FAM46C was depleted (T/NM < 1) in 93% of cases. Median FAM46C T/NM was 0.29 (IQR 0.13-0.51). Retention of FAM46C expression (defined as T/NM ≥ 0.35, n=27) was associated with superior 5-yr OS (69% vs 35%, p=0.02) and 5-yr DSS (76% vs 38%, p=0.01). The prognostic significance of FAM46C persisted in the node positive subgroup of patients (n=49; OS p=0.03, DSS p=0.04). Loss of FAM46C in the resected tumor tissue predicted distant recurrence (12/50 vs 1/27, p=0.03, Fisher's exact test), which presaged death from GCa at a median of 7 mos (IQR 4-9) following recurrence. Conclusions: Retention of FAM46C expression was associated with a better prognosis following curative-intent resection of GCa. FAM46C may be protective through its inhibition of Plk4 oncogenic function, reducing the risk of distant metastasis.

147

Gastric Cancer Peritoneal Carcinomatosis Risk Score

M.J. Selleck,[2]* L. Ji,[1] J. Morgan,[1] J. Xu,[2] S. Lum,[2] C. Garberoglio,[2] M. Reeves,[2] N. Solomon,[2] J. Namm,[2] M. Senthil.[2] *1. Loma Linda University School of Public Health, Loma Linda, CA; 2. Loma Linda University, Loma Linda, CA.*

Background: Peritoneal carcinomatosis (PC), the second most common form of metastases in gastric cancer (GC), is associated with poor prognosis. Although, several features, such as grade, histology and stage are associated with PC, cumulative risk of PC when multiple risk factors are present is currently unknown. Objective: To develop a cumulative PC risk score based on the effects of individual demographic/tumor characteristics. Methods: California Cancer Registry patient-level data (2004-2014) were reviewed by creating a keyword search algorithm to identify patients with gastric PC. Patients with unknown T-stage, node status or grade were excluded. Multivariable logistic regression was used to assess associations between demographic/tumor characteristics and PC in a random sample of half the study subjects. A discrete score was assigned to each risk factor based on the beta-coefficient from the logistic regression result, with these scores applied to the remainder of study subjects (subsample 2). Summed scores for each patient in subsample 2 formed their total risk scores. These totals were then ranked and grouped, revealing percentages of patients with PC in each score-group. Results: We identified 3911 patients with gastric adenocarcinoma (2546 males; 65.1%) having clinical data available. Median age 67 years (IQR=20). Most patients were non-Hispanic white (n=1621; 41.5%), with proximal (n=1579; 40.4%) and poorly differentiated tumors (n=2632; 67.3%). Characteristics highly associated with PC included T4 (OR=2.90; 95%CI=1.99-4.24), overlapping location (OR=2.28; 95%CI=1.50-3.48), age 20-40 years (OR=4.38; 95%CI=2.54-7.56) and Hispanic ethnicity (OR=1.66; 95%CI=1.20-2.28). Risk factor scores for demographic/tumor characteristics and percentages with PC for each score-group are shown in Table1. Conclusion: Based on demographic/tumor characteristics associated with PC in GC, it is possible to distinguish groups having varying odds of PC. Understanding the risk of PC based on the cumulative effect of the high-risk features can help customize surveillance strategies and may aid in early identification of PC.

Gastric Cancer Peritoneal Carcinomatosis Score

Patient and Tumor Characteristics	*Score*	Patient and Tumor Characteristics	*Score*
Clinical T stage		**Tumor location**	
T1	**0**	Proximal	**0**
T2	**0.5**	Distal	**2**
T3	**1**	Mid	**3**
T4	**4**	Overlapping	**3**
Tumor grade		**Age**	
Well differentiated	**0**	20-40	**4**
Moderately well differentiated	**1**	40-60	**2**
Poorly differentiated or undifferentiated	**2**	60+	**0**
Histologic subtype		**Sex**	
Intestinal	**0**	Female	**0**
NOS	**0.5**	Male	**1**
Diffuse	**1**	**Race/ethnicity**	
Mucinous	**1.5**	Asian/Other	**0**
Signet ring	**1.5**	Non-Hispanic White	**0**
		Non-Hispanic Black	**0.5**
		Hispanic	**2**

Score-group	Percent with PC
0-6	**2.8%**
6.5-9	**6.0%**
9.5-12	**14.2%**
12.5-13	**23.7%**
13+	**37.8%**

Gastric Peritoneal Carcinomatosis Score

148

New Insights into the Role of Mesothelial Cells in Peritoneal Carcinomatosis

F. Gerstenhaber,* S. Loewenstein, N. Lubezky, E. Nizri, J. Klausner, G. Lahat. *Surgery, The Tel Aviv Sourasky Medical Center, Tel-Aviv, Israel.*

Background: Angiogenesis is an important control point of intraperitoneal cancer progression, and is orchestrated by interplay between cancer and resident peritoneal cells. We studied the potential role of naïve and gastric cancer- treated mesothelial cells in angiogenesis. Methods: Cell lines were used for in vitro experiments. Gastric cancer and mesothelial exosomes were produced from cell cultures. Proliferation, migration, and invasion assays were used to evaluate the phenotypic behavior of treated endothelial cells. Matrigel formation assays demonstrated angiogenesis in vitro and in vivo. Protein array identified proangiogenic proteins in mesothelial exosomes, WB and PCR were used to investigate signaling pathways. Results: We observed a robust uptake of both mesothelial and gastric cancer exosomes by endothelial cells. These exosomes enhanced endothelial cell proliferation, motility, and invasiveness; however, mesothelial exosomes were more effective. We also demonstrate that mesothelial exosomes significantly augment in vitro and in vivo tube formation. Angiogenesis array identified 43 differently expressed regulators of angiogenesis within mesothelial exosomes. We also revealed that treatment with gastric cancer exosomes augment the secretion of these factors by the mesothelial exosomes; next, we show that this augmentation is time dependent and directly related to the exposure interval of mesothelial cells to gastric cancer exosomes. Last, we show that the above noted effects of the mesothelial exosomes were mediated by angiopoietins via the activation of MAPK and PI3K/AKT, whereas inhibition these factors significantly reduced the angiogenic effect of mesothelial exosomes. Conclusions: We report for the first time uptake of mesothelial exosomes by endothelial cells, induction of angiogenesis by these exosomes, and that interaction between gastric cancer cells and mesothelial cells augment the proangiogenic properties of mesothelial exosomes. Taken together, our data imply that mesothelial cells are important regulators of angiogenesis, thus playing an active role in the progression of intraperitoneal carcinomatosis.

149

Impact of Gallium-68 Dotatate PET/CT Imaging on the Oncologic Management of Patients with Neuroendocrine Tumors (NET)

A. Crown,* P. Raghu, B. Lin, G. Funk, A. Alseidi, M. Hubka, M. Lee, H. Kennecke, F. Rocha. *General, Thoracic and Vascular Surgery, Virginia Mason Medical Center, Seattle, WA.*

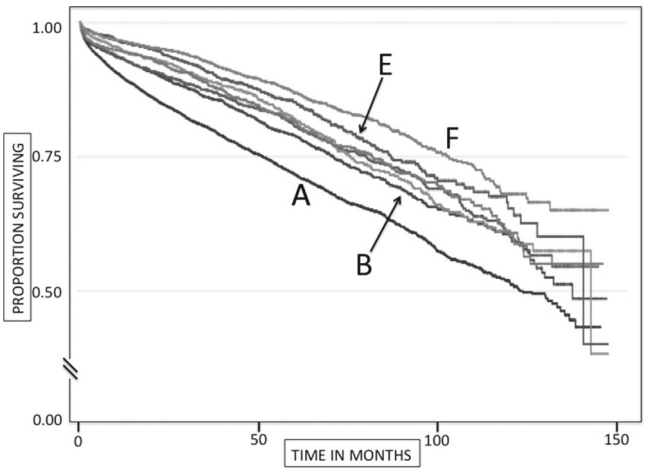
Background: Somatostatin analogue functional imaging with Ga-68 Dotatate PET/CT (NETSPOT) has demonstrated superiority in lesion detection in patients with NET. The clinical impact of this novel imaging modality on US surgical and medical oncology practices and its usefulness in different types of NET has not been established. Methods: Consecutive NET patient referred to our institution who received an initial NETSPOT between 07/2017-09/2018 were included. Clinicopathologic and treatment information was collected from the electronic medical record. NETSPOT imaging was compared to prior available CT, MRI, and/or In-111 Pentetreotide scans. Results: Among 101 eligible patients, 51/50 were female/male, site of origin was gastroenteropancreatic (GEP) (75%), unknown primary (UP) (13%), lung (8%), thymus (2%), and other (2%). All NET were histologically well/moderately differentiated and 37/51/3/10 were G1/G2/G3/unknown, respectively. NETSPOT revealed additional metastatic disease in 37 of 77(48%) patients with prior evidence of metastatic disease. Most common sites were distant lymph nodes (18), bone (15) and liver (9), and peritoneal/pleural (4). A previously UP tumor was identified in 3 patients. Results of NETSPOT imaging altered patient management in 36 (35.6%) patients as follows: 14 initiated systemic therapy due to documentation of progression, obviated need for biopsy in 4 patients, and altered surgical plans in 7/14 (50%) patients referred for surgery. In 4 patients, occult metastatic liver lesions were identified and treated in addition to the planned resection for the primary tumor. In 3 patients, NETSPOT rendered tumors unresectable. In 11 patients with no tumor Ga-68 Dotatate uptake, decisions about use of peptide receptor radionucleotide therapy and somatostatin analogues were altered. Conclusions: In this series, NETSPOT altered diagnosis and management in one third of patients and changed operative plans in half of the patients who were referred for surgical evaluation. These results supports the routine use of NETSPOT in the care of patients with early stage and advanced NET but further investigation is needed.

150

Lymphadenectomy in Small Bowel Neuroendocrine Tumors: How Many Nodes are Enough?

J. De Andrade,* A.M. Blakely, A.H. Nguyen, P. Ituarte, D. Li, B. Lee, G. Singh. *Surgery, City of Hope National Medical Center, Duarte, CA.*

INTRODUCTION: There are no national guidelines for scale of lymphadenectomy for patients with small bowel neuroendocrine tumors (SB-NETs) nor any reports associating lymphadenectomy with survival outcomes. METHODS: The National Cancer Database (NCDB) was queried for the years 2004-2013 for all patients with SB-NETs for whom data on lymphadenectomy and outcomes were present. Survival comparisons were made by Kaplan-Meier method. Ranges of lymphadenectomy were examined to identify thresholds at which a possible survival association may exist. RESULTS: 19638 patients met inclusion criteria. 7292 (37%) had 0 lymph nodes (LNs) resected, 2339 (12%) had 1-3 LNs resected, 1677 (9%) had 4-6 LNs resected, 1511 (8%) has 7-9 LNs resected, 1509 (8%) had 10-12 LNs resected, 1430 (7%) had 13-15 LNs resected, and 3879 (20%) had 16 or more LNs resected. Patients undergoing any lymphadenectomy had a higher mean overall survival (108 months) compared to those with no lymphadenectomy (92.6 months, $p<0.001$). Using stepwise survival comparison, lymphadenectomy of 1-3 nodes was associated with improved overall survival compared to 0 nodes resected ($p<0.001$) [see figure]. However, comparison of 1-3 vs 4-6 LNs removed ($p=0.147$), 4-6 vs 7-9 LNs removed ($p=0.629$), and 7-9 vs 10-12 LNs removed ($p=0.962$) showed no statistical difference in overall survival. On the other hand, further lymphadenectomy was associated with improved outcomes. 10-12 vs 13-15 LNs removed ($p=0.043$) and 13-15 vs 16 or more LNs removed ($p=0.016$) were associated with statistically higher overall survival. CONCLUSION: 37% of patients with SB-NETs underwent no associated lymphadenectomy. Lymphadenectomy is associated with improved overall survival, with the greatest benefit seen for 13 lymph nodes or more resected.



Survival of patients with small bowel neuroendocrine tumors stratified by number of lymph nodes resected.
(A) no lymph nodes removed.
(B) 1-3 lymph nodes removed, $p<0.05$ compared to (A).
(E) 13-15 lymph nodes removed, $p<0.05$ compared to 1-3 LNs removed (B) or 4-6/7-9/10-12 LNs removed (not labeled).
(F) 16 and more LNs removed, $p<0.05$ compared to (E).

ABSTRACTS

Accepted for
VIDEO PRESENTATIONS

72nd Annual Cancer Symposium
Society of Surgical Oncology
March 27–30, 2019
San Diego, CA

V1

Robotic-Extended Right Hemicolectomy with Complete Mesocolic Excision and D3 Lymph Node Dissection P. Aggarwal,* I. Hameed, M.R. Weiser. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Recent studies have shown the benefits of complete mesocolic excision and extended lymphadenectomy (D3 lymph node dissection) in patients with colon cancer. This video demonstrates a robot-assisted approach. A 62-year-old male was found to have a hepatic flexure adenocarcinoma during a screening colonoscopy. No metastatic disease was identified in the staging CT scans. A robot-assisted extended right hemicolectomy with complete mesocolic excision and D3 lymph node dissection was performed. The trocars were placed in the right lower quadrant (8 mm), lower midline (8 mm), supraumbilical (8mm, camera), and left upper quadrant (12 mm, stapler). An assistant port was placed in the left lower quadrant. With the cecum and transverse colon on tension, the ileocolic and middle colic vessels were identified along with the intervening superior mesenteric vessels. The dissection began at the superior mesenteric vein to allow resection of D3 lymph nodes. The ileocolic vessels were dissected, and a plane was developed between the mesentery and the retroperitoneum in a medial-to-lateral direction with intact visceral peritoneum. Ileocolic and middle colic vessels were transected with a vessel sealing device at their origin from the superior mesenteric vessels. Proximal transverse colon and ascending colon were mobilized by taking down lateral attachments. The intervening mesentery was transected, and the perfusion was visualized with indocyanine green fluorescence. An intracorporeal, isoperistaltic, side-to-side anastomosis was performed with a 45-mm robotic stapler. The common enterotomy/colotomy was sewn closed in two layers. Final pathology showed T3N0 adenocarcinoma with all negative margins. Twelve lymph nodes were retrieved. The patient went home on postoperative day 6 with no complications. Robotic extended right hemicolectomy with complete mesocolic excision and D3 lymph node dissection is a safe and feasible operation, with better visualization and greater degrees of freedom compared with conventional minimally invasive surgery.

V2

Robotic Complete Mesocolic Excision for Right Colectomy in a High-BMI Patient: "SMV-first" Approach Y. Yang,* S. Malakorn, S.N. Zafar, L. Sandhu, G.J. Chang. *The University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: Evidence supports complete mesocolic excision (CME) as the optimal surgical approach for right-side colon cancer, based on oncologic outcomes. Although the feasibility of a laparoscopic approach to CME has been reported, obesity is associated with increased difficulty for finding the correct plane and delineating the vascular anatomy. Methods: We utilize an approach that includes early identification of and dissection along the superior mesenteric vein (SMV) during robotic right colectomy with CME. This "SMV-first" approach is applicable to high or low body mass index (BMI), and facilitates identification of critical anatomy, complete lymphadenectomy, and correct plane dissection during robotic CME surgery. Results: This video demonstrates the SMV-first approach in a 44-year-old man with cecal cancer (clinical stage T3N2M0) whose BMI was 36.6 kg/m^2. The dissection was initiated with a transverse curvilinear incision to identify the SMV as the starting point. Then, the central vascular dissection was performed anterior to SMV plane while observing CME principles. The anterior SMV plane is a safe dissection plane as there are no anterior tributaries and it permits identification of the branches of the superior mesenteric artery. The ileocolic vein (ICV) and artery (ICA) were ligated centrally. The dissection then continued cephalad along the SMV, in order to identify the middle colic trunk, at the origin of the superior mesenteric artery. The right branch of the middle colic artery and vein were ligated, according to the oncologic principles for vascular ligation. The superior right colic vein was then ligated at the base of the gastrocolic trunk. After we completed the vascular dissection, the colon was mobilized. Conclusion: In conclusion, using the SMV-first approach, robotic CME for right colectomy can be performed on high- or low-BMI patients. This approach provides a safe plane for dissection and delineation of anatomy and facilitates performance of CME with standardized anatomic dissection.

V3

Robotic Pelvic Exenteration for Locally Advanced Prostate Cancer J.S. Peng,* K. Guru, S. Nurkin. *Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Introduction: Minimally invasive approaches to oncologic resections are being increasingly adopted, including for select patients with locally advanced malignancies. We present a patient with a prostate cancer involving the rectum and pelvic floor who was treated with robotic pelvic exenteration with en bloc resection of the prostate, bladder, and rectum. Methods: The patient was a 47-year-old male who presented with dysuria, hematuria and rectal pain. Biopsy demonstrated poorly differentiated carcinoma with basal-squamoid differentiation. Magnetic resonance imaging demonstrated a 6.6 cm prostate tumor with involvement of the anterior rectal wall and pelvic floor, and peri-rectal adenopathy. He underwent cisplatin chemoradiation with decrease in size of the tumor to 5.0 cm but with continued involvement of the rectum and pelvic floor. Results: The accompanying video demonstrates the key steps of the operation. The dissection starts with a medial to lateral mobilization of the sigmoid mesocolon. The inferior mesenteric artery is divided, along with the mesocolon. The sigmoid colon is divided and the specimen is retracted out of the pelvis to facilitate total mesorectal excision (TME). The TME dissection begins posteriorly, followed by lateral dissection until the pelvic floor is reached. The ureters are then isolated and the vesical pedicles are divided. The anterior dissection is then completed and the urethra is transected. The dissection is carried through the levators into the ischiorectal space. An ileal conduit is created for urinary diversion. Dissection is performed from the perineum until it meets the pelvic dissection plane, and an end colostomy is then matured. Pathology demonstrated residual microscopic foci of poorly differentiated carcinoma with therapy effect, without viable tumor involving the rectum. All margins were negative for cancer, and all 18 lymph nodes were negative. Conclusion: This case highlights the importance of multidisciplinary care to treat patients with locally advanced cancers. At centers with experience in robotic oncologic surgery, this approach can offer excellent oncologic outcomes with improved recovery times.

V4

Robotic Transhiatal Esophagectomy J.S. Peng,* M. Kukar, S. Hochwald. *Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Introduction: We present a patient who underwent robotic transhiatal esophagectomy with a side-to-side stapled cervical anastomosis. Methods: The patient was a 60-year-old male who presented with dysphagia and weight loss. He was diagnosed with a Siewert type I gastroesophageal adenocarcinoma, clinically staged as T3N0. He underwent neoadjuvant chemoradiation with carboplatin and paclitaxel. Positron emission tomography demonstrated metabolic response. The patient was unable to quit smoking and was recommended to undergo a transhiatal esophagectomy to avoid the morbidity associated with thoracoscopic dissection and single lung ventilation. Results: The key steps of the operation are demonstrated in the accompanying video. The gastrocolic ligament is divided, avoiding injury to the gastroepiploic vessels. The transverse mesocolon is dissected from the stomach and duodenum, and the duodenum is Kocherized. The right gastric artery is dissected and divided, and the left gastric vein and artery are dissected and divided. The gastric conduit is created using the robotic stapler starting 4 cm proximal to the pylorus. The mediastinal dissection is performed with circumferential mobilization enabled by adjustment of retraction and tension on the esophagus between the operating surgeon and bedside assistant. Care is taken to avoid injury to the membranous portion of the trachea. Aortic and lymphatic branches posterior to the esophagus are clipped. The neck dissection is performed, with careful visualization of the recurrent laryngeal nerve. The cervical esophagus is encircled bluntly and a clamp is passed to meet the mediastinal dissection. The specimen and conduit are extracted via the neck incision and a side-to-side stapled anastomosis is performed. The anastomosis is returned to the mediastinum and the excess conduit is returned to the abdomen, and tacked to the crus. Final pathology demonstrated residual poorly differentiated adenocarcinoma with treatment effect, with negative margins, and 2 of 29 lymph nodes were positive. The patient recovered uneventfully. Conclusion: Minimally invasive robotic transhiatal esophagectomy can be offered to patients with increased pulmonary risk factors with safe technical and oncologic results.

V5

Robotic Ivor Lewis Esophagectomy with Stapled Side-to-Side Intrathoracic Anastomosis J.S. Peng,* S. Nurkin, S. Hochwald, M. Kukar. *Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Introduction: Minimally invasive approaches to esophageal resections for malignancy have been increasingly utilized and have been shown to decrease pulmonary complications. We present a patient who underwent robotic Ivor Lewis esophagectomy with a side-to-side stapled intrathoracic anastomosis. We prefer a side-to-side anastomosis due to the larger anastomotic diameter compared to an end-to-end anastomosis. Methods: The patient was a 64-year-old male who presented with dysphagia and was diagnosed with a distal esophageal adenocarcinoma. The lesion was clinically staged as T3N2 due to gastrohepatic and subcarinal nodal disease. He underwent three cycles of FLOT (5-fluorouracil, leucovorin, oxaliplatin, and docetaxel) and subsequently FOLFOX chemoradiation (5-fluorouracil, leucovorin, and oxaliplatin). Positron emission tomography demonstrated a good metabolic response and he was recommended to undergo minimally invasive esophagectomy. Results: The key portions of the operation are demonstrated in the accompanying video, with tricks and tips for success. Dissection begins in the abdomen starting with the greater curve and proceeds in the clockwise fashion. The gastrocolic ligament is divided, taking care to avoid manipulation of the gastroepiploic vessels. The transverse mesocolon is dissected from the stomach and duodenum, and the duodenum is Kocherized. The right gastric artery is divided, and the left gastric vein and artery are divided. The gastric conduit is fashioned using the robotic stapler. The patient is repositioned into a left lateral decubitus position and the right lung is collapsed. The thoracic esophagus is dissected free circumferentially. The azygous vein is divided and the esophagus is divided. The conduit is pulled into the chest and the specimen is extracted. A 60-mm side-to-side esophagogastrostomy is created and a leak test is performed. Final pathology demonstrated residual carcinoma with moderate treatment effect, negative margins, and 5 of 15 lymph nodes were positive. Post-operative course was uncomplicated and the patient is tolerating an oral diet. Conclusion: Minimally invasive esophagectomy can provide excellent oncologic and functional outcomes.

V6

Robot-Assisted Distal Gastrectomy with D2 Lymphadenectomy J. Lin,[2] J. Lu,[2]* K. Chang,[2] D. Park,[3] S. Yoon.[1] *1. MSKCC, New York, NY; 2. Fujian Medical University Union Hospital, Fuzhou, China; 3. Seoul National University College of Medicine, Seoul, Korea (the Republic of).*

Introduction: Minimally invasive gastrectomy and D2 lymphadenectomy (LAD) for gastric adenocarcinoma (GA) has advantages over open surgery in terms of decreased postoperative pain and length of stay. However, this procedure, particularly portions of the LAD, aretechnically demanding. The use of robotic surgical systems may reduce the learning curve. Methods: A retrospective review was performed of patients with GA who received robot-assisted distal gastrectomy and D2 LADS by a single surgeon between 2015 and 2017. Results: Selected video footage was compiled from the operations of five patients. An 8-minute video was created describing the operative steps. The patient is placed in 15 degrees of reverse Trendelenberg position. Four 8 mm robotic ports and a 12 mm assist port are used along with the Nathanson liver retractor. Robotic instruments used include Maryland bipolar forceps, Harmonic scalpel, fenestrated bipolar forceps, large clip appliers, and large needle drivers. The assistant uses through the assistant port bowel graspers, suction-irrigator, and Endo GIA stapler. For each step, a slide demonstrates how to obtain optimal exposure and video footage shows the keys steps of dissection. Steps include division of the gastrocolic omentum, ligation of the right and left gastroepiploic vessel at their origin, dissection of the porta hepatis and liation of the right gastric vessels near their origin, dissection of the celiac axis (common hepatic artery, left gastric artery, and proximal splenic artery with ligation of the left gastric vessels near their origin, and dissection of the right paracardial and proximal lesser curvature nodes off the stomach. A Roux-en-Y reconstruction is created and the mesenteric traps are closed. Conclusion: This video provides step-by-step instructions with accompanying images to describe the robot-assisted distal gastrectomy and D2 LAD.

V7

Intraoperative Air Leak Test to Prevent Bile Leak After Right Posterior Sectionectomy with En Bloc Diaphragm Resection for Metastatic Teratoma T.J. Vreeland,[1]* E. Beaudry-Simoneau,[2] S.N. Westin,[1] R.J. Mehran,[1] W.L. Dewhurst,[1] Y. Chun,[1] T. Aloia,[1] J. Vauthey,[1] C.D. Tzeng.[1] *1. Surgical Oncology, University of Texas MD Anderson, Houston, TX; 2. Columbia University, New York, NY.*

Background: Previous publications have shown that the intraoperative air cholangiogram, or "Air Leak Test" (ALT), at the time of hepatectomy can significantly reduce the rates of bile leak and symptomatic fluid collection after high-risk cases. Because a bile leak in the setting of an en bloc diaphragm resection and biologic mesh reconstruction would be a particularly dreaded complication, herein we show the technique for resection, reconstruction, and ALT. Presentation: We present the case of a 29yr old female with metastatic teratoma with a 8x7 cm liver metastasis in segment 7 and diaphragm invasion to the level of the right hepatic vein. Operation: We performed a right posterior sectionectomy with en bloc diaphragm resection. The 12x8cm diaphragmatic defect was reconstructed using Surgimend. An intraoperative ALT identified multiple areas of bubbles under water submersion of the liver remnant, consistent with leaking from the biliary tree at the cut surface of the liver, which were all repaired with 4-0 polypropylene sutures. The ALT was repeated until no bubbles were seen at the transection line. Because there was no evidence of additional air leak, we did not have to leave an intra-abdominal drain. Total parenchymal transection time using inflow occlusion was only 25 minutes, and estimated blood loss was only 200cc. The patient did well post-operatively with no complications. Conclusion: In cases of combined liver and diaphragmatic resection, avoidance of bile leak, with subsequent contamination of the diaphragm repair and even the thoracic cavity, is particularly important. A properly performed intraoperative Air Leak Test can decrease the risk of post-operative bile leak and subsequent consequences on quality of life, adjuvant therapy, and oncologic outcomes.

EHV1

Robotic Left Adrenal Metastasectomy C.J. LaRocca,* A. Nguyen, B. Blair, M. Bassett, C. Lau, G. Singh. *Surgery, City of Hope National Medical Center, Duarte, CA.*

We describe a robotic-assisted approach for a metastatic lesion that initially appeared to involve the left adrenal gland. The patient is a 56 year old female who had a history of a multi-focal, well differentiated pancreatic neuroendocrine tumor that required a total pancreatectomy approximately four years ago. On surveillance imaging, she was found to have an enlarging mass near the left adrenal gland. She then underwent a Gallium-68 dotatate scan which demonstrated avidity in this area. The lesion was in close proximity to the inferior border of the stomach as well as the left colon. For the operation, she was positioned in the right lateral decubitus position. The operation began by taking down adhesions secondary to her previous laparotomy and continued on with mobilization of the left colon. The peri-nephric tissues were dissected to identify the left renal and gonadal veins, which were carefully preserved. Additionally, the adrenal gland was identified and the tumor abutted it, but did not invade into it. The tumor was circumferentially freed from its attachments and placed into an endo bag for extraction. The final pathology demonstrated a well-differentiated neuroendocrine tumor with negative margins that measured 5.0 cm in greatest dimension. The patient did well with no immediate complications. She was discharged home on the first post-operative day.

EHV2

Robotic Resection of Choledochal Cyst, Portal Lymph Node Dissection, and Roux-en-Y Hepaticojejunostomy E.J. Merle,[2]* L.M. Kranker,[1] M. Hellan,[1] J.R. Ouellette.[1] *1. Wright State University Boonshoft School of Medicine, Dayton, OH; 2. Medstar Georgetown University Hospital/Washington Hospital General Surgery, Washington, DC.*

A 33-year-old female presented with acutely-worsening right upper quadrant pain of several months duration. Ultrasound demonstrated a focal common bile duct dilation with choledocholithiasis. Blood chemistries and tumor markers were normal. MRCP showed a fusiform dilation, believed to be a Type I choledochal cyst, measuring 2.6 x 1.5 cm. Over 80% of choledochal cysts are diagnosed within the first decade of life, and surgical removal is standard treatment. In the adult, the risk of malignant transformation is

10 to 30%, with Type I and IV cysts having the highest rates. Using the Da Vinci Xi Surgical System, the patient underwent resection of choledochal cyst, portal lymph node dissection, and roux-en-y hepaticojejunostomy. There were no intraoperative complications. The total operative time was 3 hours and 54 minutes; total robotic time was 3 hours and 27 minutes. The specimen was completely excised with adequate margins on frozen and final pathology. Recovery was without incident or complication. In our experience, a robotic-assisted approach provides better anatomic visualization and increased dexterity for suturing the hepaticojejunostomy anastomosis, when compared to laparoscopy. Minimally-invasive excision is a safe alternative to open excision; this approach offers decreased post-operative pain and ileus, shorter hospital stay, and improved cosmesis.

EHV3

Robotic Resection of Duodenal Gastrointestinal Stromal Tumor

D. Schuitevoerder,[1]* F. Izquierdo,[2] S. Sherman,[1] K. Roggin.[1]
1. University of Chicago, Chicago, IL; 2. Clinica Santa Maria, Santiago, Chile.

The advantages of minimally invasive techniques have been widely documented and include decreased post-operative pain, shorter hospital length of stay, and improved cosmesis. For complex cases the improved instrument dexterity of robotic vs laparoscopic instruments is beneficial. Here we present a video of robotic duodenal gastrointestinal stromal tumor resection. The patient is a 74 year-old previously healthy male who presented with heme positive stool. EGD / EUS revealed a mass at the second portion of his duodenum a biopsy of which was positive for GIST. After CT abdomen confirmed tumor location and no distant disease we proceeded with robotic resection of this duodenal GIST utilizing the benefits of robotic visualization, magnification, and improved instrument dexterity to safely excise this mass and close the resulting duodenal defect. We started by mobilizing the transverse colon and hepatic flexure and then proceeded to perform a Kocher maneuver. Loose adhesions on the anterior surface of the duodenum were taken down using cautery exposing the duodenal mass. We then proceeded to excise the mass working layer by layer so as to minimize trauma to the duodenum. Stay sutures were placed in four quadrants of the duodenum adjacent to the mass and one through the mass itself to provide traction. Once the mass was excised there was a 1cm full thickness defect in the duodenum which was closed horizontally in 2 layers using interrupted absorbable suture for the internal layer and a running v-lock suture for the second layer. We finished by performing an EGD, which demonstrated good closure of the defect without leak. Final pathology showed a 2.3 cm low grade duodenal GIST with negative margins.

EHV4

Expanding Robotic-Assisted Surgery to a Large Paraaortic Retroperitoneal Extra-Adrenal Pheochromocytoma

T. Tran,[1]* A. Maker.[2] *1. University of Illinois at Chicago-MGH, Chicago, IL; 2. University of Illinois at Chicago, Chicago, IL.*

Background: Paragangliomas are rare extra-adrenal tumors arising from the neural crest. These tumors often arise in the retroperitoneum adjacent to the aorta and are challenging to remove due to risk of injury major blood vessels and life-threatening catecholamine release. Large size and retroperitoneal location are relative contraindications to minimally invasive resection, and few robotic assisted resections of these hyperfunctioning and vascular tumors have been described. Methods: A 28-year-old morbidly obese male (BMI 43) presented with uncontrolled hypertension severe headaches for the past 10 years. He had been hospitalized on multiple occasions with headaches and sinus congestion and was maintained on nifedipine 60mg twice a day and labetalol 200mg three times a day. During work-up of his hypertension he was found to elevated urine norepineprine and serum metanephrines. Cross-sectional imaging identified a 5-cm lesion near the Organ of Zuckerhandl. DOTATOC PET confirmed significant uptake in the lesion. He was aggressively titrated to symptoms with alpha-blockade in preparation for surgery. The gastrocolic ligament was divided, hepatic flexure lowered, and a Kocher maneuver was performed robotically. The mass was minimally manipulated and carefully dissected from the aorta, IVC, duodenum, and retroperitoneum without intraoperative hypertensive episodes. Feeding vessels were identified, clipped and cut. The tumor was delivered en bloc in an endocatch bag. Results: Blood loss was negligible. There were no perioperative complications. He was discharged home on postoperative day 1 on no blood pressure medications. Pathology confirmed an extra-adrenal paraganglioma, with negative nodes, no mitoses, and a Ki67<1%. Conclusion: Robotic-assisted resection of paraaortic extra-adrenal paraganglioma be safely performed for this rare, functional, and vascular tumor with excellent visualization and exposure. This approach enabled minimal blood loss and <24 hours length of stay.

ABSTRACTS

Accepted for
POSTER PRESENTATIONS

72nd Annual Cancer Symposium
Society of Surgical Oncology
March 27–30, 2019
San Diego, CA

P1

Does Race Play a Role in Breast-Conserving Surgery After Neoadjuvant Chemotherapy? Results from the National Cancer Data Base L.M. Enomoto,* C. Clark, A. Chiba, E. Levine, M. Howard-McNatt. *Wake Forest Baptist Medical Center, Winston Salem, NC.*

INTRODUCTION: Neoadjuvant chemotherapy is used for breast cancer patients to decrease disease burden, allowing for breast-conservation surgery (BCS). Racial differences in outcomes for breast cancer patients have been observed. The aim of this study was to characterize BCS rates after neoadjuvant chemotherapy in different racial groups. METHODS: The National Cancer Database was queried to identify women with American Joint Committee on Cancer stage 1 to 3 breast cancer diagnosed from 2006-2014 who underwent neoadjuvant chemotherapy and surgery. The association between race and BCS rates was determined, as well as patient demographics, tumor-related variables, and overall survival. RESULTS: 36,842 patients underwent neoadjuvant chemotherapy followed by breast surgery. When compared with white women, black women had a higher Charlson/Deyo score, tumor grade, and tumor stage (all $p<0.001$). BCS was more common in black patients when compared with whites (38.9% vs 34.0%, respectively, $p<0.001$). Overall survival was worse for black patients compared to white patients (HR 1.43, 95% CI 1.36-1.50). After adjusting for BCS, overall survival for black patients was still worse (HR 1.48, 95% CI 1.41-1.56). CONCLUSION: There is increased utilization of BCS among black women with breast cancer; however, their overall survival is worse. This is likely due to biological factors relate to the tumor and differences in comorbidities between the groups.

P2

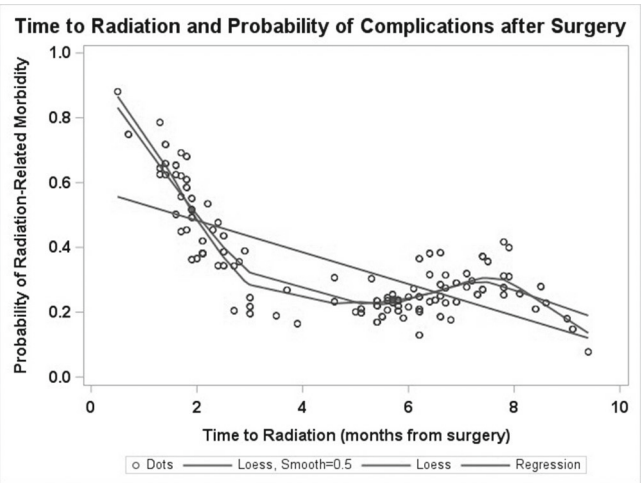
Fibroepithelial Lesions of the Breast (FELs) are Rarely Malignant and Generally Remain Stable Under Observation J. Limberg,[2]* K. Barker,[1] S.A. Hoda,[2] R.M. Simmons,[2] A.J. Swistel,[2] A. Michaels,[2] J. Marti.[2] *1. New York Presbyterian Hospital, New York, NY; 2. NYP-Weill Cornell Medical Center, New York, NY.*

Introduction: When needle core biopsies (NCB) of the breast are diagnosed as FELs, excision is often performed to rule out a phyllodes tumor (PT). The prevalence of malignancy in FELs is believed to be low, but prior analyses may have been underpowered. The natural history of observed FELs is not well described. We analyzed the risk of malignancy in FELs undergoing excision, and the natural history of observed FELs. Methods: We retrospectively studied the records of 215 patients with FELs on NCB from 2012-2018. Surgical pathology records of excised FELs, and ultrasonography of observed FELs were analyzed, and incidence of growth determined by the Kaplan-Meier method. Results: The majority of FELs (80%, n=202) were excised, and 50 FELs (20%) underwent active surveillance with ultrasounds. Of the excised FELs, 98% (n=198) were benign. Surgical pathology revealed fibroadenoma (FA) or benign breast tissue in 68% (n=137) of FELs, benign PT in 29% (n=59), LCIS arising within a FA in 1% (n=2), borderline or malignant PT in 1.5% (n=3), and invasive adenosquamous carcinoma arising from a benign PT in 0.5% (n=1). On ultrasound, malignant tumors were larger than benign lesions (mean 4.7 cm [range 3.1-7] vs. 1.6 cm (range 0.4-10, $p<0.001$). The borderline and malignant lesions often had marked vascularity and microlobulated margins on ultrasound. Fifty FELs were observed with a median follow-up of 14 months (IQR 7-32). The majority of FELs remained stable: at 3 years, 29% of tumors increased in volume by > 50%. Of those observed, 8% (n=4) ultimately underwent surgery, all with benign final pathology. Conclusion: We report clinicopathologic characteristics of a large series of breast FELs, and the first large series of the natural history of FELs that are observed. Although excision of FELs is often recommended, we find that FELs are nearly always (98%) benign. If followed, the majority will not grow. Surgery can therefore be reserved for patients with FELs that are large, growing, or exhibit suspicious radiographic findings. This could potentially spare women with FELs the unnecessary risk, anxiety, and economic cost of surgery.

P3

Surgical Outcomes of Mastectomy with Immediate Autologous Reconstruction Followed by Radiation D.R. Heller,[1] N. Parikh,[2] H. Zhuo,[3] Y. Zhang,[3] S.A. Higgins,[2] D.R. Lannin,[1] T. Avraham,[4] B.K. Killelea.[1]* *1. Dept of Surgery, Yale School of Medicine, New Haven, CT; 2. Dept of Therapeutic Radiology, Yale School of Medicine, New Haven, CT; 3. Yale School of Public Health, New Haven, CT; 4. Dept of Plastic & Reconstructive Surgery, Yale School of Medicine, New Haven, CT.*

Introduction Timing of autologous reconstruction after mastectomy + post-mastectomy radiation therapy (PMRT) is debated. Benefits of a single operation must be weighed against a heightened risk of complications from flap irradiation. We reviewed outcomes after single operation + PMRT in a large institutional cohort. Methods Retrospective health record review was performed for women with breast cancer who underwent simultaneous mastectomy and autologous reconstruction with PMRT from 2007–2016. Primary endpoints were post-radiation flap morbidity and reoperations, with predictors assessed by multivariable analysis. Non-parametric logistic regression generated a model of optimal PMRT timing projecting lowest probability of post-radiation complications. Results Among 130 women meeting criteria, 61.5% had bilateral procedures, totaling 208 flaps. Over median follow up of 35.1 months (IQR 23.6 – 56.5), 47 (36.2%) patients experienced post-radiation morbidity, commonly fat necrosis (44.1%), flap asymmetry (28.8%), and lymphedema (15.3%). Complications were higher with no adjuvant chemotherapy, shorter interval to PMRT, and internal mammary node (IMN) radiation. Among patients with complications, 32 (68.1%) underwent 70 reoperations, commonly fat grafting (51.9%), fat necrosis excision (17.1%), and wound debridement (11.4%). Reoperations were higher with 90-day perioperative morbidity after mastectomy, no adjuvant chemotherapy, and shorter interval to PMRT. On multivariable analysis, IMN radiation predicted post-radiation morbidity (OR 6.7, $p<0.01$), while 90-day perioperative morbidity (OR 4.4, $p<0.01$) and shorter interval to PMRT (OR 22.2, $p<0.01$) predicted reoperations. The lowest probability of post-radiation complications occurred when PMRT was given >3 months after surgery. Conclusions At a large-volume cancer hospital, mastectomy with immediate autologous reconstruction and PMRT is safe, with complication rates within 5% of recently published data for delayed reconstruction. IMN radiation may increase risk, while PMRT >3 months after surgery may decrease risk and enhance the safety of a single operation. Additional studies are needed to explore benefits of delayed radiation.



P5

Single Institution Experience with Reverse Axillary Mapping in Advanced Axillary Disease W.A. Young,* J.W. Jakub. *Dept of Surgery, Mayo Clinic, Rochester, MN.*

Background: Axillary reverse mapping (ARM) is a method to identify and preserve the lymphatics draining the upper extremity in order to minimize the risk of lymphedema following axillary surgery. The risk of the ARM lymph node being involved with metastatic disease from a breast cancer has been described as low in patients with clinically negative axillae. Some have

advocated preservation of the ARM node even in the setting of a clinically positive axilla. Objective: Document the incidence of nodal involvement in the ARM lymph node(s) in a contemporary patient population undergoing ALND. Methods: Single institution review of prospectively maintained single surgeon database. Results: Between May 2016 and January 2018 32 patients underwent axillary reverse mapping at Mayo Clinic Rochester by a single surgeon. The primary diagnosis was breast cancer in 25 patients (78%), melanoma in 5 patients (16%) and metastatic squamous cell cancer in 2 patients (6%). ARM lymphatic channels were identified intraoperatively via blue dye. All of the ARM channels visualized drained to an axillary lymph node contained within the boundaries of a standard ALND and therefore none of the ARM nodes were preserved. The mean lymph node count per axilla was 23.3, 21 of 32 patients had at least one positive axillary lymph node and 10 of the 21 patients with a positive axillary lymph node exhibited extranodal extension. In 16 cases the ARM node was identified, marked at the time of surgery and specifically commented on in the pathology report. In 10 of these 16 cases there was a positive node within the axillary contents and the ARM node was positive in 9 of these 10 patients. In 6 of the 9 cases (66%) with a positive ARM node, the ARM node was the only positive node. Conclusion: In a contemporary cohort of patients undergoing ALND, the ARM lymph node has a high incidence of being involved with metastatic disease and not infrequently was the only positive node in the axilla. The ARM node should not be preserved as part of an ALND in those with clinically positive nodes. Outside of a clinical trial, preserving an ARM node during an ALND is oncologically unsound given the likelihood it contains metastatic disease.

P6

The Effect of Local Therapy on Breast Cancer-Specific Mortality of Occult Breast Cancer Patients with Advanced Nodal Disease (N2/N3): A Population Analysis H.M. Johnson,* W. Irish, N.A. Vohra, J.H. Wong. *Surgery, East Carolina University/Vidant Medical Center, Greenville, NC.*

Introduction: Current NCCN locoregional therapy guidelines for occult breast cancer (OBC) recommend modified radical mastectomy, with the option for breast radiation instead of mastectomy for N1 patients. Our aim was to compare the effect of breast radiation versus mastectomy on the risk of breast cancer-specific mortality (BC-SM) of OBC patients with advanced nodal disease (N2/N3). Methods: We conducted a historical cohort study of women registered in the SEER database with T0N+M0 breast cancer diagnosed from 2004-2015. Competing risk analyses were performed to evaluate the effect of local therapy, nodal stage, and other demographic and clinical prognostic variables on risk of BC-SM. Results: A total of 353 women met the inclusion criteria. The mean age was 57.5 years (range 31-97). The majority of women were white (80.7%) and non-Hispanic (89.2%). Over half had ER positive tumors (54.4%) and 35.4% had PR positive tumors. HER2 data was unavailable for 54.1% of women. There were 203 women with N1 disease (57.5%), 76 with N2 (21.5%), and 74 with N3 (21.0%). Most received chemotherapy (88.1%). All underwent axillary lymph node dissection. 152 women received breast radiation (43.1%) and 201 underwent mastectomy (56.9%). Women treated with radiation were older (mean=60.3, range 31-97 years versus mean=55.4, range 31-88 years; p=0.0002). The two groups were comparable with respect to all other variables analyzed. During a median follow-up of 66 months, 32 women died from breast cancer (radiation: 11 women, mastectomy: 21). Five-year unadjusted cumulative incidence of BC-SM was 8.0% ± 2.6% with radiation versus 10.9% ± 2.6% with mastectomy (Gray's test p=0.309). Increasing age, increasing N stage, and ER negativity were independently associated with increased risk of BC-SM (Table 1). The type of local therapy was not significantly associated with BC-SM (p=0.2082). A sensitivity analysis to control for delayed entry bias demonstrated similar results. Conclusion: These results suggest that breast radiation is a reasonable alternative to mastectomy for OBC patients not only with N1 disease but also N2/N3.

Results of the Multivariable Cox's Cause-Specific Hazards Analysis for Breast Cancer-Specific Mortality

Variable	Comparison	Hazard Ratio	95% Confidence Interval	P-value
Local Therapy	Breast Radiation versus Mastectomy	0.621	0.296-1.304	0.2082
Nodal Stage	N2/N3 versus N1	4.114	1.758-9.628	0.0011
ER Status	Negative versus Positive/Unknown	2.338	1.121-4.876	0.0235
Chemotherapy	Yes versus No/Unknown	1.404	0.388-5.079	0.6048
Age at Diagnosis	Per year increase	1.039	1.007-1.071	0.0155
Year of Diagnosis	Per year increase	1.071	0.935-1.229	0.3225

ER = Estrogen Receptor

P7

Mastectomy is No Longer an Indication for Postoperative Narcotic Prescription at Discharge T.A. Fortes,[1]* D.M. Manasseh,[1] P.L. Flom,[2] C. Andaz,[1] P.I. Borgen,[1] K. Rojas.[1] *1. Maimonides Medical Center, Brooklyn, NY; 2. Peter Flom Consulting, New York, NY.*

Background We have previously shown that implementation of a multimodal Enhanced Recovery After Surgery (ERAS) protocol allows for the elimination of narcotic prescription after lumpectomy without compromising pain control. In the present study, we sought to employ a similar protocol in mastectomy patients to decrease the amount of narcotics prescribed at discharge. Methods A multidisciplinary team developed a 10-step protocol for patients undergoing mastectomy without reconstruction (Table 1). A pilot study was planned to minimize narcotic prescription. ERAS patients were compared to a control group undergoing surgery during the same time period. Those undergoing immediate reconstruction were excluded. In-hospital and discharge prescription of narcotics were compared between ERAS and control groups using morphine milligram equivalents (MME's). Postoperative pain scores were collected at the postoperative visit using a survey. Results Between September 2017 and August 2018, 758 breast surgeries were performed at a single institution. Of the 153 mastectomies, 57 patients met inclusion criteria. Twenty patients received the ERAS protocol and 37 underwent usual care (UC). Groups were similar in terms of race, co-morbidities, smoking status, and management of the axilla. Thirty percent of patients underwent axillary dissection. During postoperative hospital stay, the ERAS group received a mean of 2.4 (0-13) MME's while the UC group received 13.7 (0-80) (p=0.005). At discharge, the ERAS group received 2.0 (0-40) MME's and the UC group received 59.8 (0-120) (p<0.001). Nineteen of 20 ERAS patients were discharged with non-narcotic analgesia alone. The ERAS group reported a mean postoperative day 1 pain score of 3.1 (0-7), while the UC group reported 5.5 (0-10) (p=0.008). Week 1 pain scores were 1.8 (0-5) in the ERAS group and 5.8 (2-10) (p<0.001) in the UC group. There was no difference in number of days in the hospital or complication rate between the two groups. Conclusion Patients undergoing mastectomy without reconstruction on the ERAS protocol required less narcotics after surgery with significantly lower postoperative pain scores when compared to patients who received usual care.

Mastectomy Without Reconstruction ERAS Protocol

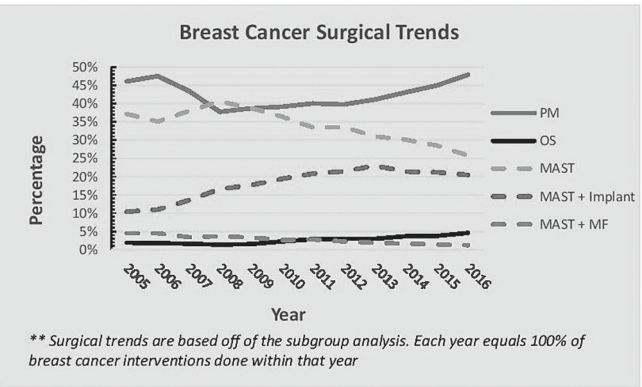
1. Preoperative counseling of postoperative expectations and non-narcotic pain control
2. Clear liquids up to 2 hours preoperatively
3. Preoperative holding area oral medication: 975mg acetaminophen, 300mg gabapentin
4. Intraoperative maintenance of euvolemia, normothermia with antiemetic protocol upon induction
5. Long-acting local analgesia injection prior to incision (1:1 of 1.3% bupivacaine liposome suspension with 0.5% bupivacaine hydrochloride)
6. At least 30cc liposomal bupivacaine mixture injected into chest wall, axilla, and drain site
7. 15 mg intravenous ketorolac during closure
8. Early cessation of intravenous fluids, early ambulation, and unrestricted diet
9. Scheduled 600 mg ibuprofen and 650 mg acetaminophen every 8 hours, alternating dose every 4 hours initiated with first oral intake
10. 5mg oxycodone every 6 hours PRN pain score >7, rescue parenteral opioid if score >7 1 hour later

P8

New Era of Modern Breast Cancer Surgery: An 11-Year Analysis of Surgical Trends with Adoption of Breast Reconstruction: NSQIP Database 2005-2016 Analysis M. Jonczyk,[1]* J. Jean,[2] R. Graham,[1] A. Chatterjee.[1] *1. Surgery, Tufts Medical Center, Boston, MA; 2. Tufts University Medical School, Boston, MA.*

Introduction: There is minimal recent literature analyzing national trends in surgery for patients with both invasive (IBC) and in situ (DCIS) breast cancer. Surgery includes partial mastectomy (PM), mastectomy without reconstruction (M), mastectomy with reconstruction (M+R), and partial mastectomy

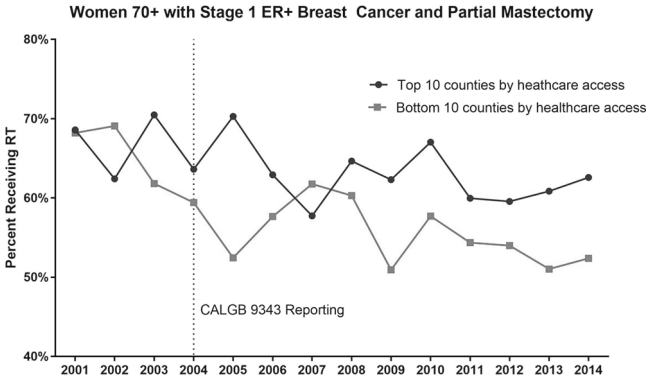
with oncoplastic reconstruction (OS). We hypothesize that the use of M is declining and likely correlates with the rise of surgery with reconstructive options (M+R, OS). Methods: A retrospective cohort analysis was conducted using the ACS-NSQIP database from 2005 to 2016 and ICD codes for IBC and DCIS. Patients were then categorized based on current procedural terminology (CPT) codes for PM, M, M+R and OS. In each group, subgroups were categorized based on additional reconstructive procedures. An ANOVA T-test was used to compare demographic variables. Data analysis was conducted via linear regression and a non-parametric Mann- Kendall test to assess a temporal trend and Sen's slope. Results: The patient cohort consisted of 256,398 patients from the NSQIP data base; 59,385 did not meet inclusion criteria (Male, no diagnosis, CPT codes with 2 surgical categories) while the remaining 197,013 were diagnosed with IBC or DCIS. Annual breast surgery trends from 2005 to 2016 changed as follows: PM 45.7% to 46.1% (p=0.21), M 36.8% to 26.4% (p=0.001), M+R 12.7% to 23.0% (p=0.03) and OS 1.8% to 4.42% (p=0.001). When analyzing the patient cohort who underwent breast conservation, subgroup analysis showed a decreased use of PM alone (96% to 91%) with an increased use of OS (4% to 9%). For the patient cohort undergoing mastectomy, M alone decreased (71% to 54%); M+R with muscular flap decreased (9% to 3%); and M+R with implant placement increased (20% to 43%) – all 3 trends p<0.0001. Conclusion: The modern era of breast surgery is identified by the increasing use of reconstruction for patients undergoing breast conservation (in the form of OS) and mastectomy (in the form of M+R). Our study provides data showing significant trends that will impact the future of both breast cancer surgery and breast training programs.



P9

Overuse of Radiation Therapy (RT) in Elderly Women with Breast Cancer: The Influence of Access to Care A.R. Marcadis,[1]* J. Marti.[2] *1. Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; 2. Weill Cornell Medical Center, New York, NY.*

Background Variation in breast cancer care indicates that some patients are being undertreated and/or overtreated. In the CALGB 9343 trial, adjuvant RT did not improve survival among women ≥70 y with stage I estrogen receptor-positive (ER+) breast cancer after partial mastectomy (PM) and hormonal therapy. Since these results were reported in 2004, the use of RT has only modestly declined. Methods Ecological study using SEER 18 examining regional variation in the use of RT and its association with access to healthcare, in 56K women ≥ 70 after PM for stage I, ER+ breast cancer, across 99 US counties with a pop. of >50K (2001-2014). Access to healthcare at the county level was measured using 10 socioeconomic factors. Associations with the probability of receiving RT were examined in multivariable logistic regression. Results Across counties, the % of women ≥ 70 receiving RT after PM for stage I ER+ breast cancer varied greatly, from 33% to 85%. Access to healthcare accounted for a significant proportion of the variability in RT use (R^2=.62, p<.0001). The use of RT was higher in counties with more access to healthcare (64% in 10 "highest access" vs. 56%, in 10 "lowest access," p<.0001). In the 3 y before CALGB 9343 (2001-2003), there was minimal difference in RT use between highest and lowest access counties (69% vs. 64%; p=.08); however, use of RT began to diverge after CALGB data were reported (2005-2007: 62% vs 49%; p<.0001) (2008-2014: 61% vs 45%; p<.0001). A number of covariates were independently associated with higher county-level use of RT: higher proportions of high school graduates (p<0.001), fewer families below poverty (p=0.008), fewer non-English speaking residents (p<0.0001), and lower % uninsured (p<0.0001). Conclusion Across the US, there was wide regional variation in the use of RT. Many elderly women with low-risk breast cancer are overtreated with RT, despite the results of CALGB 9343. Overtreatment was most prevalent in counties with higher levels of education, income, and health insurance. Reducing the use of low-value treatments is a critical aspect of quality improvement, and wider multidisciplinary engagement of oncologists is needed.



P10

Impact of Surgical Complications on Patient Reported Outcomes Following Nipple Sparing Mastectomy M. Lagendijk,[1] S. Desantis,[2] F. Nakhlis,[2] M. Duggan,[2] K. Calvillo,[2] M. Carty,[2] Y. Chun,[2] S. Caterson,[2] M. Golshan,[2] L.S. Dominici.[2]* *1. Erasmus Medical Center and Amphia Hospital, Rotterdam, Netherlands; 2. Brigham and Women's Hospital and Dana Farber Cancer Institute, Boston, MA.*

Introduction: Nipple sparing mastectomy (NSM) is felt to be oncologically safe and provides cosmetically superior outcomes to skin sparing mastectomy (SSM) in early stage breast cancer. However, NSM has higher complication rates than SSM. We collected pre- and postoperative (postop) patient reported outcomes (PROs) and assessed the impact of complications on PROs after NSM. Methods: We prospectively enrolled 63 patients who met oncologic and cosmetic eligibility criteria to undergo NSM from September 2011 until August 2014. BREAST-Q pre- and postop reconstruction modules were administered before surgery and at 1 year, respectively. Clinical data including complications were collected from the electronic health record. Analyses were performed in SPSS Statistics for Windows (version 21.0). Patients with and without complications were compared using a one-way ANOVA. Data: Sixty three women were enrolled with a median age of 46. Pre- and postop BREAST-Q data was available for 44 patients. BRCA mutations were seen in 22 pts (34.9%), and 18 patients in the cohort (28.5%) underwent prophylactic mastectomy. Most patients underwent implant-based reconstruction (N=59, 93.6%) and bilateral mastectomies (n=47, 74.6%). Patients generally had early stage breast cancers (Stage 0 n=14, 22.2%, Stage I n=17, 27.0%, Stage II n=15, 23.8%, Stage III n=1, 1.6%). No patients received preoperative systemic therapy. Seven (11.1%) patients received postmastectomy radiation therapy, and 2 (3.2%) had a history of prior radiation. Postop complications requiring surgical treatment were seen in 10 patients (15.9%) and included implant removal (n=2, 3.2%), hematoma (n=2, 3.2%), and full-thickness mastectomy flap and/or nipple necrosis (n=9, 14.2%). Two patients required nipple excision due to necrosis (3.1%). As seen in Table 1, no statistically significant differences in BREAST-Q scores were seen between patients with and without complications requiring surgery. Conclusion: Patients undergoing NSM in this study demonstrated preserved satisfaction with breasts and return of physical well being at 1 year. Experiencing a complication after initial NSM surgery is not associated with decrease in PROs.

BREAST-Q scores for patients having complications requiring surgery versus those without (one-way ANOVA). Scores listed as median [IQR].

BREAST-Q scores	Preoperative scores			Postoperative scores		
	No complications	Complications needing surgery	p-value	No complications	Complications needing surgery	p-value
Satisfaction with breast	68.5 [58-79]	64 [58-92.5]	0.91	86 [64-100] n=41	73 [63.5-90.5] n=9	0.47
Psychosocial well-being	81 [71-100]	81 [74-92.5]	0.91	79 [59.5-100] n=42	76 (61.5-100] n=9	0.97
Sexual well-being	83 [83-100]	100 [87.3-100]	0.14	60 [45-77] n=41	63 [43.5-74.5] n=9	0.77
Physical well-being chest	57 [50-67]	58.5 [54.8-63]	0.89	77 [63-85] n=42	77 [71.5-100] n=9	0.20

P11

Targeting DAMPs-Induced Inflammation in Breast Cancer
K. Landa,* E. Holl, V.N. Frazier, B.A. Sullenger, E. Hwang, S. Nair.
Surgery, Duke University Hospital, Durham, NC.

About 90% of deaths seen in breast cancer (BC) patients can be attributed to metastatic disease. Damage associated molecular patterns (DAMPs) such as cell free DNA (cfDNA), are actively and passively released from dying or stressed tumor cells and are associated with disease burden in multiple cancers. The mechanism by which cfDNA exerts its effects is not established, we postulate that it could be through DAMP-mediated activation of toll-like receptors (TLRs). We have developed an innovative method to scavenge and block DAMPs using nucleic acid binding polymers (NABPs), such as highly branched polyamidoamine dendrimer (PAMAM-G3). Our population includes patients with stages I-III BC undergoing standard of care (SOC). Samples are collected pre- and post-neoadjuvant chemotherapy (NAC), post-surgery and at 2-month follow-up. Flow cytometry analysis is performed at each time-point to examine CD3+, CD4+, CD8+, CD20+ and CD56+ cells. We have grouped samples in 3 categories: human epidermal growth factor receptor 2 (HER2+) positive, HER2 negative (HER2-) and triple-negative (TN) tumors. To-date we have analyzed 5 HER2+, 2 HER2- and 3 TN patients. Overall trends observed include: progressive decrease in total lymphocytes and post-NAC CD3+ counts for HER2- and TN tumors contrary to HER2+tumors, highest CD4+/CD8+ ratio in HER2- tumors and lowest CD20+ counts in TN tumors. Serum from each patient is used in TLR activation assays to assess effects of PAMAM-G3 on TLR activation. In the mice model, 4T1 BC cells are injected orthotopically in the 4th mammary fatpad of BALBc mice followed by treatment with PAMAM-G3 at 20 mg/kg (Figure 1). PAMAM-G3 has a therapeutic potential of blocking DAMP-mediated inflammation in patients with metastatic BC. In the murine 4T1 BC model, PAMAM-G3 prevented lung metastasis as compared to control group. We observed striking changes in immune cell profile in women with stage I-III breast cancer undergoing SOC. Although our findings are preliminary given our study size, we were able to observe distinct trends within each immune cell population in specific tumor receptor subtypes. These trends could guide sequencing of therapies, such as PAMAM-G3, in the context of SOC to prevent metastasis.

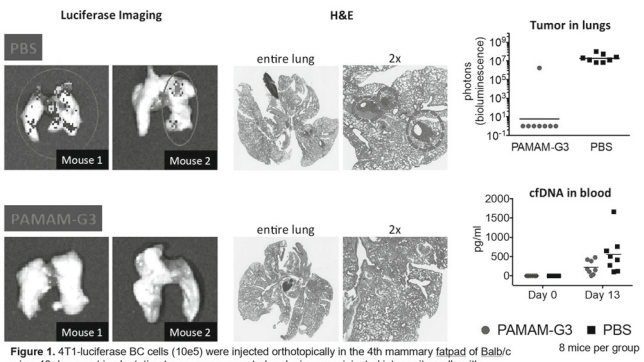


Figure 1. 4T1-luciferase BC cells (10e5) were injected orthotopically in the 4th mammary fatpad of Balb/c mice. 10 days post implantation tumors were resected and mice were injected intraperitoneally with PAMAM-G3 at 20 mg/kg twice a week starting on day 2 for two weeks. Disease progression was followed with serial luciferase imaging over the course of two weeks until the humane endpoint was reached. Metastatic disease was measured by luciferase imaging and H&E of lungs, compiled data is shown in right panel top. CfDNA levels on day 0 and 13 is shown right panel, bottom.

Figure courtesy of Eda Holl, Nikki Frazier, Smita Nair (DoD award W81XWH-16-1-0512). Unpublished data.

P12

The Risk of Positive Sentinel Lymph Node After Neoadjuvant Systemic Therapy in Clinically Node Negative Breast Cancer Patients - Implications of Postmastectomy Radiation Therapy and Immediate Breast Reconstruction
S. Samiei,[1] B. van Kaathoven,[1] L. Boersma,[2] R. Granzier,[1] S. Siesling,[3] S. Engelen,[1] L. de Munck,[4] R. van der Hulst,[1] M. Lobbes,[1] T. van Nijnatten,[1] M. Smidt.[1]*
1. Maastricht University Medical Center, Maastricht, Netherlands; 2. Maastro Clinic, Maastricht, Netherlands; 3. MIRA Institute for Biomedical Technology and Technical Medicine, Enschede, Netherlands; 4. Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands.

Introduction: Residual axillary lymph node involvement after neoadjuvant systemic therapy (NST) is one of the indications for postmastectomy radiation therapy (PMRT). If immediate breast reconstruction is performed after mastectomy, PMRT can adversely affect the reconstructed breast. Our aim was to determine the risk of a positive sentinel lymph node (SLN) for different breast cancer subtypes after NST in clinically node negative (cN0) breast cancer patients with regard to the risk of PMRT and timing of breast reconstruction. Methods: All cT1-3N0 breast cancer patients treated with NST between 2010-2016, followed by mastectomy and SLNB, were identified from the Netherlands Cancer Registry. The cN0 status at diagnosis was based on negative axillary ultrasound findings with/without biopsy. The risk of a positive SLN was determined in general and for the different breast cancer subtypes. Logistic regression analysis was performed to determine the correlation of clinicopathological variables with a positive SLN. Results: In total 788 patients were included for analyses, of whom 25.0% (197/788) had a positive SLN. Per breast cancer subtype, 10.4% (11/106) ER+HER2+, 3.7% (2/54) ER-HER2+, 35.9% (170/474) ER+HER2-, and 9.1% (14/154) triple negative (TN) patients had a positive SLN. Multivariable regression analysis showed that cT3 stage (OR 2.56, 95% CI 1.30-5.38) and ER+HER2- subtype (OR 3.94, 95% CI 1.77-8.74) were independent variables correlated with a positive SLN. cT1-3N0 ER+HER2- and cT3N0 TN patients had the highest risk of a positive SLN ranging between 24%-42% and 30%, respectively. cT1-3N0 ER+HER2+, cT1-3N0 ER-HER2+, and cT1-2N0 TN patients had the lowest risk of a positive SLN ranging between 7%-11%, 0-6%, 3%-6%, respectively. Conclusions: In cT1-3N0 ER+HER2- and cT3N0 TN patients treated with NST, immediate breast reconstruction cannot be advised due to the high risk of PMRT. In cT1-3N0 ER+HER2+, cT1-3N0 ER-HER2+, and cT1-2N0 TN patients treated with NST, immediate breast reconstruction can be advised due to the low risk of PMRT.

SLN outcome after NST for the different breast cancer subtypes

		SLN negative	SLN positive
ER+HER2+ n=106	cT1N0	26 (92.9)	2 (7.1)
	cT2N0	46 (88.5)	6 (11.5)
	cT3N0	23 (88.5)	3 (11.5)
ER-HER2+ n=54	cT1N0	5 (100)	0
	cT2N0	30 (93.8)	2 (6.3)
	cT3N0	17 (100)	0
ER+HER2- n=474	cT1N0	64 (76.2)	20 (23.8)
	cT2N0	156 (63.4)	90 (36.6)
	cT3N0	84 (58.3)	60 (41.7)
Triple negative n=154	cT1N0	33 (97.1)	1 (2.9)
	cT2N0	91 (93.8)	6 (6.2)
	cT3N0	16 (69.6)	7 (30.4)

P13

Comparison of Wire Localization, Radioactive Seed, and Savi Scout Radar for Management of Surgical Breast Disease
M. Srour,* S. Kim, F. Amersi, A.E. Giuliano, A. Chung. *Surgical Oncology, Cedars-Sinai Medical Center, Beverly Hills, CA.*

Introduction: Radioactive seed localization (RSL) and the Savi scout radar® (SSR) are newer alternatives to wire-guided localization (WL) for non-palpable breast lesions. Methods: 293 patients (pts) had a partial mastectomy (n= 194) or breast biopsy (n= 99) with pre-operative image guided localization (loc) of a single non-palpable lesion between July 2017 to July 2018. Lesions were localized by WL, RSL, or SSR. Delay in operating room start times and total perioperative times in both the hospital and ambulatory setting, loc time, explant of loc device, positive margins, volume of tissue excised, and 30-day complications were evaluated. Results: 126 pts (43%) had WL; 59 pts (20%) had RSL; 108 pts (37%) had SSR loc. SSR loc took longer to perform with an average time of 19 minutes (min), compared with 15 min for WL and

14 min for RSL (p=0.020). In 93.52% of cases, the first specimen contained both the clip and loc device, which was similar among groups (p = 0.073). There was no difference in retained biopsy clip among the groups (average 3.4%, p=0.173). For operations performed in the hospital, the time from patient arrival to the pre-operative area and incision was significantly longer in the WL group with a median of 233 min (range 56-486), 130 min (range 64-294) in RSL, and 108 min (range 59-240) for SSR (p<0.001). There was no difference in operative time among the groups with a median of 51 min (range 17-122) (p=0.108). There was however, significantly longer perioperative time of 469 min (range 210-926) in the WL group compared with 399 min (range 240-871) for RSL and 381 min (range 232-711) for SSR (p=<0.001) - similar trends were seen for the ambulatory surgery center. 131 pts (44.7%) had same day locs. Among operations with delayed start times, there was a longer average delay of 84.5 min (range 1-304) for WL group compared with 69 min (range 13-219) in RSL, and 53 min (range 0-228) in SSR (p<0.001). There was no difference in positive margin rate, volume of tissue excised, and 30-day complications [Table 1]. Conclusion: SSR and RSL loc techniques reduce perioperative time and operating room delays with few complications, compared with WL.

Comparison of Localization Techniques – Complications and Outcomes

Variable	All patients (N=293)	Wire (N=126)	Seed (N=59)	Savi (N=108)	P-value
30-day complication	21 (7.2)	10 (7.9)	4 (6.8)	7 (6.5)	0.904
Type of 30-day complication					0.965
- Seroma aspirated	8 (2.73)	4 (3.18)	2 (3.39)	2 (1.85)	
- Hematoma	5 (1.71)	3 (2.38)	1 (1.69)	1 (0.93)	
- Infection	6 (2.05)	2 (1.59)	1 (1.69)	3 (2.78)	
- Medical Complication	1 (0.34)	0 (0)	0 (0)	1 (0.93)	
Weight of specimen (grams)	11.8 (0.4 - 75)	11.2 (0.4 - 66)	10.8 (2.1 - 57.9)	12.8 (1.2 - 75)	0.942
Positive Margins [cancer only]	60/284 (21.1)	30/122 (24.6)	13/59 (22.0)	17/103 (16.5)	0.428

P14

Correlation Between Pathologic Complete Response in the Breast and Absence of Axillary Lymph Node Metastases After Neoadjuvant Systemic Therapy S. Samiei,[1] T. van Nijnatten,[1] L. de Munck,[2] K. Keymeulen,[1] J.M. Simons,[3] L. Kooreman,[1] S. Siesling,[4] M. Lobbes,[1] M. Smidt.[1]* *1. Maastricht University Medical Center, Maastricht, Netherlands; 2. Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands; 3. Erasmus Medical Center, Rotterdam, Netherlands; 4. MIRA Institute for Biomedical Technology and Technical Medicine, Enschede, Netherlands.*

Introduction: Pathologic complete response (pCR; absence of invasive and in situ cancer) rates have improved on account of more effective systemic treatment regimens. Our aim was to investigate whether pCR in the breast is correlated with absence of axillary lymph node metastases at final pathology (ypN0) in patients treated with neoadjuvant systemic therapy (NST) for different breast cancer subtypes. Methods: Patients diagnosed with cT1-3N0-1 breast cancer and treated with NST (chemotherapy with or without trastuzumab), followed by breast and axillary surgery between 2010-2016, were selected from the Netherlands Cancer Registry. The axillary nodal status was determined before NST by ultrasound with additional biopsy if required. Patients were compared according to the pathologic response of the primary tumor (pCR versus no pCR) with associated pathologic axillary outcome for different breast cancer subtypes. Multivariable analysis was performed to determine clinicopathological variables correlated with ypN0. Results: A total of 4084 patients were included for analyses, of whom 986 (24.1%) achieved breast pCR. In clinically node negative (cN0) patients, 97.7% (432/442) with breast pCR had ypN0 compared to 71.6% (882/1232) without breast pCR (p<0.001). In clinically node positive (cN1) patients, 45.0% (245/544) with breast pCR had ypN0 compared to 9.4% (176/1866) without breast pCR (p<0.001). The odds of ypN0 was decreased in case of clinical T3 stage (OR 0.59, 95% CI 0.40 – 0.87), cN1 (OR 0.03, 95% CI 0.02 – 0.04) and ER+HER2- subtype (OR 0.30, 95% CI 0.20 – 0.44), and increased in case of breast pCR (OR 4.53, 95% CI 3.27 – 6.28). Conclusions: Breast pCR achieved after NST is strongly correlated with ypN0 in cN0 patients, especially in ER+HER2+, ER-HER2+ and triple negative subtypes. Identifying breast pCR can provide insights for future axillary treatment with the potential of omitting axillary surgery in these selected patients.

Overview of number of lymph node metastases for each breast cancer subtype differentiated between breast pCR and without breast pCR after NST

Breast pCR (n=986)		Number of Lymph Node Metastases on Final Pathology (%)				
		0	1	2	3	4
ER+HER2+ (n=236)	cT1N0	29 (100)	0	0	0	0
	cT2N0	73 (99)	1 (1)	0	0	0
	cT3N0	20 (95)	1 (5)	0	0	0
	cT1N1	9 (60)	6 (40)	0	0	0
	cT2N1	33 (53)	26 (42)	0	2 (3)	1 (2)
	cT3N1	16 (46)	17 (48)	0	1 (3)	1 (3)
ER-HER2+ (n=247)	cT1N0	13 (100)	0	0	0	0
	cT2N0	72 (100)	0	0	0	0
	cT3N0	12 (100)	0	0	0	0
	cT1N1	12 (48)	13 (52)	0	0	0
	cT2N1	33 (43)	42 (55)	1 (1)	1 (1)	0
	cT3N1	25 (52)	23 (48)	0	0	0
ER+HER2- (n=208)	cT1N0	27 (94)	1 (3)	1 (3)	0	0
	cT2N0	44 (94)	3 (6)	0	0	0
	cT3N0	12 (92)	1 (8)	0	0	0
	cT1N1	4 (17)	12 (49)	4 (17)	0	4 (17)
	cT2N1	25 (35)	33 (46)	6 (8)	2 (3)	6 (8)
	cT3N1	9 (39)	10 (43)	0	2 (9)	2 (9)
Triple negative (n=295)	cT1N0	29 (97)	0	1 (3)	0	0
	cT2N0	99 (100)	0	0	0	0
	cT3N0	2 (67)	1 (33)	0	0	0
	cT1N1	16 (49)	15 (45)	1 (3)	0	1 (3)
	cT2N1	47 (47)	45 (44)	6 (6)	1 (1)	2 (2)
	cT3N1	16 (55)	10 (35)	2 (7)	0	1 (3)
No Breast pCR (n=3098)		**Number of Lymph Node Metastases on Final Pathology (%)**				
		0	1	2	3	4
ER+HER2+ (n=349)	cT1N0	25 (83)	5 (17)	0	0	0
	cT2N0	87 (89)	8 (8)	2 (2)	0	1 (1)
	cT3N0	18 (72)	5 (20)	1 (4)	0	1 (4)
	cT1N1	9 (33)	10 (37)	2 (7)	1 (4)	5 (19)
	cT2N1	15 (13)	63 (53)	10 (8)	7 (6)	24 (20)
	cT3N1	15 (30)	13 (26)	4 (8)	3 (6)	15 (30)
ER-HER2+ (n=114)	cT1N0	2 (100)	0	0	0	0
	cT2N0	14 (88)	2 (12)	0	0	0
	cT3N0	12 (92)	0	1 (8)	0	0
	cT1N1	2 (50)	0	0	2 (50)	0
	cT2N1	14 (33)	13 (30)	6 (14)	4 (9)	6 (14)
	cT3N1	9 (25)	14 (39)	6 (17)	4 (11)	3 (8)
ER+HER2- (n=2128)	cT1N0	97 (75)	24 (18)	5 (4)	0	4 (3)
	cT2N0	341 (67)	124 (24)	23 (4)	10 (2)	12 (3)
	cT3N0	107 (53)	58 (29)	11 (5)	4 (2)	23 (11)
	cT1N1	7 (4)	63 (34)	34 (18)	19 (10)	63 (34)
	cT2N1	36 (5)	217 (31)	111 (16)	88 (13)	249 (35)
	cT3N1	22 (6)	72 (18)	45 (11)	46 (12)	213 (53)
Triple negative (n=507)	cT1N0	27 (87)	4 (13)	0	0	0
	cT2N0	126 (89)	12 (8)	2 (2)	1 (1)	0
	cT3N0	26 (79)	4 (12)	2 (6)	0	1 (3)
	cT1N1	5 (12)	15 (37)	4 (10)	5 (12)	12 (29)
	cT2N1	35 (20)	64 (36)	20 (11)	15 (8)	45 (25)
	cT3N1	7 (9)	18 (22)	10 (12)	7 (9)	40 (52)

P15

Did the SSO-ASTRO Margin Guidelines Reduce Additional Surgery in Patients with Invasive Lobular Breast Cancer? A. Mamtani,* E. Zabor, M. Stempel, L.H. Rosenberger, M. Gemignani, M. Morrow. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction The SSO-ASTRO guidelines defined a negative margin for BCT as no ink on tumor, and use of this definition has reduced rates of additional surgery in patients with invasive ductal cancer (IDC). Outcomes in invasive lobular cancer (ILC) are uncertain due to its discontinuous growth pattern, and poorer clinical and radiographic definition. Methods We identified patients with stage I-II pure ILC treated with BCT from 1/2010-1/2018. All patients had separately submitted cavity-shave margins. Guidelines were uniformly adopted on 1/1/2014. Clinicopathologic characteristics, margin status, and re-excisions were compared before and after adoption, and to patients with pure IDC treated from 5/2013-2/2015. Results Among 745 early-stage ILC treated with BCT, 312 (42%) were treated pre-guideline and 433 (58%) post-guideline. Characteristics were similar between groups (Table). Most tumors were T1 (74%), ER+ (98%), and had classical morphology (80%). There was a significant decline in additional surgery (31.4% to 23.1%, p=0.01) after guideline adoption, seen for re-excisions (19.9% to 15.2%) and conversions to mastectomy (11.5% to 7.8%)(p=0.04). Between eras, there was no difference in incidence of positive margins (ink on tumor), margin width ≤2mm, or number of margins ≤2mm (all p=0.2). On multivariate analysis, larger tumor size (OR 1.55, 95%CI 1.3-1.8), younger age (OR 0.96, 95%CI 0.94-0.97), earlier surgery year (OR 0.89, 95%CI 0.82-0.96), and pre-guideline era (OR 0.62, 95%CI 0.44-0.87) were independently associated with additional surgery. Only younger age was predictive of mastectomy (OR 0.96, 95%CI 0.93-0.99). In the IDC cohort of 431 pre-guideline and 601 post-guideline patients, re-excisions declined from 20.8% to 14.1% (p=0.005), and conversion to mastectomy was rare (0.5%).

The magnitude of reduction in re-excisions (interaction p=0.56) and additional surgery (interaction p=0.92) was similar between ILC and IDC. Conclusion Despite differences in growth pattern and conspicuity between ILC and IDC, guideline adoption significantly reduced additional surgery for patients with ILC, with a magnitude of benefit similar to that seen for IDC.

Clinicopathologic features

	All N = 745	Pre-guideline N = 312	Post-guideline N = 433	P
Age, years (range)	62 (53, 70)	61 (53, 70)	63 (53, 70)	0.35
Breast density				0.1
Fatty	43 (6%)	19 (6%)	24 (6%)	
Scattered fibroglandular	233 (31%)	83 (26%)	150 (35%)	
Heterogenous	392 (53%)	172 (55%)	220 (51%)	
Extremely dense	77 (10%)	38 (12%)	39 (9%)	
MMG/US size, cm* (range)	1.1 (0.8, 1.7)	1.2 (0.8, 1.6)	1.1 (0.8, 1.7)	0.46
MRI performed	382 (51%)	151 (48%)	231 (53%)	0.2
MRI size, cm* (range)	1.6 (1.1, 2.4)	1.5 (1.0, 2.3)	1.7 (1.1, 2.5)	0.23
Pathologic tumor size, cm (range)	1.4 (0.9, 2.1)	1.4 (0.9, 2.0)	1.3 (0.9, 2.1)	0.99
Associated lobular carcinoma in situ	686 (92%)	298 (96%)	388 (90%)	0.004
Receptor subtype**				0.64
ER+/HER2-	713 (96%)	296 (95%)	417 (96%)	
ER+/HER2+	17 (2%)	7 (2%)	10 (2%)	
ER-/HER2+	4 (1%)	3 (1%)	1 (0.2%)	
ER-/HER2-	7 (0.5%)	3 (1%)	4 (1%)	
Morphology				0.42
Classic	596 (80%)	248 (80%)	348 (80%)	
Pleomorphic	133 (18%)	60 (19%)	73 (17%)	
Other	16 (2%)	4 (1%)	12 (3%)	
Lymphovascular invasion	80 (11%)	50 (16%)	30 (7%)	<0.001
Positive margins (ink on tumor)	121 (16%)	50 (16%)	71 (16%)	0.2
Pathologic T classification				0.45
T1	553 (74%)	236 (76%)	317 (73%)	
T2	183 (25%)	74 (24%)	109 (25%)	
T3	9 (1%)	2 (0.6%)	7 (2%)	
Pathologic stage				0.43
I	485 (65%)	195 (63%)	290 (67%)	
IIA	210 (28%)	94 (30%)	116 (27%)	
IIB	50 (7%)	23 (7%)	27 (6%)	

MMG, mammography; US, ultrasound; ER, estrogen receptor; *Continuous variables reported as median (interquartile range) and categorical variables reported as frequency (%)*; *Numeric size not stated or occult on MMG/US in N = 91, and on MRI in N = 39; **Not performed in N = 4 patients due to microinvasive tumor only

P16

Real-Time Electromagnetic Navigation in Breast-Conserving Surgery: A Phase 2 Study C.T. Yeo,[1]* G. Gauvin,[2] T. Ungi,[1] A. Lasso,[1] D. Jabs,[1] T. Vaughan,[1] J.F. Rudan,[1] R. Walker,[1] S. Merchant,[1] G. Fichtinger,[1] J. Engel.[1] *1. Surgery, Queen's University, Kingston, ON, Canada; 2. Fox Chase Cancer Center, Philadelphia, PA.*

Positive margins in breast cancer surgery is associated with an increased risk of local recurrence despite adjuvant therapy, resulting in re-operation to excise the positive margin. We developed a real-time electromagnetic-based navigation (EMN) system that uses ultrasound to contour the tumor margins, then tracks the tumor location intraoperatively (Figure 1). The purpose of this study was to evaluate the safety and efficacy of EMN in patients with non-palpable invasive breast cancer. Patients with ultrasound visible single foci non-palpable invasive breast cancer who were scheduled to undergo needle-localized partial mastectomy (NLPM) were enrolled prospectively in this study from 2016 to 2018. Outcomes were compared to retrospective data (2015) of patients at our institution with invasive breast cancer who underwent NLPM without EMN (NL, N=52). The primary outcome was positive margin rate. Secondary outcomes included specimen volume, operating time, contouring time, and safety. Surgeon feedback was also evaluated. 36 patients were recruited and underwent NLPM with EMN. The positive margin rate was 22.2%EMN vs. 21.1%NL(p=1.0). 6 patients underwent re-excision for a positive circumferential margin (16.7%EMN vs. 13.5%NL); 1 invasive and 5 ductal carcinoma in situ (DCIS). 1 re-excision contained <1mm DCIS and 5 were negative for residual disease (2.7%EMN vs. 7.7%NL). 2 patients did not undergo re-excision due to positive skin or chest-wall margins (5.5%EMN vs. 7.6%NL). The median specimen volume was 71±77cm^{3}EMN vs. 144±154cm^{3}NL(p<0.01). The median operative time was 66±18minEMN vs. 68±22minNL(p=0.98), including a median contouring time of 3.2±1.3min (EMN). Sterility was maintained for all cases and there were no immediate patient complications secondary to EMN. Surgeon feedback concluded that EMN was easy to use. The EMN positive margin rate is similar to NL, with significant reduction in resected specimen volume. This has an impact on cosmetic outcomes and patient body image. There was no difference in length of operative time, or compromise to surgical sterility and patient safety. This study suggests that EMN is safe and may improve treatment outcomes in breast-conserving surgery.

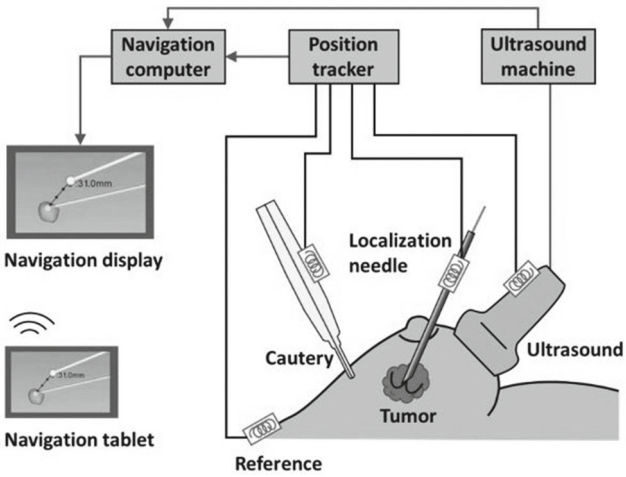


Figure 1. Operating room setup for electromagnetic navigation system. The coils represent electromagnetic position sensors. The navigation tablet allows the surgeon to contour the tumor location in a sterile fashion. This produces a virtual 3D tumor that is tracked relative to needle and cautery in real-time and displayed on an overhanging monitor.

P17

Concordance of Intraoperative Touch Prep Sentinel Lymph Node with Final Pathology in the Context of Neoadjuvant Chemotherapy M. Kupsik,[1]* R. Henry-Tillman,[1] S. Klimberg,[2] S. Korourian,[1] I. Makhoul,[1] A. Pennisi,[1] M. Preston,[1] D. Ochoa.[1] *1. Surgery, University of Arkansas for Medical Sciences, Little Rock, AR; 2. University of Texas Medical Branch at Galveston, Galveston, TX.*

BACKGROUND: Sentinel lymph node biopsy (SLNB) is an important tool used in staging the axilla in breast cancer. The results guide further local, regional and systemic treatments. Touch prep (TP) has been validated as a highly reliable technique for SLNB evaluation and at our institution has a sensitivity of 96% and specificity of 100%. Neoadjuvant chemotherapy (NAC) is known to cause treatment effects to the lymph nodes which has led investigation into intraoperative axillary staging in the context of NAC. There is a paucity of data validating TP in this context. METHODS: This study is a retrospective chart review of SLNB undergoing TP in women who underwent NAC. Pathology records were accessed to define TP and permanent section (PS) results in this cohort. The accuracy of TP was then calculated. RESULTS: A total of 360 SLNB were identified from 202 patients who underwent NAC, between 1/2006-1/2018. TP had 26(7.2%) false negatives and 3(0.8%) false positives. 1 FP was from micrometastasis seen on PS. Sensitivity and specificity were 66.2% and 98.9% respectively. The positive predictive value was 94.4% and the negative predictive value was 91.5%, for an overall accuracy of 91.9%. Of the 26 false negative results amongst 18 women, TP resulted in the following: 3 slides with atypical cells, 6 specimens of breast tissue, 1 paucicellular smear and the remaining 16 showing benign lymphoid cells. 13(3.6%) of lymph nodes demonstrated micrometastses and only one of those resulted in a false positive result. The rest were negative on TP and PS. Sensitivity decreased from 96% to 66% when the axilla was treated with NAC. CONCLUSION: In conclusion, the probability of correctly making a dichotomous classification of the SLN intraoperatively after NAC remains a challenge. In our review, although feasible, the sensitivity was greatly reduced.

TABLE 1.
Result Summary, n=360

	(%)	95% CI
SENSITIVITY	66.2	55-77
SPECIFICITY	98.9	97-100
PPV	94.4	85-98
NPV	91.5	89-94
Accuracy	91.9	89-95

P19

What is the Risk of Poor Outcome of Breast Conservation Therapy in Patients with Augmented Breasts? A. Tadros,* T. Moo, E. Zabor, R. Allen, Jr., M. Morrow, L. Braunstein. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Cosmetic outcomes and rate of implant loss are poorly characterized among breast cancer patients with previous breast augmentation(BA) who undergo breast conservation therapy(BCT). We sought to determine frequency of capsular contracture and implant loss after BCT among patients receiving contemporary whole-breast radiotherapy(WBRT). Methods: From 2006-2017, 71 breast cancers in 70 patients with a history of BA electing BCT were identified from a prospectively collected institutional database. Clinicopathologic, treatment, and outcome variables were examined. WBRT included conventional and hypofractionated schedules, both with and without a boost. Baker grade was determined by physician assessment and used to compare patients with new/worse contracture following treatment. Results: Median age was 52 years and median tumor size was 0.9cm. 54.9% of patients received radiation using hypofractionated whole-breast tangents and 81.7% received a boost (Table). 18 of 71 cases (25.4%) developed a new/worse contracture after BCT with a mean follow-up of 1.9 years. 9 of 71 cases (12.7%) were referred to a plastic surgeon for revisional surgery. There were no cases of implant loss. On univariate analysis, location of implant (retropectoral vs. subglandular), year of implant placement, type of radiation therapy(RT), RT boost, body mass index, and tumor size were not associated with new/worse contracture. Of 12 patients with existing contracture, only 2 patients developed worsening contracture. Inframmamary augmentation incision placement was associated with higher frequency of new/worse contracture when compared to other incision types (p=0.04). Patients with a new/worse contracture were less likely to have a post-BCT clinician cosmetic assessment of excellent (p<0.001). 87% of patients had an excellent/good cosmetic outcome. Conclusion: BCT for breast cancer patients with a prior history of BA has a low risk of implant loss. Hypofractionated RT does not adversely affect implant outcomes. Patients should be counseled regarding risk for capsular contracture (25%), but the majority have good/excellent outcome so BA does not represent a contraindication to BCT.

Patient, treatment, and outcome characteristics

	Frequency (%)
Carcinoma Subtype	
Ductal Carcinoma in Situ	8 (11.3%)
Invasive Ductal Carcinoma	55 (77.5%)
Invasive Lobular Carcinoma	6 (8.5%)
Other	2 (2.8%)
Receptor Status	
ER+	59 (83.1%)
ER-/HER2+	2 (2.8%)
Triple Negative	9 (12.7%)
Unknown	1 (1.4%)
Nodal Status	
Negative	60 (84.5%)
Positive	11 (15.5%)
Location of Implant	
Retropectoral	62 (87.3%)
Subglandular	9 (12.7%)
Type of Radiation Therapy	
Conventional	28 (39.4%)
Hypofractionation	39 (54.9%)
Unknown	4 (5.6%)
Chemotherapy	
Yes	34 (47.9%)
No	35 (49.3%)
Unknown	2 (2.8%)
Clinician Cosmetic Assessment after BCT	
Excellent	43 (60.6%)
Good	19 (26.8%)
Fair	6 (8.5%)
Poor	3 (4.2%)

ER=Estrogen Receptor; BCT=Breast Conservation Therapy

P20

Effectiveness and Safety of Magseed-localization for Excision of Breast Lesions: A Prospective Trial P. Singh,* M. Scoggins, A. Sahin, R. Hwang, H. Kuerer, A. Caudle, E. Mittendorf, A. Thompson, I. Bedrosian, M. Teshome, S. DeSnyder, F. Meric-Bernstam, K. Hunt. *Breast Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: Since FDA approval in 2016, use of Magseed has been increasing for localization of non-palpable lesions due to advantages over wires or radioactive seeds. Here we report the first prospective trial evaluating effectiveness of Magseed to localize breast lesions. Methods: From 1/2017-2/2018, women with lesions requiring localization for excision were enrolled at a single institution. Primary endpoint was Magseed retrieval rate. Secondary endpoints were adverse events, accuracy and duration of placement, surgery duration, positive margin rate and second procedure rate. Surgeons, radiologists and pathologists were surveyed for ease of placement and localization using a Likert scale. Descriptive statistics and Fisher's exact test to assess univariate associations with positive margins were done. Results: 107 subjects underwent placement of 124 Magseeds by image-guidance followed by surgical excision. Mean age was 61 years (range 28-87). 25 subjects had neoadjuvant chemotherapy. The majority were masses (62%) followed by calcifications (24%), architectural distortion (7%) and other (7%). Median lesion size on imaging was 13mm (range 0-60). One marker was placed in 93 subjects, 2 markers in 11 and 3 markers in 3. Median localization time by radiology was 5 min (range 1-45). All Magseeds were within 10mm of the target lesion: 118 within 5mm and 99% placed on first attempt. The 124 Magseeds were surgically retrieved with median operative time of 15 min (range 4-47). No device-related adverse events occurred. Pathology showed 92 malignant (70 invasive, 22 DCIS) and 15 benign lesions. For malignant lesions, 10 (11%) had positive margins and 7 required a second surgery for additional margins. On univariate analysis, age ≤ 50 was significantly associated with positive margins (31.3% vs 6.5%, p=0.01). Table 1 shows clinician rating of ease of Magseed use. Conclusions: The Magseed system for localization of non-palpable lesions was effective and safe; all markers were successfully placed and retrieved with margin-negative resections in 89%. Clinicians rated Magseeds easy to use in most cases. This study supports use of Magseed for localization of breast lesions.

Table 1. Survey of clinicians assessing Magseed placement and localization in 107 subjects

	Rating	n (%)
Radiologist		
Ease of placement?	Very Easy	65 (60.8)
	Fairly Easy	40 (37.4)
	Difficult	2 (1.9)
Surgeon		
Ease of transcutaneous location?	Very Easy	67 (62.6)
	Fairly Easy	32 (29.9)
	Fairly Difficult	4 (3.7)
	Difficult	2 (1.9)
	Unable to localize transcutaneously	2 (1.9)
Ease of intraoperative localization?	Very Easy	64 (59.8)
	Fairly Easy	29 (27.1)
	Fairly Difficult	11 (10.3)
	Difficult	3 (2.8)
	Unable to localize intraoperatively	0 (0.0)
Pathologist		
Ease of marker identification and retrieval in specimen?	Very Easy	82 (76.6)
	Fairly Easy	21 (19.6)
	Fairly Difficult	3 (2.8)
	Difficult	0 (0.0)
	Unable to retrieve	0 (0.0)
	Missing data	1 (0.9)

P21

Implant Sparing Mastectomy: An Alternative for Women Undergoing Mastectomy with Retropectoral Implants E.E. Burke,* C. Laronga, W. Sun, S. Naqvi, B. Fridley, B.J. Czerniecki, S.J. Hoover, N. Khakpour, J.V. Kiluk, M.C. Lee. *Surgical Oncology, Moffitt Cancer Center, Tampa, FL.*

Introduction: Implant sparing mastectomy (ISM) is a novel skin-sparing mastectomy preserving a retropectoral implant that potentially eliminates the need for tissue expansion or complex reconstruction. The aim of this study was to determine oncologic and surgical outcomes, including reconstruction patterns, in patients (pts) undergoing ISM. Methods: A single institution, retrospective review of pts undergoing ISM from 2006 to 2018 was performed. Patient/tumor characteristics, stage, adjuvant therapy use, 90-day complication rates, reconstruction type, and disease recurrence were collected. Descriptive statistics provided. Results: A total of 121 ISM in 73 women were performed. Median age was 48yrs (range 27-79). Seventy (57.9%) ISM were for breast cancer (BC) treatment and 51 (42.1%) for prophylaxis. Among BC cases, 73.8% were cT1/cT2 and 73.8% were cN0; (70.8%) received systemic therapy and 32.3% received radiation therapy (XRT). Predicted number of deaths due to BC at 5yrs was 3-5. Median follow up was 35 months (0.5-140mos). There were 3 deaths due to BC. Among 5 recurrences, 4 were distant and 1 was local (mastectomy flap). There was no BC identified for prophylactic ISM. Total 90-day complication rate per ISM was 15.7% similar to the 10-20% reported rate for mastectomy with immediate reconstruction. Rates were 0.8% for both seroma and wound infection, 2.5% for wound dehiscence, 3.3% for hematoma, and 8.2% for skin necrosis. Neoadjuvant therapy, XRT, ISM for prophylaxis vs. BC treatment, clinical stage, receptor status, and node dissection were not associated with complications. The majority of pts (56.2%) had delayed reconstruction requiring only implant exchange (Figure 1). Overall usage of autologous reconstruction was low (12.3%); 7/9 (77.8%) flaps were performed in pts receiving XRT. Conclusion: ISM is a unique approach for pts pursuing mastectomy for BC treatment or prevention with equivalent oncologic outcomes and complication rates to skin sparing mastectomy with reconstruction. Reconstruction for the majority of these pts was markedly simplified by elimination of tissue expansion while maintaining a low rate of flap reconstruction.

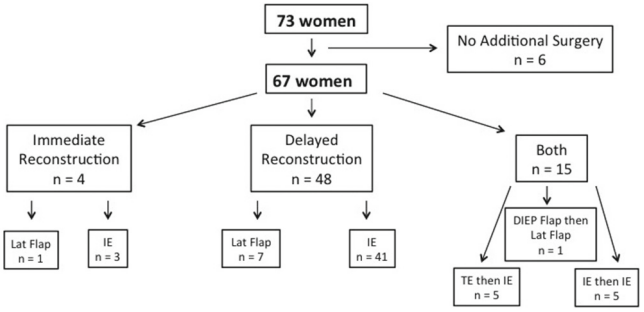
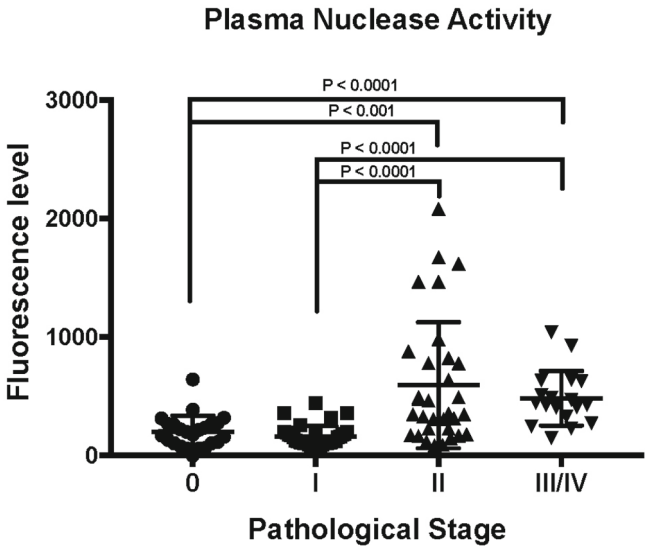


Figure 1. Breakdown of timing and type of reconstruction performed. Immediate reconstruction performed at time of ISM. Delayed reconstruction performed at any time after ISM. IE – implant exchange. TE – tissue expander. Lat Flap – Latissimus dorsi flap, implant removed. DIEP Flap – Deep inferior epigastric perforator flap, implant left in place.

P22

Plasma Nuclease Activity is Elevated in Stage II-IV Breast Cancer S. Shubham,[1] S. Kruspe,[1] M.A. Curry,[2] S.D. Phadke,[1] S. Sugg,[1] J.O. McNamara,[1] P.H. Giangrande,[1] C.H. Chan.[1]* *1. Department of Surgery, University of Iowa, Iowa City, IA; 2. Holden Comprehensive Cancer Center, Iowa City, IA.*

Background: Upregulation of various nucleases has been shown in breast cancer. Using a fast and simple fluorescence-based nuclease-activated probe (NuCAP) assay, we have previously detected nuclease activity in circulating tumor cells (CTCs) isolated from stage IV breast cancer patients in comparing to healthy controls. CTCs may be useful to predict outcome or to monitor response to therapy. Here we aim to determine if we can detect free plasma cancer-associated nucleases in loco-regional disease, and if there is a difference in nuclease activity among the different breast cancer subtypes as determined by receptor status. Methods: Under an IRB-approved protocol, breast cancer patients were consented for prospective tissue and clinical data collection. Blood samples were freshly processed and plasma samples were stored frozen. Patients with stage 0-IV breast cancer were randomly selected. Plasma nuclease activity was determined by the NuCAP assay and reported as fluorescence signal generated from digested NuCAP probes. Activity levels were correlated with pathological stage and molecular subtype. Two-tailed student t-tests with 95% confidence intervals and one-way ANOVA were used for statistical analysis. A p-value of less than 0.05 was considered statistical significance. Results: We obtained 109 plasma samples from patients with stage 0-IV breast cancer. Plasma nuclease activity was significantly higher in stage II-IV (N=50) in comparing to stage 0/I (N=59) (555 vs. 179, P<0.001). For patients with stage II-IV disease, ER/PR+HER2- cancers (N=29) tended to have higher nuclease activity than those with HER2+ (N=10) and triple negative (N=10) breast cancers (669 vs. 408 vs. 384, ANOVA P=0.11). Conclusion: Elevated nuclease activity can be detected in plasma of patients with loco-regional and metastatic breast cancer using a simple NuCAP assay. Nuclease activity elevation correlated with more advanced disease and tended to be higher in ER/PR+ tumors. Although further studies are required, this novel assay could potentially be used to detect the presence of CTCs in breast cancer patients.



P23

Trends in Axillary Management of Breast Cancer Patients With 1 to 3-Positive Nodes Undergoing Mastectomy: A NCDB Analysis L. Kopicky,[1]* B. Pople,[1] P. Karabon,[2] M. Danko,[2] N. Dekhne.[1]
1. Surgery, William Beaumont Hospital, Royal Oak, MI; 2. Oakland University William Beaumont School of Medicine, Rochester, MI.

INTRODUCTION: Axillary lymph node dissection (ALND) with consideration for post mastectomy radiation therapy (PMRT) is current standard of care for patients undergoing mastectomy who have N1 disease. Axillary radiation therapy and ALND both provide comparable regional control for patients with N1 disease. This study examines nationwide trends in axillary management of patients with 1 to 3 positive lymph nodes undergoing mastectomy. METHODS: A NCDB analysis was conducted of breast cancer patients who underwent mastectomy and were found to have 1-3 positive lymph nodes between 2010 and 2014. One-Way Analysis of Variance (ANOVA) or T-Tests are used to compare continuous variables while categorical variables are compared using Chi-Square Tests. Cochran-Armitrage Tests for Trend were used to examine treatment trends over time. Further analysis was conducted of four subgroups: neither ALND nor PMRT, ALND only, PMRT only, and ALND plus PMRT. RESULTS: From 2010 to 2014, the proportion of mastectomy cases that received ALND decreased from 73.41% to 68.55% ($p< 0.0001$) and the cases that received PMRT increased from 21.40% to 29.72% ($p< 0.0001$). Trends of each subgroup showed the proportion of mastectomy cases that received neither ALND nor PMRT increased from 20.80% to 22.23% ($p=0.4385$), ALND only decreased from 57.80% to 48.05% ($p< 0.0001$), PMRT only increased from 5.79% to 9.21% ($p< 0.0001$), and both ALND and PMRT together increased from 15.61% 20.51% ($p < 0.0001$). Patients who had 3 positive lymph nodes were more likely to receive both ALND and PMRT ($p<0.0001$). Patients treated at academic centers were less likely to have PMRT only compared to other subgroups ($p<0.0001$). Factors associated with greater use of PMRT include young age, immediate breast reconstruction, and contralateral mastectomy. CONCLUSION: There is a significant decrease in surgical management alone (ALND) and increasing use of PMRT in breast cancer patients who have 1-3 positive nodes, indicating earlier adoption of the 2014 AMAROS trial results by community centers.

	No ALND or PMRT (n = 15,909)	ALND Only (n = 38,392)	PMRT Only (n = 5,341)	ALND + PMRT (n = 13,774)	P-Value
Age (Years)					
Mean (Standard Deviations)	58.49 (14.06)	58.52 (13.95)	53.91 (12.79)	54.19 (12.59)	< 0.0001
Breast Reconstruction					
Yes	5,607 (35.24%)	13,218 (34.43%)	1,982 (37.11%)	4,977 (36.13%)	< 0.0001
No	10,302 (64.76%)	25,174 (65.57%)	3,359 (62.89%)	8,797 (63.87%)	
Removal of Contralateral Breast					
Yes	4,811 (30.24%)	11,226 (29.24%)	1,877 (35.14%)	4,633 (33.64%)	< 0.0001
No	11,098 (69.76%)	27,166 (70.76%)	3,464 (64.86%)	9,141 (66.36%)	
Regional Lymph Nodes Positive					
1	12,020 (75.55%)	21,603 (56.27%)	3,428 (64.18%)	5,430 (39.42%)	< 0.0001
2	2,761 (17.35%)	10,706 (27.89%)	1,259 (23.57%)	4,661 (33.84%)	
3	1,128 (7.09%)	6,083 (15.84%)	654 (12.24%)	3,683 (26.74%)	
Regional Lymph Nodes Positive					
Mean (Standard Deviations)	1.32 (0.60)	1.60 (0.75)	1.48 (0.70)	1.87 (0.80)	< 0.0001
Facility Type					
Community Program	8,599 (54.05%)	20,676 (53.85%)	2,782 (52.09%)	6,792 (49.31%)	< 0.0001
Academic Program	4,363 (27.42%)	10,953 (28.53%)	1,309 (24.51%)	3,771 (27.38%)	
Other or Unknown Program	2,947 (18.52%)	6,763 (17.62%)	1,250 (23.40%)	3,211 (23.31%)	

P24

Superparamagnetic Iron Oxide Nanoparticles (SPIO): A Sentinel Node (SN) Tracer with Novel Applications A. Karakatsanis,[1]* A.F. Hersi,[2] S. Abdsaleh,[3] H. Olofsson,[4] L. Pistiolis,[5] L. Esserman,[6] S. Eriksson,[2] H. Lundgren,[1] F. Wärnberg.[1] *1. Department for Surgical Sciences, Uppsala University, Uppsala, Sweden; 2. Centre for Clinical Research, Uppsala University, Västerås, Sweden; 3. Aleris Mammography Unit, Uppsala, Sweden; 4. Department for Clinical Pathology, Uppsala, Sweden; 5. Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy at University of Gothenburg, Sahlgrenska University Hospital, Gothenburg, Sweden; 6. UCSF Carol Franc Buck Breast Care Center, San Francisco, CA.*

Introduction: SPIO is a tracer for SN biopsy (SNB) comparable to radioisotope (RI) and ink. SPIO injection 2-27 days before surgery enhances SN detection from 89 to 96% and remains in the SN for at least four weeks. The timing and technique of injections can be varied to improve logistics and reduce morbidity. We present a series of ongoing studies that will enable innovation in surgical management Methods/Results: The SentiNot trial includes women with a preoperative diagnosis of DCIS where SNB is planned because of mastectomy or high risk for upgrading to invasive cancer. SPIO is injected at primary surgery but SNB is performed later, only in those upgraded. In 185 women, 25% were upgraded. SentiNot approach reduced SNB by 75%. At SNB 9-47 days after primary surgery, RI+ink was also used. SPIO outperformed RI both as sole tracer (85% identification vs 59%) and combined with ink (96% vs 70%). Cost was reduced by 26% in women with pure DCIS. In the MagUS trial (n=20), MRI is performed before and after peritumoral SPIO injection and facilitates a focused ultrasound (US) of the SN. Transcutaneous magnetic probe localisation of the SN guides the US and a "targeted" core biopsy of the SN is done. The MagUS technique was 24% more sensitive than ordinary US and 100% specific for macro-metastases. A peritumoral injection of SPIO 1-1.5ml, resulted in negligible or no MRI breast artefacts, 3-12 months after surgery, in women without skin staining (PostMagMRI, n=20). A deeper injection gave less skin staining and most of the SPIO was removed at surgery. Combining peritumoral SPIO for SN detection with a magnetic clip for tumor localisation showed feasibility in a pilot study (n=32). The breast excisions were radical with small resection volumes and successful SN detection in all cases. The seed placement and SPIO injection was performed by the radiologist up to four weeks before surgery, simplifying logistics. Conclusion: SPIO for SN detection can lead to innovations in delivery of care. It can be extended, leveraging the persistence in nodes and with an ability to localize both tumor and SN.

P25

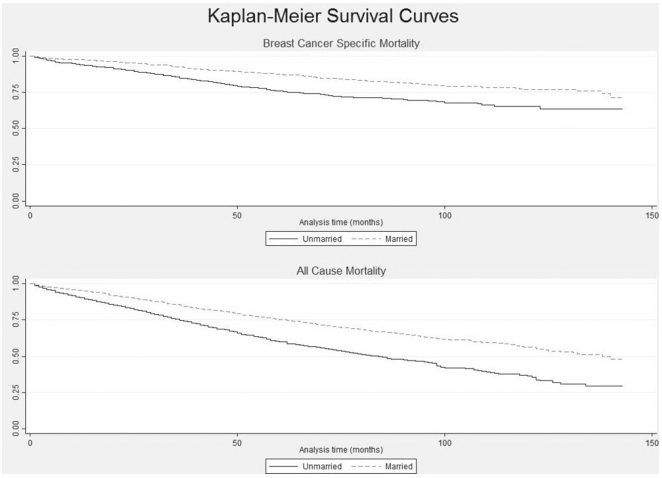
Frequency of ESR1 Mutation and Resistance Factors of CDK4/6 Inhibitor in ER-Positive Breast Cancer Cohorts T. Takeshita,* E. Katsuta, L. Yan, K. Takabe. *Surgical Oncology, Roswell Park Comprehensive Cancer Center, Williamsville, NY.*

Introduction: Endocrine therapy in combination with CDK4/6 inhibitors is becoming a mainstay of treatments for estrogen receptor (ER)-positive metastatic breast cancer (MBC), but resistance to this combination therapy is inevitable. Recently, resistance factors of each drug have become clear. ESR1 mutation is a resistance factor of endocrine therapy and it is a useful predictive biomarker. Further, Rb1 mutation and amplification of cyclin E1 (CCNE1) and CDK6 are now known as resistance factors of CDK4/6 inhibitors. However, it is not clear whether coexistence of these genetic alterations is a predictor of effect of these combination therapies. Here we studied the frequency of ESR1 mutation and resistance factors of CDK4/6 inhibitor (Rb1 mutation, and amplification of CCNE1 and CDK6) in ER-positive breast cancer cohort. Methods: We analyzed genetic alterations using an ER-positive primary breast cancer (PBC) cohort from TCGA data (n = 525), MBC cohort 1 (n = 84), and MBC cohort 2 (n = 140). Results: In the MBC cohort 2 with only 83.9% of the patient underwent endocrine therapy, ESR1 mutation was identified in 13.5%, Rb1 mutation in 4.2%, amplification of CCNE1 in 0.7%, and amplification of CDK6 in 5.7%. We were unable to find any case with both ESR1 mutation and resistance factors of CDK4/6 inhibitor. In the PBC cohort and the MBC cohort 1 with only 7% aromatase inhibitor treatment, the proportion of ESR1 mutation was very small and mutual relationship could not be verified. These results indicated that treatment-naïve patients with both tolerance factors of combination therapy are rare and it is speculated that the tolerance factors are acquired as each treatment is added. Conclusion: We showed the clinically important frequency of ESR1 mutation and resistance factors of CDK4/6 inhibitor in ER-positive breast cancer cohorts.

P26

The Impact of Marital Status on the Stage at Diagnosis and Survival in Males with Breast Cancer J.H. Fieber,* C. Wirtalla, R.R. Kelz, J. Tchou. *University of Pennsylvania, Philadelphia, PA.*

Introduction: The incidence of breast cancer among men is increasing. In part, due to detection bias, outcomes for male breast cancer patients are poor compared to females. Marriage has been shown to influence treatment and life expectancy in multiple malignancies. We investigated the effect of marital status on the diagnosis and survival of males with breast cancer. Methods: The SEER database (2004-2015) was queried to identify male adults diagnosed with invasive breast cancer. Patients were defined as married or unmarried (divorced, separated, single, widowed). Logistic regression was used to analyze the stage of diagnosis defined as AJCC Stage I compared to Stage II-IV in married compared to unmarried males. Cox regression was used to analyze breast cancer specific and all-cause mortality of married compared to unmarried males. Results: Of the 3,699 males with breast cancer that were included in our cohort, the average age of diagnosis was 65.7 years-old (Std Dev: 12.4). The AJCC tumor Stage at the time of diagnosis was Stage I in 30.4%, Stage II in 43.4%, Stage III in 17.1% and Stage IV in 9.1% of patients. Over 90% of tumors were ER positive, 50% of tumors were 2-4.99 cm, and 48% were moderately differentiated. Almost 70% of men with breast cancer were married. Married men were 50% (OR: 1.50, CI: 1.28-1.76, p<0.001) more likely to be diagnosed with Stage I disease versus a higher stage than unmarried men. There were 536 deaths (14.5% of patients) attributed to breast cancer and 1,097 (29.6% of patients) deaths from all causes during the study period. Married men were less likely to die of their breast cancer (Hazard ratio: 0.68, CI: 0.57-0.82, p<0.001) as well as less likely to die from any cause (Hazard ratio: 0.67, CI: 0.59-0.76, p<0.001) after adjusting for demographics, stage, and tumor characteristics. Conclusion: Unmarried males are significantly more likely to present with more advanced breast cancer and die of their disease or other causes than married males. This study emphasizes the potential impact of the social network on cancer diagnosis and survival and suggests that unmarried males may benefit from additional support.



P28

FOXP3 Expression: A Marker of Immunosuppression in Breast Lobules with Epithelial Proliferation W. Young,[1]* T. Hoskin,[1] M. Arshad,[1] S. Winham,[1] M. Frost,[1] R. Brahmbhatt,[1] A. Pena Jimenez,[1] M. Stallings Mann,[2] L.M. Murphy,[1] L. Denison,[1] M. Sherman,[2] J.M. Carter,[1] K. Knutson,[2] D.W. Visscher,[1] D.C. Radisky,[2] A.C. Degnim.[1] *1. Mayo Clinic, Rochester, MN; 2. Mayo Clinic Florida, Jacksonville, FL.*

Background: Resident immune cells in the breast may inhibit tumorigenesis or provide a permissive microenvironment for breast cancer (BC) development. Regulatory T cells (Treg) dampen the immune response and are of interest in the tumor immunosurveillance hypothesis. We evaluated FOXP3 immunostaining for Tregs in benign breast disease (BBD) biopsies and assessed its association with epithelial abnormalities. Methods: We performed a 1:1 matched case-control analysis of 46 women (median age 57 years) with BBD who developed incident BC (cases), and 46 women who remained BC-free (controls). We assessed <10 lobules per biopsy for number FOXP3+ cells and density (FOXP3+ cells / lobule area) in digitized immunostained sections with ImageScope and Aperio software. Analysis of Tregs versus epithelial proliferation was performed using zero-inflated Poisson models with the logarithm of lobule area as the offset and fit using a generalized linear mixed model to account for data among multiple lobules per patient. Results: Only 8% of the 839 lobules evaluated [48% normal (NL), 28% fibrocystic nonproliferative (NP), 25% proliferative/atypical (PA)] contained FOXP3+ cells. The 68 lobules containing any FOXP3+ cells showed staining in a median of 6.4 per 10,000 nuclei (range: 0.6-781), with a median density of 8.3 FOXP3+ cells/mm^2 (range: 0.75-887). Overall, the presence of any FOXP3 expression did not differ between cases (7.0%) and controls (9.2%), p=0.80. In per lobule analyses of cases and controls, the presence of any FOXP3 expression increased from NL lobules (4.8%) to NP (9.0%) to PA lobules (13.6%), zero-inflation model component p=0.008 for linear trend, see Table. Conclusion: We observed increased detection of FOXP3+ cells in breast lobules with increasing epithelial proliferation. We suggest that analysis of Tregs in BBD biopsies warrants further study in relationship to BC risk.

FOXP3 Expression by Lobule Type

Lobule Type	FOXP3 Absent N (%)	FOXP3 Present N (%)
Normal (N=399)	380 (95.2)	19 (4.8)
Fibrocystic Non-proliferative (N=234)	213 (91.0)	21 (9.0)
Fibrocystic Proliferative/Atypia (N=206)	178 (86.4)	28 (13.6)

P29

Whole Breast Radiation Therapy Following Intraoperative Radiation Therapy is Associated with Increased Surgical Site Complications A. Crown,[1]* C.J. Hillenbrand,[1] F. Rocha,[1] J. Grumley.[2] *1. General, Thoracic and Vascular Surgery, Virginia Mason Medical Center, Seattle, WA; 2. John Wayne Cancer Institute, Santa Monica, CA.*

Introduction: Identifying candidates for IORT is a challenge since the true extent of disease and presence of risk factors can only be confirmed on final pathology. As a result, some patients require post-operative WBRT. We hypothesized that multiple radiation treatments to the surgical bed may contribute to poor wound healing. Methods: The electronic medical records of all women with invasive breast cancer who underwent partial mastectomy with IORT from February 2011 to October 2016 were reviewed. Final surgical pathologic specimens that demonstrated high-risk features, defined as multifocal or large extent of disease, positive nodes, lymphovascular invasion, or inadequate margins, were indications for additional treatment with WBRT. Surgical site complications were correlated to receipt of IORT or IORT+WBRT. Results: Of 238 patients treated with IORT, 184 (77.3%) patients had IORT only while 54 (22.7%) received IORT+WBRT. Patient age (IORT 62.9 years vs WBRT 62.2 years, p=0.69), body mass index (IORT 28.5 kg/m^2 vs WBRT 30.2 kg/m^2, p=0.21), tumor size (IORT 14.2 mm vs WBRT 16.7 mm, p=0.83), tumor histology (p=0.53), and receptor status (ER+ p>0.99, PR+ p=0.86, Her2+ p=0.57) were similar between groups. One WBRT patient had a rib fracture on bone scan, not visible on chest x-ray. No other major complications occurred. Overall, 29 (12.2%) patients experienced 34 surgical site complications with 12 (22.2%) patients in the WBRT group compared to 17 (9.0%) patients in the IORT group (RR 3.2, 95% CI 1.7-6.2, p<0.001). Addition of WBRT was associated with an increased rate of complications on both univariate and multivariate analyses. Advanced age, obesity, diabetes, and smoking were not associated with increased complications. Two patients in the WBRT group underwent seroma aspiration; no other complications required invasive interventions. Conclusion: IORT combined with WBRT is associated with an increased rate of minor surgical site complications; however, most complications did not require invasive interventions. Additional studies are needed to identify strategies to mitigate complications associated with WBRT after IORT.

Complications	IORT (n=184)	WBRT (n=54)	p-value
Rib fracture	0 (0%)	1 (1.9%)	0.23
Dehiscence	8 (4.3%)	8 (14.8%)	0.01
Infection	2 (1.1%)	2 (3.7%)	0.22
Nipple deformity	1 (0.5%)	2 (3.7%)	0.13
Fat necrosis	3 (1.6%)	0 (0%)	0.59
Seroma	5 (2.7%)	2 (3.7%)	0.50
Multiple complications	2 (1.1%)	3 (5.6%)	0.08

P30

Modern Risks for Capsular Contracture After Mastectomy and Implant-based Reconstruction J.B. Hammond,[1]* H. Kosiorek,[4] R. Gray,[1] P. Cronin,[1] A. Rebecca,[2] W. Casey,[2] C.E. Vargas,[3] W. Wong,[3] S.R. Keole,[3] T. Vern-Gross,[3] L. McGee,[3] M. Halyard,[3] B. Pockaj.[1] *1. Mayo Clinic Dept. of Surgical Oncology, Phoenix, AZ; 2. Mayo Clinic Dept. of Plastic & Reconstructive Surgery, Phoenix, AZ; 3. Mayo Clinic Dept. of Radiation Oncology, Phoenix, AZ; 4. Mayo Clinic Dept. of Research Biostatistics, Scottsdale, AZ.*

Background Breast reconstruction after mastectomy is a common technique which continues to evolve. Capsular contracture is a known complication that creates pain, poor cosmesis, and need for revisions. The goal of this study was to analyze the incidence of capsular contracture and risk factors for its development. Methods We performed a retrospective review of patients who underwent mastectomy with implant-based reconstruction from 2010-17 for ductal carcinoma in situ, invasive cancer or local recurrence. Risks for capsular contracture were analyzed using univariate and multivariate analysis. Results A total of 395 patients underwent implant-based reconstruction following mastectomy. Mean age was 51 years, and mean BMI was 25.2. Incidence of capsular contracture was 8%. Most underwent skin (35%) or nipple-sparing mastectomy (59%). Majority of patients had direct to implant reconstruction (74%). Implant location was subpectoral in 84%, with acellular dermal matrix (ADM) used in 81%. Factors were evaluated for association with capsular contracture (Table). Capsular contracture was not associated with BMI, stage, type of reconstruction, adjuvant therapies, or acute postoperative complications (hematoma, infection, skin necrosis, or seroma). Factors associated with capsular contracture included young age (p=0.032), adjuvant radiotherapy (RT, p<0.001), and neoadjuvant therapy (p=0.004). The rate of capsular contracture was 18% among patients with post-mastectomy RT vs 6% for those without. The rate of capsular contracture among six patients receiving proton beam RT was 33%. Prior RT was not associated with capsular contracture, but there were only 14 such patients. Multivariate analysis showed that adjuvant RT but not neoadjuvant therapy was associated with capsular contracture. Adjuvant chemotherapy was found to be protective (OR=0.212, 95% CI 0.06-0.746)). Among patients who developed capsular contracture 68% underwent surgical revision. Conclusion The incidence of capsular contracture in the modern era is lower than previously reported. Adjuvant RT remains a significant risk factor, but current surgical techniques and radiation delivery may have reduced the risk of this complication.

Capsular Contracture

Characteristics	Capsular Contracture		Total N (%)	P-Value
	Yes N (%) 31 (8)	No N (%) 364 (92)		
Age, Years (Mean, SD) (Range)	47.1 (10.1) (22-82)	51.6 (11.0) (17.3-46.3)		0.032
BMI (Mean, SD) (Range)	24.5 (5.1) (18.3-38.4)	25.3 (5.1) (17.3-46.3)	25.2 (5.1) (17.3-46.3)	0.277
Stage				0.073
0	6 (19)	79 (22)	85 (21)	
I	7 (23)	137 (37)	144 (36)	
II	13 (42)	109 (30)	122 (31)	
III	3 (10)	35 (10)	38 (10)	
IV	2 (6)	4 (1)	6 (2)	
Type of Surgery				0.240
Mastectomy	0 (0)	22 (6)	22 (6)	
Skin-Sparing Mastectomy	14 (45)	126 (35)	140 (35)	
Nipple-Sparing Mastectomy	17 (55)	216 (59)	233 (59)	
Implant Placement				0.679
Subpectoral	27 (87)	306 (84)	333 (84)	
Subglandular	4 (13)	57 (16)	61 (16)	
ADM	24 (77)	293 (81)	317 (81)	0.657
Adjuvant Hormone Therapy	14 (45)	188 (52)	202 (51)	0.488
Adjuvant Chemotherapy	3 (10)	90 (25)	93 (24)	0.058
Neoadjuvant Chemotherapy	15 (14)	89 (86)	104 (26)	0.004
RT	13 (42)	59 (16)	72 (18)	<.001

P31

Preoperative Delays and Outcomes in Stage III Breast Cancer Patients: Differences by Histologic Features D. Sachs,* N. Melchior, K. Ruth, E.R. Sigurdson, A. Aggon, J. Daly, R. Bleicher. *Breast Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

BACKGROUND Time to surgery (TTS) after diagnosis in Stage I-II breast cancer patients adversely affects survival; however, this has not yet been demonstrated for stage III cancers. This study was performed to analyze the effect of preoperative delay on Stage III patients, and to determine if specific histological subsets are more adversely affected by delays than others. METHODS Women diagnosed from 2004 to 2014 with their first and only breast cancer treated without neoadjuvant chemotherapy were identified from the National Cancer Database. Patients were limited to those having AJCC pathologic Stage III disease, excluding T4 tumors. Differences in TTS were assessed for patient demographics, tumor characteristics, histology, nodal status, and treatment. Cox proportional hazards regression evaluated the interaction of tumor-related predictors and TTS with overall survival (OS), with control for demographic, tumor, and treatment characteristics. RESULTS Among 43,970 women, mean tumor size was 4.2 cm, and patients had an average of 7.8 nodes positive. Mean (±SD) TTS after diagnosis was 32.4 (± 21.4) days. TTS by tumor size was similar for T1, T2, and T3 primaries (p=0.67), while TTS was slightly shorter when node positivity increased from N1 to N2 and N3 (p<0.001). OS was lower for all patients when TTS was >90 days (adjusted HR for >90 days vs 1-30 days=1.18, 95% CI=1.04-1.33 p=0.009). Association of TTS and OS did not differ by histology (p=0.70), grade (p=0.65), or tumor size (p=0.85), however delays made less of a difference in outcome for patients having greater numbers of positive nodes (p=0.008). CONCLUSION Preoperative delays in the Stage III non-neoadjuvant setting adversely affect survival. Tumor size, grade and histology do not change the effect of delay, but tumors having greater nodal involvement are less affected by greater TTS. This suggests that greater nodal disease may confer a predetermination of outcomes as versus the biologic behavior for stage III tumors whose primaries are large. Efforts to minimize excessive preoperative delays remain important even in stage III disease.

P32

Ductal Carcinoma In Situ Management Among Indiana Breast Cancer Patients: Does Race Matter? S. Obeng Gyasi,* L. Timsina, S.A. Adrian, T.J. Ballinger, C.S. Fisher. *Department of Surgery, Indiana University School of Medicine, Indianapolis, IN.*

Introduction: Black women in Indiana have a higher incidence and mortality from breast cancer compared to their white counterparts. The objective of this study is to evaluate differences in sociodemographic, clinical and treatment variables that may contribute to racial disparities in clinical outcomes among patients diagnosed with Ductal Carcinoma In-Situ (DCIS) Methods: The Indiana Cancer Registry was queried for black and white women ages 18-90 with a diagnosis of DCIS from 01/01/2006-12/31/2016. The data was divided into two groups based on race (black, white). Bivariate analyses were conducted to determine intergroup differences between races on sociodemographic, clinical and treatment variables. Results: The study population included 2,213 patients. Black women comprised approximately 11% (n=243) of the sample. A higher percentage of black women lived below the federal poverty level (black 17.9%, white 14.2%, p =0.00l), in a metropolitan area (black 98%, white 74%, p=0.001) and had Medicaid insurance (black 7.9%, white 3% p = 0.002). There was no significant difference in the groups on tumor grade (p=0.453), hormone receptor status (estrogen p=0.111, progesterone p=0.858), surgical treatment (p=0.393), radiation therapy (p=0.134) and hormone therapy use among estrogen positive patients (p= 0.398). Black patients were more likely to experience longer wait times from biopsy to surgery (black 46 days [IQR 6-347], white 33 [IQR 1-380], p <0.001) and from surgery to radiation (black 80 days [IQR 22-246], white 64[IQR 10-244], p 0.001) than their white counterparts. Conclusion: Despite differences in sociodemographic variables between white and black Indiana DCIS patients, there was no difference in the treatment (surgery, radiation and hormone therapy) between the two groups. Our study results of longer waits times for surgery and radiation indicate black women in Indiana may face barriers in accessing these treatment modalities. This is significant as studies have shown treatment delay to worsen anxiety and clinical outcomes. Future studies should focus on identifying institutional and patient related variables resulting in increased delays for black patients.

P33

High-risk for Developing Breast Cancer: Differences Between White and African American Women Q.P. Le,* S.D. Nathanson, L.L. Susick. *Henry Ford Health System, Detroit, MI.*

Background: Although African American (AA) women are more likely to die from breast cancer (BrCa) than White Americans (WAs), they are less likely to get the disease. We hypothesized that AAs are also less likely to exhibit a high risk for getting BrCa than WAs. Methods: 4585 women undergoing screening mammograms between May 2017 and August 2018 completed an iPad-based cancer risk assessment (Hughes riskApp). This technology allowed rapid evaluation of demographic, family, and other pertinent risk factors and enabled a comparison of lifetime risks of BrCa between AAs and WAs. Results: Based on the Hughes riskApp, 655/4585 (14.3%) had a >20% lifetime risk of developing BrCa; High risk was identified in 535/3546 (15.1%) of WAs compared to 120/1039 (11.6%) AAs (Chi square 6.018; p=0.014). None of these patients had breast cancer at the time of study. Conclusions: In this single institution study, women who had otherwise not been identified as being at high risk for developing BrCa were identified by the Hughes riskApp to be eligible for more intense imaging and preventive measures, including testing for deleterious gene mutations. AA women were significantly less likely to have a high lifetime risk (>20%) of developing breast cancer than WAs. This new information parallels population statistics that show AAs are less likely to have developed breast cancer than WAs. Both WAs and AAs are likely to benefit from increased imaging with more BrCas potentially diagnosed early.

P34

Radiofrequency Technology as a Non-Radioactive Alternative to Wire Localization for Excision of Non-Palpable Breast Cancers M.L. DiNome,[1]* A.M. Kusske,[1] D.J. Attai,[1] C.P. Fischer,[2] A.C. Hoyt.[2] *1. Department of Surgery, UCLA, Los Angeles, CA; 2. Department of Radiologic Sciences, UCLA, Santa Monica, CA.*

Introduction: Despite the logistical challenges and patient inconveniences, wire localization (WL) remains the most common method for targeting non-palpable breast cancers for surgery. Radioactive seed localization, as the most studied alternative, requires special handling and tracking of the ^{125}I seeds. Our study compared the surgical outcomes of a new radiofrequency technology to standard wire localization to assess the suitability of this approach for guiding surgical excision of breast cancers. Methods: An IRB-approved retrospective review of patients who had undergone lumpectomy using a radiofrequency localization system (RFLS) compared to patients who underwent standard wire localization was performed. Clinical-pathologic features were matched. Imaging modality used to guide localization, tumor volume excised, positive margin rates and re-excision rates were assessed. Results: Our study compared the outcomes of a cohort of breast cancer patients localized with radiofrequency technology (n=33) to patients who subsequently were localized using standard wire (n=50). Mammography was used to guide wire placement in 64% of patients (32/50) compared to 42% (14/33) for radiofrequency tag placement, with ultrasound used for the remainder. The volume of tissue removed was similar in both groups (WL 35.25 cm^3 vs RFLS 36.3 cm^3). Positive margin rates (WL 8.0% vs RFLS 3.0%) and re-excision rates (WL 10% vs RFLS 6.1%) were not statistically different. Conclusion: Radiofrequency technology appears to be a suitable alternative to wire localization for guiding the surgical excision of breast cancers, with similar positive margin and re-excision rates. Unlike radioactive seed localization, which has been the most studied alternative to wire, RFLS is non-radioactive and utilizes a technology that is in use worldwide, most commonly in the microchipping of pets. The inherent challenges to operating room efficiency and patient satisfaction with same day WL warrants the evaluation of alternative methods for localization prior to surgery. We anticipate that RFLS, a non-radioactive alternative, will be a more readily adoptable option across all institutions.

P35

Axillary Management After Neoadjuvant Endocrine Therapy A. Weiss,* S. Wong, M. Golshan, E. Mittendorf, T.A. King. *Surgery, Brigham and Women's Hospital, Boston, MA.*

Background: Clinical trials evaluating axillary management in patients receiving upfront surgery or neoadjuvant chemotherapy (NAC) have led to a shift towards less axillary lymph node dissection (ALND). How these data have impacted management of the axilla in patients receiving neoadjuvant endocrine therapy (NET) remains unknown. Methods: The National Cancer Database was used to identify stage II and III HR+, HER2- breast cancer patients treated from 2012-2015. Patients with T4d and/or N2,3 disease were excluded. Clinico-pathologic characteristics and type of axillary surgery (SLNB +/- ALND) were examined by primary treatment (surgery, NAC, or NET) using pairwise comparisons and logistic regression. Residual nodal micromets were considered pN1. Results: 95,476 patients met eligibility criteria: 81,988 (85.9%) underwent upfront surgery; 11,286 (11.8%) received NAC; 2,202 (2.3%) received NET. NET use increased over the study period (1.9% to 2.9%, P<.0001). Among cN0 patients (n=62,858), SLNB attempt was more likely in patients treated with upfront surgery (48,588/56,394 (86.2%)) and NET (1379/1610 (85.7%)) compared to patients treated with NAC (3859/4384 (79.5%), p<0.001 for both comparisons). Among cN1 patients (n=32,618), SLNB attempt was also more likely in patients treated with upfront surgery (11,907/25,594 (46.5%)), when compared to NET (246/592 (41.6%) p=0.02) or NAC patients (2551/6432 (39.7%) p<.0001). The difference between upfront surgery and NET did not persist on adjusted analysis (Table). Among all patients with SLNB attempt, 23,520/68,333 (34%) had pN1 disease. In this setting ALND was more likely after NAC (1281/2134 (60%)) as compared to upfront surgery (11,298/20,837 (54%) p<.0001) or NET (222/549 (44%) p<.0001). On adjusted analyses, use of NAC was associated with reduced odds of SLNB attempt; whereas in pN1 disease by SLNB attempt, use of NET was associated with reduced odds of ALND (Table). Conclusions: In Stage II-III HR+ Her2- patients, SLNB use did not differ between upfront surgery and NET in cN0 or cN1 disease. In patients with pN1 disease by SLNB attempt, NET patients were less likely to undergo ALND. Outcomes data are needed to guide axillary management in this setting.

	Adjusted Odds Ratio for SLNB attempt		Adjusted Odds Ratio for cALND after SLNB attempt
	cN0 (n=62,858)	cN1 (n=32,618)	pN1 (n=23,520)
Upfront Surgery	Ref	Ref	Ref
NET	1.01 (0.87-1.17)	0.93 (0.79-1.11)	0.74 (0.62-0.89)
NAC	0.73 (0.68-0.79)	0.87 (0.82-0.92)	0.99 (0.90-1.01)

P36

588-Nipple-Sparing Mastectomies at a Single Institution C. Gan,* D. Hook, Y. Yan, J. Margenthaler. *Washington University School of Medicine, Saint Louis, MO.*

Nipple sparing mastectomy (NSM) is a cosmetically pleasing alternative to skin sparing mastectomy in the appropriately selected patient. The aim of this study was to review our experience with NSM and evaluate for oncologic safety. Patients who underwent NSM at our institution from September 2008 to August 2017 were identified. Data collected included patient age, tobacco use, tumor size, hormone receptor status, lymph node status, radiation and chemotherapy treatment, incision type, reconstruction type, and follow-up length. Statistical analyses were performed using an ANOVA test for numerical variables and a chi-squared test for categorical variables. A total of 322 patients underwent 588 NSM, of which 83% percent were bilateral and 17% were unilateral. Thirty-two percent of NSM were performed for breast cancer prophylaxis. A total of 399 (67.9%) NSM were performed for malignancy, including Stage 0 (26.5%), I (44.4%), II (25.2%) and III (3.8%) breast cancer. The overall rate of wound complications was 18.6 %; >90% of patients with a complication required at least one additional surgical intervention. Patients using tobacco at the time of surgery had increased rates of complication (37.5%|16.3%, p<0.001), as were those who required adjuvant radiation therapy after NSM (31.4%|17.4%, p=0.014). Patients with lymph node involvement and larger tumor size had higher rates of complications (31.3%|17.2%, p=0.016; p=0.033). Patients undergoing circumareolar incisions had a higher rate of complications than lateral, inframammary fold, or curvilinear incisions (43.5%|17.4%|17.4%|14.3%, p=0.018). Six (1%) local chest wall recurrences occurred during the follow-up period. Four patients (1.2%) suffered a distant recurrence during the follow-up period. Performance of NSM at our institution has increased dramatically during the study period and the majority of procedures are now performed in patients with malignancy. The oncologic safety is confirmed by the low locoregional recurrence rate. Tobacco use and adjuvant radiation therapy remain the most significant risk factors for complications, highlighting the need for careful patient selection and patient counseling regarding modifiable risk factors and expected outcomes.

P37

Tracking the Fate of Individual Disseminated Tumor Cells to Determine the Role of Premetastatic Conditioning A.H. Coste,[1]* L. Boriello,[2] Y. Wang,[3] M. Oktay,[4] J.S. Condeelis,[5] D. Entenberg.[3]
1. Department of Surgery, Department of Anatomy and Structural Biology, and Gruss-Lipper Biophotonics Center at Albert Einstein College of Medicine/Montefiore, Bronx, NY; 2. Department of Anatomy and Structural Biology, and Gruss-Lipper Biophotonics Center at Albert Einstein College of Medicine/Montefiore, Bronx, NY; 3. Department of Anatomy and Structural Biology, Gruss-Lipper Biophotonics Center, and Integrated Imaging Program at Albert Einstein College of Medicine/Montefiore, Bronx, NY; 4. Department of Anatomy and Structural Biology, Gruss-Lipper Biophotonics Center, Integrated Imaging Program and Department of Pathology at Albert Einstein College of Medicine/Montefiore, Bronx, NY; 5. Department of Surgery, Department of Anatomy and Structural Biology, Gruss-Lipper Biophotonics Center and Integrated Imaging Program at Albert Einstein College of Medicine/Montefiore, Bronx, NY.

For the last 100 years, the process of metastasis has been studied using the experimental metastasis (EM) assay: tail vein injection of tumor cells followed by histological analysis of the lung weeks later. While providing some insights, EM is limited in that it is unable to follow the fate of the individual tumor cells, nor can it track spontaneously metastasizing (SM) tumor cells. Recent technological advancements have allowed direct visualization of this process at the secondary site in vivo by surgically implanting an optical imaging window into the chest wall of a mousen, named the Window for High Resolution Imaging of the Lung (WHRIL). Using the WHRIL, we investigated the fate of disseminated tumor cells to determine whether the lung is altered by the presence of the primary tumor, or whether the tumor cells themselves are educated by their residency in the primary tumor. Real-time images of tumor cell dissemination were captured using the WHRIL in both EM and SM models. Metastatic potential was analyzed by comparing the percentage of tumor cells survival in the lung over time, the time-to-extravasation and the percent of cells that develop into metastases. In addition, the primary tumor and lung tissue were stained for several factors, including dormancy, stemness, and expression of proteins linked with increased invasiveness to determine role these factors play in the progression of metastasis. SM tumor cells show a ten-fold higher rate of survival in the lung and three times greater efficiency in forming metastases compared to EM cells. Comparison of survival times for intravascular and extravascular tumor cells indicates that the ability to extravasate is a critical step for disseminated tumor cell survival. Of those tumor cells that do survive, they are significantly more dormant in the case of spontaneous dissemination. These results indicate that EM alone does not accurately reflect the true clinical process and, that either preconditioning of spontaneously disseminating tumor cells in the primary tumor, or education of the recipient lung tissue by the primary tumor has a significant influence on the survival and growth of disseminated cells.

P38

Impact of Axillary Dissection Among Sentinel Node Positive Mastectomy Patients J. Sun,[1]* W. Sun,[1] B. Mathias,[1] W. Fulp,[2] J. Zhou,[2] J.V. Kiluk,[1] C. Laronga,[1] M.C. Lee.[1] *1. Moffitt Cancer Center, Department of Breast Oncology, Tampa, FL; 2. Moffitt Cancer Center, Department of Biostatistics and Bioinformatics, Tampa, FL.*

Axillary lymph node dissection (ALND) is the standard operation for axillary lymph node positive breast cancer. The 2010 ACOSOG Z0011 trial supports omission of ALND after breast conserving surgery with a positive sentinel lymph node biopsy (SLN). We hypothesize that ALND also does not impact outcome in women with clinically node-negative (N_0), pathologically SLN-positive breast cancer undergoing mastectomy. We performed a single institution, retrospective review of SLN-positive invasive primary breast cancer patients diagnosed from 1999-2018. Pathology, treatment, recurrence and survival data were collected. Patients with SLN alone were compared to those receiving SLN with ALND. Patients that received neoadjuvant therapy or had prior diagnosis of breast cancer were excluded. Statistical analyses were performed using Kruskal Wallis, Chi-square, and Fisher's exact tests. Recurrence and overall survival (OS) were analyzed using Cox Proportional Hazard models and Log-rank test. Of our cohort of 340 clinically N_0, SLN-positive breast cancer patients receiving mastectomy; 60% had ALND (n=204), 40% (n=136) had SLN alone. Median age at diagnosis was 54 (range 21-85); 92.6% patients were Caucasian with median BMI 26.4 kg/m^2 (range 16.7-61.1 kg/m^2). Median SLN sampled was 3 (IQR 2-4), with median number of positive nodes of 1 (IQR 1-2). Median follow-up was 4.24 years (range 0.03-18.2 years). Patients with ALND were younger with a median age of 52.4 compared to 57.5 for the patients that did not have ALND. (p=0.003). The rate of ALND increased by stage; 24.4% of Stage 1, 57.9% of Stage 2 and 87.3% of Stage 3 (p<0.0001). The rate of ALND increased for ER negative (78.4%, p=0.006) and PR negative patients (74.3%, p=0.007); no association between Her2 status and ALND. Rate of ALND decreased after 2010. There was no association between ALND and OS (p=0.22; Fig 1) or local/distant recurrence. Completion of adjuvant radiation was associated with improved OS (HR=0.42, p=0.02), but not local/distant recurrence. In patients with clinically node-negative, SLN-positive breast cancer, ALND does not prevent recurrence or improve OS. Completion of post-mastectomy radiation was associated with improved OS.

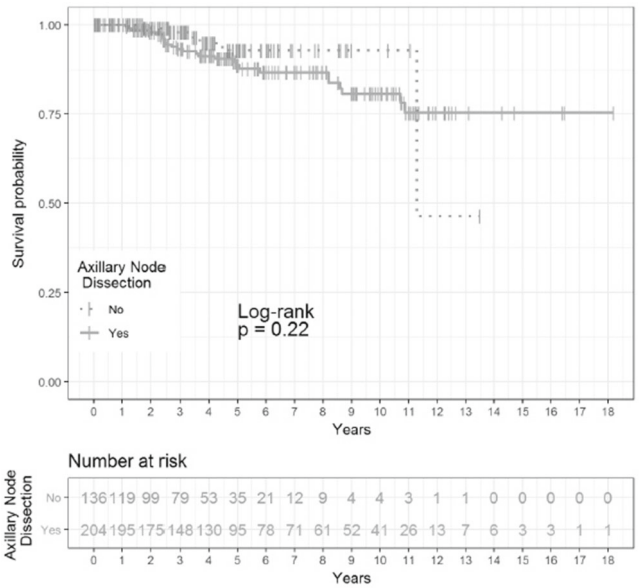


Figure 1: Kaplan-Meier curve for overall survival by ALND

P39

Radiomics Based on Baseline DCE-MRI is Predictive of Tumor Pathological Complete Response to Neoadjuvant Systemic Therapy in Breast Cancer Patients R. Granzier,[3] A. Ibrahim,[3] H. Woodruff,[3] T. van Nijnatten,[1] S. Samiei,[3] M. de Boer,[1] E. Heuts,[1] F. Hulsmans,[2] P. Lambin,[3] M. Smidt,[1]* M. Lobbes.[1] *1. Maastricht University Medical Center+, Maastricht, Netherlands; 2. Zuyderland, Sittard-Geleen, Netherlands; 3. Maastricht University, Maastricht, Netherlands.*

Purpose To evaluate the applicability of radiomics models based on baseline (i.e., prior to treatment) dynamic contrast-enhanced MRI (DCE-MRI) for the prediction of pathologic complete response (pCR) of breast tumors to neoadjuvant chemo(targeted)therapy (NCT) in breast cancer patients. Methods Two independent cohorts from 2 centers were used to train and validate a radiomics-based classification model. The training cohort included 102 patients with 129 breast tumors. The external cohort (120 patients, 125 breast tumors) was split into testing (n=63) and validation cohorts (n=62). All patients received NCT and underwent a baseline DCE-MRI scan. All tumors were delineated manually by 3 individuals on MRIs acquired 2 minutes after contrast injection. Features were extracted using the validated OncoRadiomics research software. Overall concordance correlation coefficient was used to assess feature stability among observers. Feature ranking and selection of stable features was achieved via support-vector machine recursive feature elimination with correlation bias reduction. Random forest binary classification algorithms were generated using the training cohort and hyper-parameters tuned on training and test cohorts. The area under the receiving operator characteristics curve (AUC) was used to independently assess model performance on the external validation cohort. Results 30.2% of tumors in the training cohort achieved breast pCR while 23.8% and 32.2% of tumors achieved pCR in the test and validation cohorts

respectively. 1322 features were extracted, of which 1094 features were stable. The 20 top-ranked features were selected to build the model for predicting pCR, of which sixteen were wavelet-filtered features. The model performed better than chance with an AUC of 0.68 (range 0.53-0.82) in both the training cohort and the external validation. Conclusion Our results demonstrate that baseline DCE-MRI radiomics analysis on pretreatment MR exams can be used to predict tumor pCR after NCT. Further studies with larger sample sizes are needed to confirm these results and to expand the model with patient- and tumor characteristics.

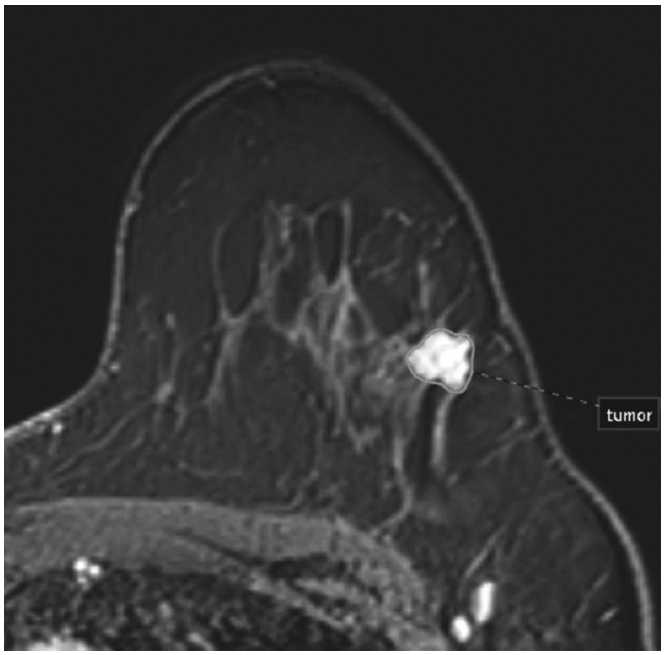


Figure 1. Manual delineation of an invasive breast tumor in the left breast (pink margin) on a 2 minute post-contrast DCE-MRI.

P40

The Growth Factor Receptor Bound Protein 7 (GRB7) Predicted Non-Sentinel Lymph Nodes (NSLN) Metastasis in Sentinel Lymph Node (SLN)-Positive Breast Cancer Patients E. Goldin,[1]* C. Benna,[2] S. Pasquali,[3] H. Monticelli,[2] S. Rajendran,[2] A. Marchet,[2] D. Nitti,[2] S. Mocellin.[4] *1. Surgical department, San Bortolo Hospital Vicenza, General Surgery, Padova, Italy; 2. Department of Surgery Oncology and Gastroenterology, University of Padova, Padua, Italy; 3. Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; 4. Surgical Oncology Unit, Istituto Oncologico Veneto (IOV-IRCCS), Padua, Italy.*

Aims The aim of this study was to investigate a panel of genes expressed in primary breast cancer for predicting NSNL metastasis in SLN-positive patients Materials and Methods This was a retrospective analysis conducted on a prospectively collected database and associated patient tumour samples. Using the resources of the institutional Biobank, we firstly tested 88 genes in 24 frozen tissue samples from patients with positive SNL who underwent axillary lymph node dissection, of them 12 patients had negative NSLN and 12 with positive NSLN (testing group). Genes significantly associated with NSLN metastasis were tested, with qRT-PCR, in 79 frozen tissue samples from breast cancer patients who underwent SLN biopsy, thus including patients with negative SLN (validation group). The associations between gene expression value, NSNL status and other characteristics were analyzed with chi-square test and Student's T-test. Univariate and multivariable logistic regression analysis was performed. Results 5 genes were associated with NSLN metastasis (THBS1, IGF1, ERB2, GRB7, MGMT) in the testing group. These genes were analyzed in the validation group, where GRB7 level was differently expressed between patients with a positive SNL biopsy and negative NSNL (mean level:3.14) and those patients with both SLN and NSLN metastasis (mean level:6.76, p=0.014). Vascular invasion and frozen section analysis were predictive factors of NSNLs status on univariate logistic regression analysis (p<0.05) among clinic-pathological features. Multivariate logistic regression analysis confirmed that GRB7 was an independent predictive factor of NSNLs (p=0.017) also when adjusted for clinic-pathological predictors together with frozen section analysis (p=0.047). The receiver operating characteristic (ROC) curves for this model suggested high accuracy for predicting NSLN (AUC=0,77). Conclusion This study suggested the association between expression level of GRB7, a gene encoding a growth factor receptor-binding protein that interacts with epidermal growth factor receptor leading to cell migration, in primary breast cancer and NSLN metastasis.

Multivariate logistic regression

	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf. Interval]
grb7	1.116578	.0516715	2.38	0.017	1.01976 1.222587
frozen section	8.664052	9.41185	1.99	0.047	1.03051 72.84338
vascular invasion	2.560662	1.467849	1.64	0.101	.8325644 7.875657

P41

Sentinel Lymph Node Positivity in Patients with Mastectomies for Ductal Carcinoma In Situ A. Price,* F. Schnabel, J. Chun, E. Kaplowitz, J. Goodgal, A. Guth, F. Darvishian. *Surgery, NYU Langone Health, New York, NY.*

Introduction Sentinel lymph node biopsy (SNLB) should be strongly considered, as per NCCN guidelines, for patients who are having a mastectomy for a preoperative diagnosis of ductal carcinoma in situ (DCIS). This practice is supported by the finding that invasive cancer may not be conclusively ruled out by preoperative core biopsy, and the inability to map sentinel nodes after a mastectomy procedure. The purpose of this study was to examine the clinical and pathologic factors, rates of upstaging on final pathology, and SLN positivity for patients undergoing mastectomy with a preoperative diagnosis of DCIS on preoperative core biopsy. Methods The Institutional Breast Cancer Database was queried for patients with a preoperative diagnosis of pure DCIS who underwent mastectomy procedures from 2010-2018. Patients were divided into two groups according to their final diagnosis (DCIS or invasive cancer). Variables of interest included age, method of presentation, tumor characteristics, and outcomes. Statistical analyses included Pearson's Chi Square and multivariate analyses. Results Out of 3145 women with breast cancer, 172 (5%) had pure DCIS on preoperative core biopsy and underwent total mastectomy with SLNB. The median age was 52 years with a median follow up of 5.2 years. Of 120 patients with no change in diagnosis, there were no cases of positive sentinel nodes. 52 patients had invasive carcinoma identified in their mastectomy specimens. Of these, 7 (13%) had at least 1 positive sentinel node. Factors associated with upstaging to invasive cancer included younger age (p=0.039), presentation with a palpable finding (p<0.0001), and a mass on pre-op imaging (p=0.021). (Table) Conclusion Our data suggest that SLNB may be omitted in a subset of patients undergoing mastectomy procedures who are asymptomatic and have limited disease on preoperative evaluation as the risk of upstaging is extremely low. However, patients who present with clinical findings and a mass on pre-op imaging, have a meaningful risk of upstaging to invasive cancer, and SLNB remains an important part of their surgical treatment.

Clinical Characteristics of Patients by Final Diagnosis

VARIABLES	DCIS on Mastectomy N=120 (70%)	Invasive Cancer on Mastectomy N=52 (30%)	P-value
AGE AT DIAGNOSIS			0.039
Median (range)	54 years (29-80)	49 years (27-73)	
PALPABILITY			p<0.0001
Palpable	12 (10%)	20 (39%)	
Non-palpable	104 (90%)	31 (61%)	
METHOD OF PRESENTATION			0.005
Breast exam	15 (13%)	18 (36%)	
Mammogram	95 (79%)	31 (62%)	
Ultrasound	2 (2%)	0 (0%)	
MRI	8 (7%)	1 (2%)	

P42

30-Day Postoperative Morbidity in Patients with Breast Cancer Following Neoadjuvant Chemotherapy M. Srour,* M. Lee, S. Wallcott-Sapp, S. Kim, F. Amersi, A.E. Giuliano, A. Chung. *Surgical Oncology, Cedars-Sinai Medical Center, Beverly Hills, CA.*

Introduction: The rate of bilateral mastectomy for treatment of breast cancer is rising even among patients treated with neoadjuvant chemotherapy (NAC). The purpose of this study was to compare post-operative complication rates among patients treated with partial mastectomy (PM), unilateral mastectomy (UM), and bilateral mastectomy (BM) after NAC. Methods: 398 patients with breast cancer who had NAC from 2008 to 2016 were identified from a prospectively maintained database. Complications for each type of breast operation were examined. The primary outcome was 30-day post-operative morbidity. Results: 125 patients (31%) underwent PM, 107 patients (27%) UM, and 166 (42%) BM. Compared with the UM group, patients who had a BM had a higher rate of implant or tissue expander reconstruction (86.1% vs 50.5%) and a lower rate of autologous tissue reconstruction (2.5% vs 6.0%). The median age in the BM group was significantly younger than the PM or UM groups (45 vs. 54 vs. 52, p<0.001). There was no significant difference among the 3 groups with respect to histology (ductal: 96% PM, 88.8% UM, 92.6% BM, p=0.161). Groups were similar with respect to estrogen receptor positivity (overall 58.5%, p=0.331) and triple negative biomarker status (overall 23.9%, p=0.559). The PM group had a higher rate of Her2 positive disease (n=58, 47.5%, p=0.012). Patients who underwent PM had a lower clinical T Stage (p=<0.001), fewer axillary lymph node dissections (n=32, 25.6%, p=<0.001), and a higher rate of pathologic complete response (n=48, 38.4%, p=0.037) compared with patients who underwent mastectomies. Overall, 52 patients (13.8%) had a complication within the 30 day post-operative period. 30-day complication rates were significantly higher in the BM group compared to the PM and UM groups: 6.4% (n=8) for PM, 12.2% (n=13) for UM, and 18.7% for BM, (p=0.008). There was increased wound dehiscence, delayed healing, and skin necrosis in the BM group compared with the PM group (n=7 vs. 0, p=0.032) [Table 1]. Conclusion: Bilateral mastectomy is associated with higher rates of 30-day morbidity compared to partial and unilateral mastectomy in patients who received NAC.

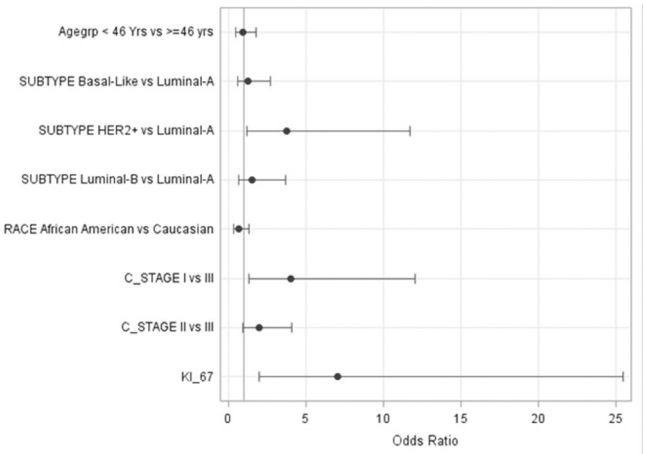
Table 1. 30-day Postoperative Complications by Type of Operation

Variable	All patients (N=398)	Partial Mastectomy (N=125)	Unilateral Mastectomy (N=107)	Bilateral Mastectomy (N=166)	P-value
30-day complication	52 (13.1)	8 (6.4)	13 (12.2)	31 (18.7)	0.008
Type of 30-day complication					0.184
Axillary seroma aspirated	4 (7.7)	3 (37.5)	0 (0)	1 (3.2)	0.249
Breast seroma aspirated	5 (9.6)	0 (0)	3 (23.1)	2 (6.5)	0.182
Hematoma with intervention	2 (3.9)	0 (0)	0 (0)	2 (6.5)	0.340
Infection	26 (50.0)	5 (62.5)	7 (53.9)	14 (45.2)	0.235
Wound dehiscence, delayed healing, and skin necrosis	9 (17.3)	0 (0)	2 (15.4)	7 (22.6)	0.032
Deep vein thrombosis	1 (1.9)	0 (0)	0 (0)	1 (3.2)	1.000
Medical complication	5 (9.6)	0 (0)	1 (7.7)	4 (12.9)	0.195

P43

Biological Predictors of Pathological Complete Response in Breast Cancer for Surgical Planning A. Johnson,[1]* M. Mubasher,[2] R. Rollins,[1] c. ramirez,[1] J. McKnight,[1] H. Pabbathi,[1] D. Hansra,[1] M. Ninan,[1] R. Alvarez.[1] *1. Breast Surgical Oncology, Cancer Treatment Centers of America, Newnan, Ga; 2. Morehouse School of Medicine, Atlanta, GA.*

Background: Pathological Complete response (pCR) in breast cancer has been associated with a better long-term outcome. pCR has been demonstrated in 20-61% of breast cancer patients undergoing neoadjuvant chemotherapy. This study was designed to identify clinical and tumor factors that will assist surgeons in predicting a pCR in patients undergoing neoadjuvant chemotherapy for breast cancer. Methods: The study included patients treated with neoadjuvant chemotherapy between 2013 and 2017. A retrospective analyses of our database was used to compare those with and without a pCR in terms of frequencies and proportions as well as using the logistic regression to model the likelihood of having a pCR classification as a function of age, cancer subtypes, marker proliferation noted as the Ki 67 score, race and stage. pCR was defined in our study as having the absence of invasive tumor in the breast as well as the axilla. Results: A total of 393 patients were included in this study. 34.7% of patients <46 years old (n=143) vs 63.0% of patients >= 46 years old (n=250) demonstrated a pCR. Tumor subtypes demonstrating a pCR included basal like 42.9% (n=136), her 2 neu + 13.3% (n=34), luminal A 23.5% (n=150), and luminal B 20.4% (n= 73). 60.2% (n=248) of African American patients demonstrated a pCR vs 39.8% (n=145) of Caucasian patients. The median Ki 67 score pCR vs non-pCR was 70.0% vs 52.5%. A pCR was demonstrated in 13.3% stage I, 58.2% of stage II and 28.6% of stage III. Conclusion: In this population, age nor race were found to be statistically significant predictors of pCR. The high risk tumor subtype her 2 neu +, the marker proliferation Ki-67 score and notably stage III disease was a predictor of pCR. Certain biological tumor markers can assist surgeons in predicting a pCR and may assist with surgical planning in the management of the axilla.



Odds Ration with 95% Confidence Limits

P44

Patterns of Radiographic Follow-up Using NCCN Guidelines for Non-BRCA1/2 Mutations: A Single Institutional Review L. Hudson,* N. Gower, S. Lenarcic, S. Trufan, R.L. White, Jr. *Levine Cancer Institute, Charlotte, NC.*

Analysis of BRCA1/2 genes has been available since 1996 and multigene panel sequencing is increasingly available. The National Comprehensive Cancer Network (NCCN) developed clinical practice guidelines for germline mutations in high penetrant genes, such as TP53 and PTEN, and in moderate penetrant genes, such as CHEK2, ATM and PALB2. For genetic mutations other than BRCA1/2, however, we lack an understanding of patterns of radiographic follow-up. We assessed whether patients who receive genetic counseling for mutations other than BRCA1/2 receive recommended radiographic follow-up. A retrospective review was performed. 7667 patients received genetic counseling at Levine Cancer Institute between January 1, 2007 through December 31, 2017. Patients with negative results, variants of uncertain significance, BRCA1/2 mutations, a previous diagnosis of breast cancer, and mutations not associated with breast cancer were excluded. Patients with genetic mutations in ATM, CDH1, CHEK2, NBN, PALB2, PTEN, STK11 and TP53 genes were included. Of 87 patients with these mutations, 25 were men and 20 were women too young for recommended radiographic follow up. Records of 42 remaining patients, with mutations in ATM, CDH1, CHEK2, NBN, PALB2, PTEN, STK11 and TP53, were reviewed to assess adherence to recommendations for annual mammography and consideration of MRI according to NCCN guidelines. Twenty of 42 (48%) patients did not have radiographic follow up. Twelve of 42 (29%) patients only received a mammogram. Ten of 42 (23%) patients received both mammography and MRI. Three of 42 (7%) patients were diagnosed with DCIS or invasive breast cancer within three years of genetic testing. Two of these patients underwent mammography and MRI. For patients with genetic mutations other than BRCA1/2, data from a single institution suggest variation in adherence to recommendations for radiographic follow-up according to NCCN guidelines. More education for clinicians and patients may improve adherence with current practice guidelines. Improved radiographic follow-up after genetic counseling may be an opportunity to enhance patient care.

Radiographic follow-up for patients with non-BRCA1/2 mutations

Mutation	Recommendations	Number of women included	Annual mammogram	Annual MRI	Adherence to both
ATM (38-69% lifetime risk)	Women ≥ 40	13	4	2	2/13 (15%)
CDH1 (39-52% lifetime risk)	Women ≥ 30	2	0	0	0/2 (0%)
CHEK2 (28-37% lifetime risk)	Women ≥ 40	15	10	5	5/15 (33%)
NBN	Women ≥ 40	4	2	0	0/4 (0%)
PALB2 (14-35% lifetime risk)	Women ≥ 30	5	4	2	2/5 (40%)
PTEN (high penetrance)	Women ≥ 30	2	1	0	0/2 (0%)
STK11 (8-45 % lifetime risk)	Women ≥ 25	1	1	1	1/1 (100%)
TP53 (90-100% lifetime risk)	Women ≥ 30	0	n/a	n/a	n/a
				Total adherence to mammogram and MRI	10/42 (23%)

P45

Adherence to NCCN Guidelines for Genetic Testing in Breast Cancer Patients: Who are We Missing? J. Alberty-Oller, S. Weltz, A. Santos, k. pisapati, A. Miller, M. Ru, C. Weltz, H. Schmidt, E. Port.* *Dubin Breast Center, Mount Sinai Medical Center, New York, NY.*

Background: Genetic predisposition accounts for 5-10% of all breast cancers (BC) diagnosed. NCCN guidelines help providers identify appropriate candidates for counseling and testing. Concerns about underutilization of genetic testing have spurred interest in broader population testing to identify mutation carriers eligible for prevention and high-risk screening strategies as well as potentially guiding surgery in those with BC. We evaluated surgeon adherence to NCCN guidelines and study patterns of testing in newly diagnosed BC patients. Methods: 397 patients were identified with newly diagnosed BC treated at our institution between 2016-2017 with no prior genetic testing. Eligibility for genetic testing based on NCCN criteria, referral, and patient compliance were recorded. Results: 212/397 (53%) met NCCN testing criteria. Most common criterion met was family history-based (diagnosis at any age with 2+ relatives with BC at any age). We identified 11 (3%) patients with a BRCA1 or BRCA2 mutation, as well as 5 (1%) patients with pathogenic mutations in other high-risk genes. 59/212 (28%) patients went untested despite meeting one or more criteria. 14/59 (24%) were referred but did not comply. Most common criteria among missed patients were family history-based (2+ relatives with breast cancer any age, 1+ relative with breast cancer younger than 50, and 1+ relative with ovarian cancer). Age >50 years old and non-Ashkenazi Jewish descent were predictive of missed referral (p<0.01). 7 patients chose to undergo testing despite not meeting any NCCN criteria, and 1 BRCA2 mutation was identified. Conclusions: Our data highlight the underutilization of genetic testing due to both patient and physician factors. Even in the setting of a full service breast center with readily available genetic counseling/testing for BC patients, there is a substantial miss rate for identifying patients eligible for testing, most likely related to assessment of complex family history and patient compliance. In addition, NCCN guidelines will exclude some mutation carriers. Broader population testing should be considered, and higher compliance rates with patients referred should be sought.

P46

Contralateral Prophylactic Mastectomy Use After Neoadjuvant Chemotherapy N. Christian,* E. Zabor, M. Stempel, M. Cassidy, M. Morrow, M. Gemignani. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Background Neoadjuvant chemotherapy (NAC) for breast cancer is known to increase rates of breast conservation (BCT), but many women opt for mastectomy with contralateral prophylactic mastectomy (CPM). Here we evaluate factors associated with CPM use in patients undergoing mastectomy after NAC. Methods A prospective database review identified patients with clinical stage I-III, unilateral invasive breast cancer receiving NAC and undergoing unilateral (UM) or bilateral (CPM) mastectomy from 9/2013-12/2017. Clinical/pathologic characteristics, imaging and presence of contraindications to BCT post-NAC were compared between patients undergoing UM and CPM, with subset analysis of BCT candidates. Multivariable logistic regression was used to adjust for potential confounders. Results Of 569 NAC patients having mastectomy, 297(52%) had UM and 272(48%) had CPM. Rates of UM and CPM were similar across the study period(p=0.73). Table 1 compares characteristics between groups. On univariable analysis, younger age, BRCA+, more favorable disease as evidenced by lower pre NAC clinical stage, pCR rate, and extent of axillary surgery were associated with CPM(all p<0.01). Favorable post-NAC clinical factors of no residual palpable disease, clinically negative nodes, complete response on breast imaging, and no post-NAC contraindication to BCT were also associated with CPM(all p<0.01). On multivariable analysis, only young age(OR .93, 95%CI 0.91-0.95), lower pre NAC stage(0.51, 0.34-0.77) and no contraindication to BCT(3.07, 1.99-4.75) were significantly associated with CPM. On subset analysis of 203(35%) patients who had no contraindication to BCT post NAC, 145(71%) underwent CPM. BRCA+, family history, and patient preference were associated with CPM on univariable analysis(p<0.001). Conclusions In our study, CPM was performed in 48% of patients undergoing mastectomy after NAC; younger patients with earlier-stage cancers were more likely to undergo CPM. While increased use of CPM in patients with more favorable disease is medically appropriate, our findings indicate lost opportunity for use of less morbid BCT in this group. Further study into patient decision making factors is necessary to understand this trend.

Table 1. Patient and disease characteristics by mastectomy group. P-values are from the Wilcoxon rank-sum test for continuous variables, and Fisher's exact test for categorical variables.

Variable	Overall (n = 569)	unilateral mastectomy(UM) (n = 297)	bilateral mastectomy (CPM) (n = 272)	p-value
Age	48 (40, 57)	53 (45, 63)	44 (37, 50.2)	<.001
Tumor stage				<.001
T1/Tis/Tx	52	8 (15.4)	44 (84.6)	
T2	273	127 (46.5)	146 (53.5)	
T3	159	91 (57.2)	68 (42.8)	
T4	85	71 (83.5)	14 (16.5)	
Overall stage				<.001
1	18	1 (5.6)	17 (94.4)	
2	320	141 (44.1)	179 (55.9)	
3	231	155 (67.1)	76 (32.9)	
Tumor subtype				<.001
ER-, PR-, HER2-	142	56 (39.4)	86 (60.6)	
ER-, PR-, HER2+	85	54 (63.5)	31 (36.5)	
ER/PR+, HER2-	211	125 (59.2)	86 (40.8)	
ER/PR+, HER2+	131	62 (47.3)	69 (52.7)	
BRCA status				<.001
negative	250	105 (42)	145 (58)	
positive	56	2 (3.6)	54 (96.4)	
vus	14	7 (50)	7 (50)	
Not tested	249	183 (73.5)	66 (26.5)	
pCR (invasive)				0.006
no	378	213 (56.3)	165 (43.7)	
yes	191	84 (44)	107 (56)	
Axillary Surgery				<.001
Sentinel lymph node alone	268	104 (38.8)	164 (61.2)	
Completion ALND	301	193 (64.1)	108 (35.9)	
No contraindication to BCT Post-NAC				<.001
borderline	2	2 (100)	0 (0)	
no	364	237 (65.1)	127 (34.9)	
yes	203	58 (28.6)	145 (71.4)	
Residual palpable disease				<.001
no	379	173 (45.6)	206 (54.4)	
yes	190	124 (65.3)	66 (34.7)	
Clinical axillary nodal status				0.005
negative	517	260 (50.3)	257 (49.7)	
positive	52	37 (71.2)	15 (28.8)	
Persistent abnormality on any imaging (Mammo and/or MRI) post NAC				<.001
no	75	25 (33.3)	50 (66.7)	
yes	332	199 (59.9)	133 (40.1)	

Numbers are median (interquartile range) for continuous variables and number (percent) for categorical variables. ER, estrogen receptor; PR, progesterone receptor; vus, variation of unknown significance; pCR, pathologic complete response; ALND, axillary lymph node dissection; BCT, breast-conserving therapy; NAC, neoadjuvant chemotherapy

P47

Impact of Age on Locoregional Recurrence after Mastectomy for Ductal Carcinoma In Situ +/- Microinvasion A. Mamtani,[1]* F. Nakhlis,[2] S. Downs-Canner,[1] E. Zabor,[1] M. Stempel,[1] M. Morrow,[1] T.A. King,[2] K. Van Zee.[1] *1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Brigham and Women's Hospital, Boston, MA.*

Background Locoregional recurrence (LRR) risk after breast-conserving surgery (BCS) for ductal carcinoma in situ (DCIS) is increased in young women. While LRR after mastectomy for DCIS+/-microinvasion (MI) is uncommon, we sought to examine the impact of age on LRR. Methods We identified consecutive patients with DCIS+/-MI treated with mastectomy from 1995-2017 at two large cancer centers. LRR was defined as any recurrence at the ipsilateral chest wall or regional lymph nodes. The association of age and LRR was assessed. Results 3063 cases were identified; 431 (14%) had DCIS+MI. Median age was 49 yrs (range 22-83). Median follow-up was 76 months; 33 LRR were observed: 32 (97%) of LRR were invasive; 22 (67%) occurred in the chest wall, 8 (24%) in regional lymph nodes, and 3 (9%) in both. Overall, the cumulative 10-year incidence of LRR was 1.4%. Of 33 LRR, characteristics of the initial DCIS+/-MI were: 31 (94%) <50, 25 (76%) high nuclear grade, 13 (39%) DCIS+MI, 2 (6%) close margins. Women <40 more often had close/positive margins (p=0.007), high nuclear grade (p<0.001), and DCIS+MI (p=0.02). Age<50, high nuclear grade, and DCIS+MI (all p<0.001) were associated with LRR; margin status was not (p=0.2). Adjusting for high nuclear grade (HR 3.4, 95%CI 1.4-7.9, p=0.005) and DCIS+MI (HR 3.3, 95%CI 1.6-6.7, p=0.001) on multivariable analysis, age<50 (HR 14, 95%CI 3.4-59, p<0.001) was associated with LRR. Compared to women ≥50, the youngest women (<40) had the highest risk of LRR (HR 26, 95%CI 5.9-117) with women 40-49 having intermediate risk (HR 11, 95%CI 2.6-48). Cumulative 10-yr incidence of LRR was 4.2% for women <40, 2.1% for 40-49, 0.2% for ≥50 (Fig). Overall, the 10-yr distant disease (DD) rate was 1% (95%CI 0.6-1.5%). Women <40 had a higher 10-year DD rate of 2% as compared to ages 40-49 (0.8%) and ≥50 (1%) (p=0.008). Grade, DCIS+MI, and margin status were not associated with DD. Conclusions LRR after mastectomy for DCIS+/-MI is uncommon, but is significantly more frequent among women <50, especially in those <40. Yet, the 10-year LRR rate in this youngest group remains low at 4.2%. Young age is a risk factor for LRR after BCS or mastectomy.

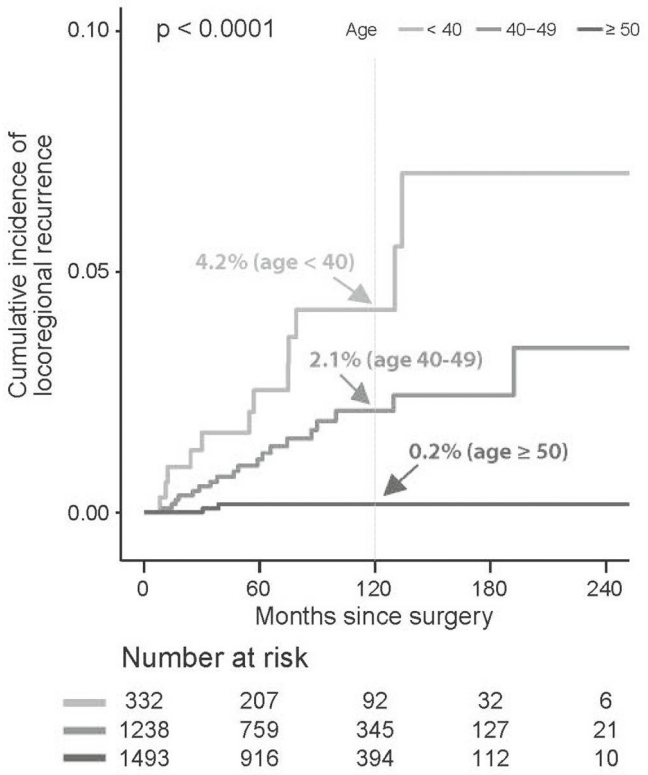
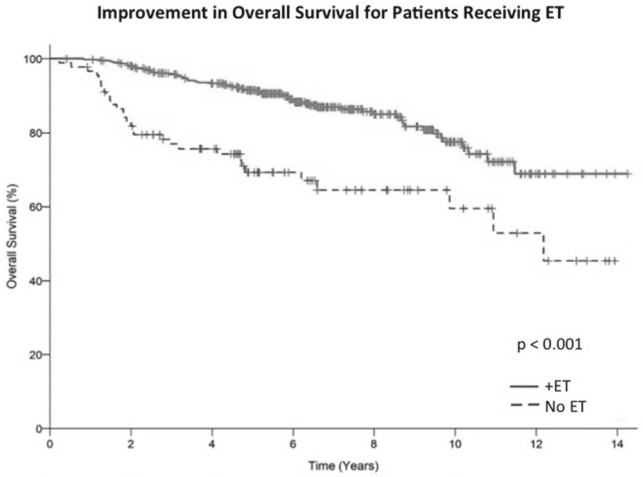


Fig: Locoregional recurrence, by age at surgery (age <40, 40-49, or ≥50 years)

P48

Administration of Adjuvant Endocrine Therapy is Associated with Improved Disease-Free and Overall Survival in Elderly Breast Cancer Patients J.G. Rand,* J. Johnson, J. Bao, S. Kim, R. Basho, F. Amersi, A.E. Giuliano, A. Chung. *Cedars Sinai Medical Center, Los Angeles, CA.*

Introduction: There is controversy regarding whether elderly patients with early invasive breast cancer gain a survival benefit from endocrine therapy (ET). Methods: A review of a prospectively maintained database identified 483 women ≥ 70 years old who underwent breast-conserving therapy for stage I-III estrogen receptor positive tumors at a single institution from 2004 to 2013. We compared clinicopathologic characteristics, locoregional recurrence (LRR), disease-free survival (DFS), overall survival (OS) and breast cancer specific survival (BCSS) for those who received ET (n=393) versus those who did not (n=90). Results: Compared to those who did not receive ET, patients receiving ET were younger (median age 76 vs 78 years, p<0.01) and had larger tumors (median size 15 vs 12.5mm, p<0.02). Patients receiving ET were also more likely to undergo sentinel lymph node (LN) biopsy (84 vs 68%, p<0.01), have positive LNs (26 vs 10%, p<0.01) and receive radiation (XRT, 76 vs 43%, p<0.010). There were no significant differences between groups in American Society of Anesthesiologist (ASA) score, tumor grade, HER2 status or receipt of adjuvant chemotherapy. With a median follow-up of 79.3 months, receipt of ET was associated with improved LRR on univariable analysis (HR 0.25; 95% CI 0.09-0.70; p<0.01); however, after adjusting for grade and XRT this was not statistically significant on multivariable analysis (HR 0.38; 95% CI 0.13-1.08; p = 0.069). ET was associated with improved DFS (HR 0.42; 95% CI 0.28-0.64; p<0.01), independent of age, LN status, tumor grade and XRT. ET was also associated with improved OS (HR 0.44; 95% CI 0.25-0.77; p<0.01), after adjusting for ASA score, age, LN status, tumor grade and XRT. There was no significant difference in BCSS between groups (HR 0.59; 95% CI 0.16-2.16; p=0.43). Conclusions: ET was associated with significant improvements in DFS and OS, regardless of clinicopathological features and receipt of other adjuvant therapies. However, receipt of ET did not impact BCSS. Larger cohorts of patients and longer follow up can help clarify the inconsistency between these clinical outcomes.



P49

Evolving Strategies in Axillary Management in Breast Cancer: The Use of a New Magnetic Localizing Seed J.M. Wong,* H. Greenwood, R. Mukhtar, C. Ewing, L. Esserman, E. Price, M. Alvarado. *University of California, San Francisco, San Francisco, CA.*

Background: Axillary management in breast cancer is moving away from complete lymph node dissections due to the associated morbidity. In patients with node positive disease, ensuring excision of the positive node remains a concern, especially with the use of neoadjuvant therapy. We describe a novel use of a magnetic localizing seed, Magseed (Endomag) and its efficacy in localizing previously biopsied nodes for excision. Methods: We used ultrasound guidance to place 24 Magseeds in previously biopsied axillary nodes in 23 patients between January 2017 and August 2018; 18 (75%) also had clip

placement. Magseeds were placed within 1 week of surgery and the Senti-Mag probe was used intra-operatively to guide node identification and verify removal of the Magseed. All sentinel lymph node biopsies were done with Lymphoseek, with the addition of blue dye in 33%. Results: Magseed was used for 20 sentinel lymph node biopsies, 3 targeted lymph node excisions, and 1 axillary lymph node dissection. There were no complications related to Magseed placement. All Magseeds were identified at surgical excision, 21 (87%) were also confirmed with specimen radiograph. All of the clipped nodes were retrieved; 16 were identified with specimen radiograph and 2 with direct visualization of the clip and Magseed. Ten (42%) of Magseed localized nodes were negative on surgical pathology following neoadjuvant therapy, with 4 patients (16%) having pathologic complete response. In 15 patients (75%), the Magseed localized lymph node was also the sentinel lymph node. Conclusions: Magseed is a novel and feasible system for localizing previously positive lymph nodes after neoadjuvant therapy and can be used together with a radioactive tracer and/or blue dye. While node-positive patients have historically been treated with axillary dissection, newer data confirm the safety of targeted node removal to confirm response to therapy. Avoiding axillary dissection can be facilitated by Magseed localization.

P50

Disparities in Multimodal Treatment of Patients with Breast Cancer J. Gunn,* R. Lemini, K.N. Partain, T. Almerey, T. Yeager, S.P. Bagaria, S. McLaughlin, E. Gabriel. *Mayo Clinic, Jacksonville, FL.*

Background: It has been shown that disparities in breast cancer multidisciplinary management can impact patient outcomes. The purpose of this study was to evaluate for disparities among women receiving treatment for breast cancer at multiple facilities of varying acuity across the United States. Methods: We queried the National Cancer Data Base (NCDB) for female breast cancer patients <70 who received multimodal treatment, including surgery, chemotherapy, and radiation. Patient demographic, clinical, and treatment characteristics, including time to treatment were analyzed. Overall survival (OS) was calculated using standard Kaplan-Meier methods. Multivariable analysis was performed to study the association of disparate patient factors on OS. Results: A total of 1,048,575 patients were included. With regards to race, a statistically significant difference in OS was noted between black vs white patients (HR=1.23, 95% CI 1.17-1.28) and Asian vs white patients (HR=0.72, 95% CI 0.65-0.81). This difference was also noted with regards to ethnicity (non-Hispanic origin vs Hispanic HR=0.73, 95% CI 0.67-0.79). Disparate outcomes in OS were also identified with respect to treating facility (Table 1). There was a statistically significant difference in mean days from diagnosis to treatment between races: white 29.9, black 36.4, Native American 34.2, Asian 34.3, other 34.6 ($p<0.001$). This disparity was seen with regards to mean days from diagnosis to definitive surgery as well: white 77.5, black 101.0, Native American 87.6, Asian 89.8, other 90.0 ($p<0.001$). Conclusion: There exists significant disparities in the treatment and OS for breast cancer patients based on race, ethnicity, and facility type. Further study is warranted to address the issues underlying these disparities as they are shown to impact care and outcomes.

Multivariate Analysis, Overall Survival

Variable		Hazard Ratio (95% CI)	p-value
Facility Type	Other vs Community Cancer Program	0.93 (0.87, 0.99)	<.001
	Academic/Research Program vs Community Cancer Program	0.86 (0.81, 0.90)	
	Comprehensive Community Cancer Program vs Community Cancer Program	0.95 (0.91, 1.00)	

P51

Adequate Sentinel Node Harvest Can Avoid Axillary Dissection in Node-Positive Breast Cancer Patients Even if Clipped Node is Not Identified T.L. Sutton,[2]* N. Johnson,[1] J.R. Garreau.[1] *1. surgical oncology, Legacy Cancer Institute, Portland, OR; 2. OHSU, Portland, OR.*

Introduction: Targeted axillary dissection (TAD) reduces the false negative rate of axillary lymph node sampling after neoadjuvant chemotherapy (NAC) in patients with clinically node-positive breast cancer (NPBC) when compared with sentinel lymph node biopsy (SLNB) alone. However, the Sentina study indicated that identification of at least 3 sentinel nodes also led to a low false negative rate (FNR) in this population. The aim of the present study was to determine if an adequate SLN harvest, when negative, might allow omission of ALND if the clipped node cannot be identified. Methods: A retrospective review of the Legacy Health System Breast Cancer Database was performed to identify patients receiving NAC between 2011 and 2016. Women with NPBC at diagnosis and those managed with SLNB and TAD were identified. Results: 456 patients received NAC in the study time frame. Of these, 188 patients had clinically NPBC. SLNB was performed in 46 and TAD in 29. A SLN was identified in 44 (96%) of patients; the median SLN harvest was 4 nodes. In TAD, there was pathologic concordance between the clipped and sentinel nodes in 25 cases (86%). In two of these cases, the clipped node was negative while a SLN was positive. Overall, the clipped node was a SLN in 20 cases(69%). ALND was indicated for inability to find the clipped node despite negative SLN in 4 patients (14%). In two cases, greater than 3 negative SLN were identified, and there were no additional positive nodes identified with ALND. In two cases, fewer than 3 negative SLN were identified and no axillary dissection was performed. Both of these patients had axillary recurrence within one year. Conclusions: In patients with NPBC receiving NAC, an adequate SLN harvest with negative intraoperative pathology may allow omission of axillary dissection even if the clipped node is not identified. ALND for clip identification is essential if there is inadequate SLN harvest.

P52

A Population-Based Evaluation of Post Mastectomy Radiotherapy Disparity in Appalachian Kentucky T. Gan,[1]* Q. Chen,[2] B. Huang,[3] E. Marcinkowski.[1] *1. University of Kentucky Department of Surgery, Lexington, KY; 2. University of Kentucky Department of Biostatistics, Lexington, KY; 3. University of Kentucky Markey Cancer Center, Lexington, KY.*

Introduction: Appalachian Kentucky (AK) has one of the highest breast cancer mortality rates in the United States. The Commission on Cancer (CoC) developed accountability measures to improve cancer care implemented through the National Accreditation Program for Breast Centers. This study evaluates compliance of Kentucky patients to the CoC quality measure of post mastectomy radiotherapy (PMRT). Methods: A retrospective review of patients who underwent mastectomy with 4 or more positive lymph nodes from 2006 to 2015 was obtained through the Kentucky Cancer Registry. Compliant radiation treatment was defined as starting radiotherapy within 365 days of diagnosis. Those with metastatic disease and age younger than 18 were excluded. Cox-regression analysis and Kaplan Meier plots were performed. Results: 1676 patients met inclusion criteria. Of these, 1104 (66%) received PMRT while 572 (34%) did not. AK patients were less likely to receive PMRT (58%) compared to non-AK patients (69%, $p < 0.001$). Factors associated with poor compliance included: older age (62% ≥ 50 years old vs 76% < 50 years old, $p < 0.001$), higher tumor grade (62% vs 69% in lower grade tumors, $p = 0.007$), insurance status (Medicare 51% vs 79% in private insurance, $p < 0.001$), non-academic centers (52% vs 71% in academic centers, $p < 0.001$), high poverty (57% vs 69% in low poverty, $p < 0.001$), and low education (58% vs 71% in high education, $p < 0.001$). Multivariate analysis demonstrated significantly lower compliance in those ≥ 50 years old (vs < 50 years old), Medicare and Medicaid (vs private insurance) and non-academic centers (vs academic centers). Despite significantly lower compliance in AK patients, there was no difference in survival in AK vs non-AK ($p = 0.122$, Figure 1). There was a significant survival difference in those who received PMRT vs no PMRT, ($p < 0.001$) highlighting the importance of PMRT in this population. Conclusion: Several factors contribute to the poor PMRT compliance of AK patients. The lack of difference in survival between AK and non-AK is likely due to the poor compliance of the Kentucky population overall, further demonstrating the need for accredited breast cancer centers.

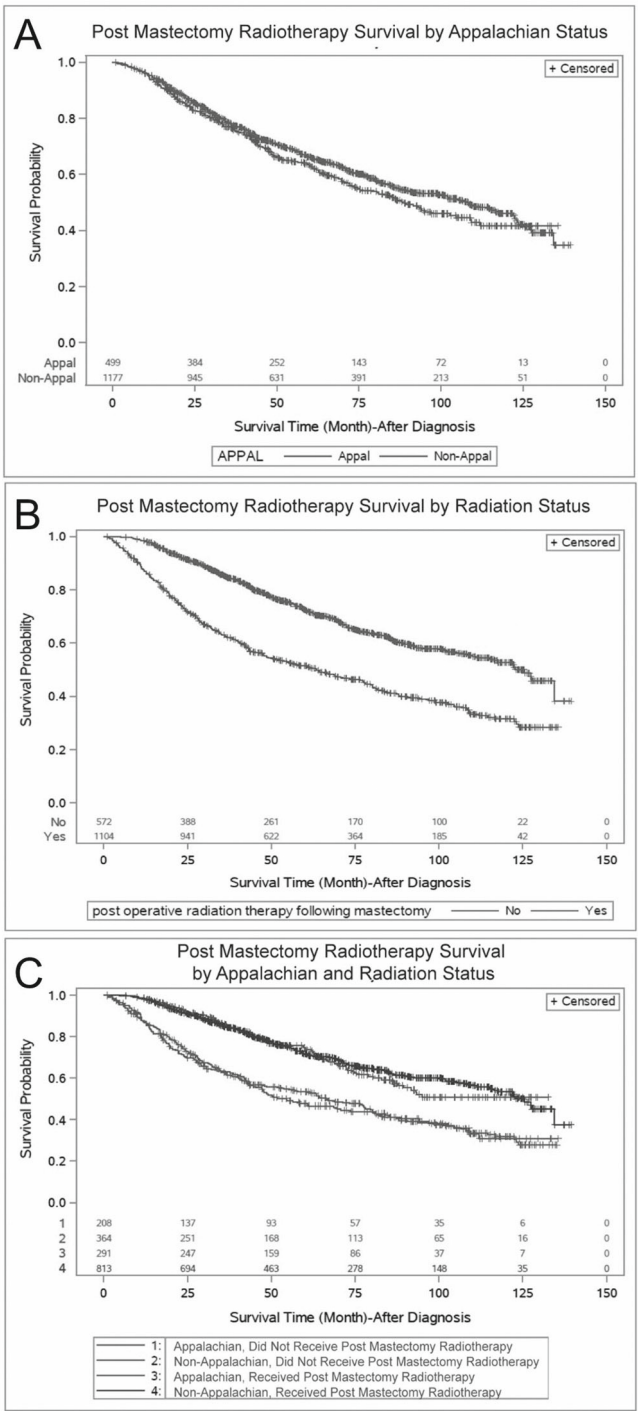


Figure 1: Post Mastectomy Radiotherapy (PMRT) Survival by Appalachian and Radiation Status. A) PMRT by Appalachian vs non-Appalachian. B) PMRT by radiation vs no radiation. C) PMRT by both Appalachian status and Radiation status.

P53

Excision of Atypical Lobular Hyperplasia is Not Associated with Malignancy Upstaging Even in Patients with a Synchronous Breast Cancer P. Jadeja,[1]* R. Ha,[2] E. Desperito,[2] L. Friedlander,[2] E. Ayala-Bustamante,[2] R.T. Wynn,[2] B. Taback.[2] *1. Breast Surgery, Summit Medical Group, Florham Park, NJ; 2. Columbia University Medical Center, New York, NY.*

Background: Improvements in breast screen imaging increase detection of atypia. There has been an effort to curtail excision for atypical lobular hyperplasia (ALH). In the setting of a malignancy, additional sites of atypia may result in an increase in excisions or even conversion to mastectomy in patients otherwise eligible for limited breast conserving surgery. The goal of this study was to evaluate the outcomes of patients undergoing excision of ALH. Methods: Single-institution, IRB approved, HIPAA compliant retrospective review of the electronic medical record identified patients who underwent surgical excision of ALH diagnosed by percutaneous biopsy. Site of excision, diagnoses of synchronous cancers, upgrades to a malignant pathology (ductal carcinoma in situ or invasive breast cancer), and long-term follow-up were analyzed. Results: Sixty patients were identified who underwent surgical excision after percutaneous biopsy identifying ALH. Among 60 patients, mean age was 55 years (range: 40-82) with 16 patients (26.7%) demonstrating a synchronous malignancy. Forty-four patients (73.3%) underwent excisional biopsy, 11 (18.3%) synchronous malignant lumpectomy and excisional biopsy, and 5 (8.4%) bilateral mastectomy. Among all patients undergoing excision, 6 patients (10%) upstaged from an initial diagnosis of ALH to DCIS (n=2) or invasive carcinoma (n=4), 5 (83.3%) of these demonstrated a mass and imaging-pathologic discordance. Among patients undergoing definitive surgical treatment for a synchronous malignancy, only 1 patient (1.7%) upstaged to DCIS at the previous ALH biopsy site. At median 6 year follow-up, 57 patients (95%) remained without evidence of disease; 2 patients (3.3%) developed a contralateral malignancy, and 1 patient (1.7%) contralateral atypical ductal hyperplasia. Conclusion: Excision of ALH, even in the setting of a synchronous malignancy does not result in upgrade. Patients otherwise eligible for breast conserving surgery who have additional sites of ALH identified, may be spared concomitant excision without evidence of long-term risk of relapse.

P54

Adjuvant Endocrine Therapy Impacts Local Recurrence and Distant Metastasis in Breast Cancer Treated with Intraoperative Radiation K.K. Broman,[1]* L. Joyal,[2] W. Sun,[1] J. Zhou,[1] B. Fridley,[1] R. Diaz,[1] C. Laronga.[1] *1. Surgical Oncology, Moffitt Cancer Center, Temple Terrace, FL; 2. University of South Florida, Tampa, FL.*

Background: Lumpectomy with whole breast radiation (WBXRT) is standard treatment for breast cancer. The ELIOT and TARGIT-A randomized trials supported IORT as an alternative to WBXRT in low risk patients using consensus eligibility criteria. To inform patient selection for IORT, we sought to identify additional factors that predict local recurrence (LR) and distant metastasis (DM). Methods: We performed a single institution, retrospective review of women with estrogen-receptor positive, clinically node-negative breast cancer who underwent lumpectomy with IORT from 2011-2015. We evaluated the association of demographics, clinicopathologic factors, operative data and adjuvant treatment with LR and DM. Statistical analyses used Wilcoxon rank-sum and Fischer exact tests. Results: The study cohort included 195 cases in 193 patients (pts) (2 had bilateral ER+ cancer). Median age was 70.0yrs (range: 51.6-88.5). On final pathology 92.8% had invasive ductal cancer (IDC), median tumor size was 1.0cm (range: 0.0-2.5), and 93.7% were node-negative. At a median follow-up of 44.3mos (range: 0.49-92.0), there were 14 (7.2%) recurrences [12 LR (6.2%), 3 DM (1.5%), 1pt had both LR+DM (0.5%)]. Six additional pts developed contralateral breast cancer (CBC), not included as LR or DM. Patients with LR or DM had longer follow-up (p=0.007), higher grade tumors on initial biopsy (p=0.040), higher mitotic indices (p=0.010) and lymphovascular invasion on final pathology (p=0.038), and were less likely to receive endocrine therapy (p=0.010). Most pts with CBC (4 of 6) also declined or did not receive endocrine therapy. Among pts followed at least 5 years (N=61), 9 (14.8%) recurred [7 LR (11.5%), 3 DM (4.9%), 1 LR+DM (1.6%)]. At five years, pts with recurrence were older (p=0.037) and less likely to receive endocrine therapy (p=0.011). Conclusion: Both LR and DM were higher than reported in the ELIOT and TARGIT-A trials. Receipt of endocrine therapy was the most significant factor impacting local recurrence, contralateral breast cancer, and distant metastasis.

Table. Clinicopathologic Factors Associated with Recurrence after Lumpectomy with Intraoperative Radiation

Characteristic	Local Recurrence			Any Recurrence *		
	No N=182	Yes N=13	*P-value*	No N=180	Yes N=15	*P-value*
Age (years), median [range]	69.7 [51.6, 88.5]	72.1 [66.4,84.0]	*0.073*	69.7 [51.6,88.5]	72.8 [66.4,84.0]	***0.024***
Biopsy histologic grade, N (%)						
1	82 (44.8)	2 (16.7)	*0.084*	82 (45.3)	2 (14.3)	***0.040***
2	88 (48.1)	8 (66.7)		86 (47.5)	10(71.4)	
3	13 (7.1)	2 (16.7)		13 (7.2)	2 (14.3)	
Tumor size (cm), median [range]	1.0 [0, 2.5]	0.9 [0.4,2.1]	*0.924*	1.0 [0,2.5]	0.95 [0.4,2.1]	*0.886*
Node positive, N (%)	12 (6.7)	0 (0)	*1.000*	11 (6.2)	1 (7.1)	*1.000*
Final margin < 2mm, N (%)	14 (7.7)	1 (8.3)	*1.000*	14 (7.8)	1 (7.1)	*1.000*
Lymphovascular invasion, N (%)	10 (5.6)	2 (18.2)	*0.145*	9 (5.1)	3 (23.1)	***0.038***
OncotypeDx Score, median [range]	18 [2,46]	17 [8,37]	*0.855*	18 [2,46]	17 [8,37]	*0.734*
Follow-up (months), median [range]	42.7 [0.5,89.0]	67.0 [20.0,92.0]	***0.026***	42.7 [0.5,89.0]	67.9 [20.0,92.0]	***0.007***
No endocrine therapy, N (%)	34 (18.6)	6 (50.0)	***0.018***	33 (18.2)	7 (50.0)	***0.010***

P55

Patients Seeking Second Opinions for Breast Surgery at a Safety Net Hospital: A Retrospective Study E. Warnack,* K. Joseph. *Surgery, NYU Langone Health, New York, NY.*

Introduction: Newly diagnosed women with breast cancer often seek second opinions. We sought to analyze the management of underserved women who sought second opinions at an urban safety net hospital in NYC. Methods: Our breast cancer database was used to identify patients with breast cancer who had been seen in clinic over an eight-year period (2008-2016). Patients who presented to our SNH from an outside hospital (OSH) for second opinion for surgical management were identified by chart review. Characteristics of second opinion (SO) patients, including outside hospital diagnostic work up and subsequent management at SNH, were obtained. Mammogram readings from the OSH were compared to those from our SNH using BIRADS scoring. Chi Square test was used to compare second opinion patients vs. other patients seen in breast clinic. Results: 945 patients presented to our breast clinic over the time period studied. Most patients were Asian (18.5%), with Medicaid insurance (85.3%). 72 patients (7.6%) presented to this SNH seeking a second opinion for surgical management. The most common stage at presentation were stage 1 (29.9%) and stage 2 (28%). Compared to other patients seen in clinic, SO patients were more likely to be Asian (40.3% vs. 26.7%, p = .04) and undergo modified radical mastectomy (22.2% vs. 9.7%, p = .01). Of SO patients, most were first seen at a community hospital (34.7%), and a majority received a mammogram as part of their diagnostic work up (86.1%). There was a discrepancy in mammogram read in 15 patients (20.8%), and 30 patients (41.6%) had a new cancer diagnosis, while 9 patients (12.5%) were found to have additional area of cancer not previously appreciated. Conclusions: There was often a discrepancy in breast imaging impression between outside hospitals and our institution, and new cancer diagnoses were also common. This suggests that second opinions may be particularly useful in surgical management for underserved patients referred to safety net hospitals who face significant roadblocks to high quality screening, diagnosis and treatment.

Table: Second Opinions, 2008-2016 (n= 72)

Second Opinions	# Patients (%)
OSH Type	
Academic	5 (6.9%)
Safety Net Hospital	23 (31.9%)
Private Hospital	9 (12.5%)
Community Hospital	25 (34.7%)
International	6 (8.3%)
Unknown	4 (5.6%)
OSH Diagnostic Work up	
Mammogram	62 (86.1%)
Breast U/S	45 (62.5%)
Breast MRI	2 (2.7%)
Biopsy	48 (66.6%)
OSH Treatment	
Surgery	11 (15.2%)
Chemotherapy	4 (5.5%)
XRT	2 (2.7%)
BHC Diagnostic Work up	
Mammogram	29 (40.2%)
Breast MRI	28 (38.8%)
Metastatic work up	29 (40.2%)
Biopsy (either LN FNA or breast core)	65 (90.2%)
Breast core biopsy	58 (80.5%)
BHC Biopsy Results (breast only, n= 58)	
IDC	39 (63.7%)
IDC + DCIS	1 (1.7%)
DCIS	12 (20.6%)
LCIS	1 (1.7%)
ILC	3 (5.1%)
Benign	2 (3.4%)
Difference in Mammogram Read	15 (20.8%)
New Cancer Diagnosis	30 (41.6%)
Additional Area of Cancer Found	9 (12.5%)

P56

Development of the New Prognostic Score for Predicting the TNBC Patients' Survival M. Oshi,* E. Katsuta, L. Yan, K. Takabe. *Surgical oncology, Roswel Park Cancer Institute, Buffalo, NY.*

Background: Triple-negative breast cancer (TNBC) has the worst prognosis among all breast cancer subtypes, and the vast majority of death is the consequence of metastasis. Thus a prognostic score that predict the likelihood of metastasis is expected to help identify the patients with high risk. Here, we aimed to develop such prognostic score utilizing gene profile of metastatic clone of TNBC cells. Method: Gene expression profile of human TNBC cell line MDA-MB 231 and its lung metastasis clone LM2-4 were analyzed by RNA-sequence data. The least absolute shrinkage and selection operation (LASSO) Cox regression model was applied for METABRIC cohort to construct a prognostic score. Result: There were 534 upregulated genes in metastatic clone (LM2-4) compared with originated MDA-MB 231 with adjusted $P<0.05$ and fold-change > 2.0. Among them, 17 genes were epithelial mesenchymal transition (EMT) related genes. Employing publicly available large cohort METABRIC, we built a scoring system to predict TNBC patients' disease-specific survival (DSS) utilizing these 17 genes by LASSO Cox regression model. Among 17 genes, four genes were identified to establish our prognostic scoring system. When we applied this four-mRNA-based classifier in 250 TNBC patients of METABRIC cohort, we identified the cutoff of top 17% score showed the highest impact on patients' DSS (5-year DSS rates; 39.0 vs 68.4 months, $p<0.001$). This scoring system was validated with 160 TNBC patients in The Cancer Genome Atlas project (TCGA) cohort. Utilizing top 17% cutoff, high score patients showed significantly worse overall survival than low score patients (5-year survivals; 44.6 vs 79.5 months, $p=0.033$). Conclusion: We developed a prognostic tool based on four-mRNAs for TNBC patients. This scoring system is expected to be a useful tool to predict patients' survival.

P57

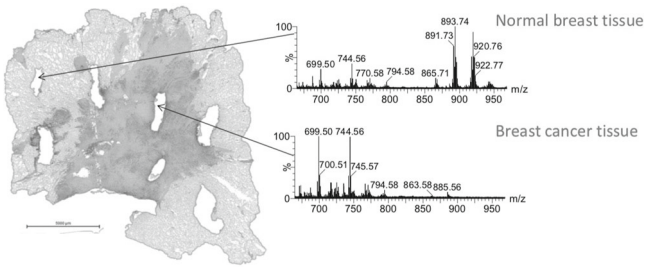
Elevation of Naïve CD4 Cells, Naïve B-Cells, Gamma Delta T-Cells, and Regulatory T-Cells is Associated with Long-term Disease-free Survival in Breast Cancer A.L. Butash,[1]* M. Asaoka,[1] T. Kawaguchi,[2] L. Yan,[1] K. Takabe.[1] *1. Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY; 2. Kyoto Prefectural University of Medicine, Kyoto, Japan.*

Introduction It is well known that increased tumor infiltrating lymphocytes (TILs) is associated with attaining pathologic complete response (pCR) to neoadjuvant chemotherapy (NAC) and a better survival in breast cancer. One limitation of these data is that the lymphocyte infiltration is evaluated by pathological evaluation where there is a possibility of bias. Our group and others are able to estimate immune cell counts by utilizing a computer algorithm, CIBERSORT, on gene expression data. We hypothesized that tumors that recur early, in less than 3 years, have less favorable immune cell composition compared to patients with disease free survival (DFS) beyond 5 years. Methods 894 breast cancer patients with DFS data available in The Cancer Genome Atlas (TCGA) were analyzed, comparing the short survival group (DFS<3 years) and the long survival group (DFS>5 years). CIBERSORT was used to estimate immune cell composition and genomic expression. Results Patients who had long DFS had composition fractions of higher naïve CD4 T cells (p=0.036), higher naïve B cells (p=0.01), higher gamma delta T cells (p=0.033), higher regulatory T cells (p=0.01), and lower CD8 T cells (p=0.044) when compared to patients with short DFS. The remaining 17 types of immune cells did not show a significant difference when comparing the groups. Estimated counts of TILs, leukocytes, lymphocytes, cytolytic activity score, T cell receptor repertoire, and B cell receptor repertoire demonstrated the trend to be higher in the long DFS group, however, the differences were not significant. There were also no significant differences seen when comparing intra-tumoral heterogeneity, Mutant Allele Tumor Heterogeneity, mutation load, and homologous recombination deficiency. Gene expression of CD274 (PDL-1 gene) was higher in the long survival group compared to the expression in those in the short survival group (p=0.023), whereas PDCD1 (PD-1 gene) expression showed no difference. Conclusion Elevation of naïve CD4 cells, naïve B cells, gamma delta T cells, and regulatory T cells is associated with long term disease free survival in breast cancer.

P58

Rapid Evaporative Ionization Mass Spectrometry of Electrosurgical Vapors Classifies Normal Breast and Breast Cancer Tissues P. Vaysse,[1] L. Kooreman,[2] S.W. M. Olde Damink,[2] R.M. A. Heeren,[1] M. Smidt,[2]* T. Porta Siegel.[1] *1. Maastricht University, Maastricht, Netherlands; 2. Maastrict University Medical Centre, Maastricht, Netherlands.*

An important component of oncologic surgery is the achievement of radical margins. Nevertheless, in the current setting, they can only be determined in detail by the pathologist after the operation. Rapid Evaporative Ionization Mass Spectrometry (REIMS) has emerged as a promising tool for real-time classification of biological tissues to assist intraoperative decision-making (Balog et al., 2013). In this study, we investigated the classification of normal breast and breast cancer tissues by ex vivo REIMS analysis (St John et al., 2017) to build the foundation towards our implementation during surgery. Patients undergoing surgery for breast tumor were included following an approved ethic protocol. After examination of the resected specimen, a pathologist could select tumor and normal tissue samples for the study. For each sample, several spots were sampled by cauterisation for a few seconds by using a blade connected to an electrosurgical heat-generator (Covidien). For each spot, the produced vapours were analysed by REIMS (Xevo-Q-TOF, Waters) to generate a molecular profile. The tissues were then sectioned and H&E stained. A breast pathologist examined the tissues on the surroundings of each spot to attribute tissue components to each molecular profile. The accuracy of the REIMS tissue classification model based on principal component analysis-linear discriminant analysis was tested with a leaving out 20% cross validation (AMX, Waters). In total, 520 REIMS profiles were collected from 40 patients. 237 profiles were included as tumor (i.e. minimal tumor component of 20%). 283 profiles were included as normal tissue. The REIMS classification model distinguished tumor and normal breast profiles with a classification rate of 93%. 40% of the misclassified profiles were sampled on tumor edges while being annotated as normal breast tissue. Moreover, a classification rate of 93% was obtained to distinguish lobular and ductal invasive carcinomas when only considering tumor profiles. The REIMS ex vivo analysis distinguishes tumour and normal breast tissues in few seconds confirming its potential for future intraoperative in vivo analysis.



P59

A Comparative Analysis of Genomic Profiles of Matched Primary Breast Tumors and Metastatic Lymph Nodes in Non-triple Negative Breast Cancer N. Liao,[1]* G. Zhang,[1] Y. Wang,[1] L. Guo,[1] L. Cao,[1] C. Ren,[1] L. Wen,[1] K. Li,[1] M. Jia,[1] S. Chuai,[2] X. Chen,[1] B. Chen.[1] *1. Department of Breast Cancer, Cancer Center, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China; 2. Burning Rock Biotech, Guangzhou, China.*

Background: There are significant differences in biology behavior and genomic profiling between triple-negative breast cancer (TNBC) and ER, PR and/or HER2neu expressing breast cancer (non-TNBC). Meanwhile, little is known about differential mutation spectrums in synchronous breast tumors and matched metastasis in axillary lymph nodes. Here, we determined the genomic mutational profiles in synchronous primary lesion (PL) and metastatic lymph nodes (MLN) of non-TNBC by using ultra-deep targeted sequencing. Methods: The mutational profiles were compared between the matched PL and MLN samples from 55 of treatment naïve non-TNBC patients with invasive breast cancer and axillary lymph node metastasis by targeted next-generation sequencing of 520 cancer related genes. KEGG enrichment analysis was further performed. Results: In this paired cohort, 877 genomic aberrations were identified in 217 genes, including 384 single nucleotide variants (SNVs), 63 insertions or deletions, 425 copy number amplifications (CNAs), and 5 translocations. Although 546 (62.3%) events were shared in PL and MLN samples, 204 (23.3%) mutations and 127 (14.4%) mutations were specific PL and MLN samples, respectively. Twenty patients (36.4%) had PL specific mutations, but had no MLN specific mutations. In contrast, 5 patients (9.1%) only had MLN specific mutations and the remaining 23 patients (41.8%) had both PL and MLN specific mutations. In addition, 7 of patients (12.7%), ki67 significantly lower than other patients, all of whom are hormonal receptor (HR) positive, harbored completely similar mutation spectrum between PL and MLN. KEGG pathway enrichment analysis revealed that aberrant activation of Proteoglycans pathway and JAKSTAT signaling, as well as aberrant HIF1 pathway, was specifically occurred in the MLN samples, suggesting crucial roles for these signaling pathways in the involvement of lymph node metastasis. Conclusions: Our study focused on non-TNBC and revealed genomic heterogeneity between primary tumors and lymph nodes, and identified mutations as well as pathways that are potentially relevant to lymph node metastasis.

P60

MicroRNA-34a Levels Are Associated with Subtype-Specific Immune Cell Composition in Breast Cancer J.C. Sporn,* E. Katsuta, L. Yan, K. Takabe. *Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

MicroRNAs are short RNA molecules of about 18 to 24 nucleotides in length that target certain messenger RNAs preventing them from coding for a specific protein. MicroRNA-34a (miR-34a) was found to be decreased in many different cancers, suggesting a role as a tumor suppressor, and re-expression of miR-34a has been investigated as a potential cancer treatment. We have previously shown that miR-34a plays a dual role in breast cancer. Within the estrogen receptor positive (ER+) cohort, patients with low expression of miR-34a had an improved disease-free survival (DFS) compared to patients with high expression of miR-34a. Interestingly, this effect was reversed in

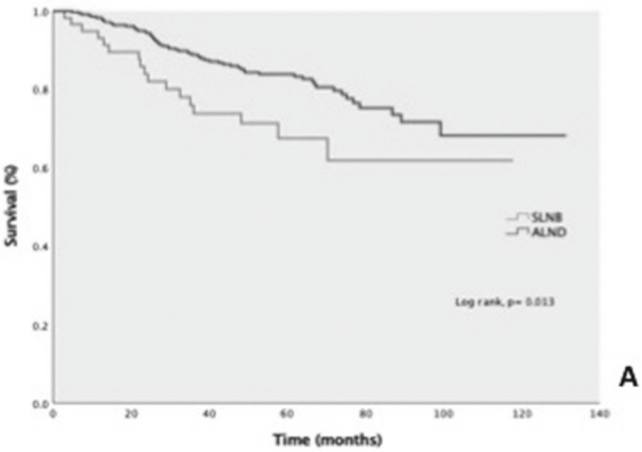
the ER negative (ER-) cohort where high miR-34a expression was associated with improved DFS compared to low expression. We hypothesized that part of these differences were due to subtype-specific immunoediting. We utilized The Cancer Genome Atlas containing genetic and molecular data, clinical profiles and survival information for 985 breast cancers. Survival analysis compared a group with low expression of miR-34a to a group with high expression within the ER+ and ER- cohorts and within the triple negative breast cancer (TNBC) and non-TNBC cohorts. The CIBERSORT algorithm was used to calculate the cell fractions of 22 immune cell types in each tumor. In the ER+ cohort, miR-34a high tumors -associated with a worse prognosis- are characterized by a relative abundance of activated mast cells, M0 and M2 macrophages, neutrophils, regulatory T and T follicular helper cells, and a relative scarcity of naïve B cells, resting dendritic cells, resting mast and resting memory CD4 cells ($p<0.05$ for all). In the ER- cohort, miR-34a high tumors -associated with an improved prognosis- do not show this abundance with the exception of an abundance of M2 macrophages ($p=0.042$). The most notable difference in the TNBC versus non-TNBC cohorts is seen with T follicular helper cells which show a relative abundance in the miR-34a high group in non-TNBC, but a relative scarcity in the miR-34a high group in TNBC. These findings suggest a subtype-specific intratumor immune cell composition associated with varying miR-34a levels.

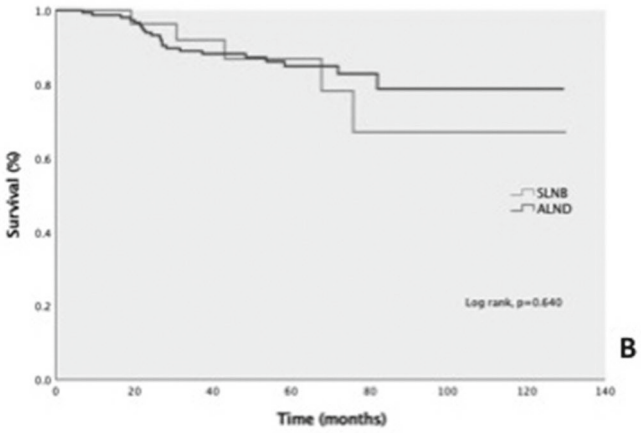
P61

Surgical Management of the Axilla in Patients with Occult Breast Cancer (cT0N+) Who Underwent Neoadjuvant Chemotherapy

F. Macedo,* B. Azab, R. Fayne, D. Yakoub, D. Franceschi, N. Goel, S.B. Kesmodel, E. Avisar. *Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL.*

INTRODUCTION: Occult breast cancer (OBC) represents a rare clinical entity and its surgical management is yet controversial. Axillary lymphadenectomy (ALND) has been widely recommended with or without mastectomy. We sought to investigate the role of sentinel lymph node biopsy (SLNB) in patients with OBC who underwent neoadjuvant chemotherapy (NAC). METHODS: National Cancer Data Base (NCDB) was queried for patients with cT0N1-2 breast cancer diagnosed from January 2004 to January 2014. Actuarial estimates for overall survival (OS) were calculated using Kaplan-Meier methods. Log-rank and Cox multivariable regression analysis were performed to compare the outcomes of ALND versus SLNB. RESULTS: A total of 684 patients with OBC were included in the analysis: 470 (68.7%) patients underwent surgery upfront and 214 (31.3%), NAC. Mean age was 61.6 and 55.6 years ($p<0.001$), respectively. Of NAC patients, 34 (15.9%) underwent SLNB and 180 (84.1%), ALND. There was no difference in pCR between the 2 groups (34.3% vs. 24.5%, $p=0.245$, respectively). ALND was superior to SLNB in patients undergoing surgery upfront (median survival 54 vs. 49.1 months, log rank, $p=0.013$, Fig 1A), however no significant difference was found in patients undergoing NAC (median survival 55.4 vs. 54.8 months, log rank, $p=0.640$, Fig 1B). Radiotherapy (HR 0.615, 95% CI 0.225-1.682), mastectomy (HR 0.865, 95% CI 0.147-5.082), ALND (HR 0.277, 95% CI 0.063-1.210), or pN2 (HR 4.873, 95% CI 0.853-27.833) were not independent predictors of improved survival in NAC patients. CONCLUSIONS: This is the first analysis assessing the surgical management of the axilla in patients with OBC who underwent NAC. SLNB has similar outcomes compared to ALND in this population, and therefore should be considered in the management of the axilla after NAC. NAC followed by SLNB and breast RT should be attractive for patients with OBC who opt for a less invasive approach.



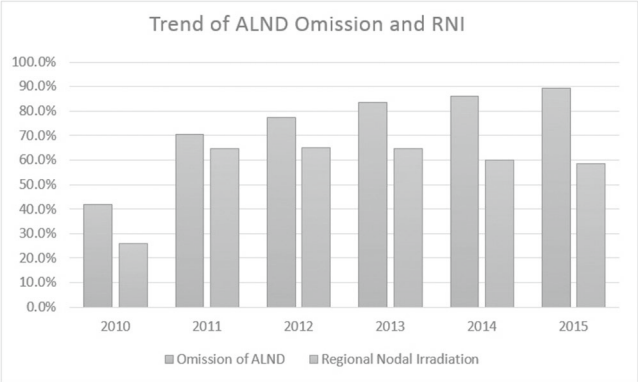


P62

Trends in Regional Nodal Management of Breast Cancer Patients with Low Nodal Burden B.M. Raber,* H. Lin, Y. Shen, S. Shaitelman, I. Bedrosian. *Breast Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: ACOSOG Z0011 (Z11) 10 year data confirms the safety of omission of axillary lymph node dissection (ALND) and regional nodal radiation (RNI) in breast cancer patients with 1-2 positive (+) sentinel nodes (SN), with no negative impact on disease free (DFS) and overall survival (OS). The NCIC MA20 trial showed improved DFS in node + patients undergoing ALND and receiving RNI, with no difference in OS. We sought to examine how these data have influenced management of patients with limited nodal burden. Methods: Using the National Cancer Database, patients diagnosed between 2010-2015 with a cT1-2 N0M0 breast cancer treated with lumpectomy and no more than 2 + SN were queried for omission of ALND (Z11 compliant) or completion ALND (Z11 non-compliant). Logistic regression was used to analyze factors associated omission of ALND and use of RNI, respectively. Regression analyses of survival data based on the Cox proportional hazards model were conducted on OS. Results: 26,689 patients met study criteria. Omission of ALND rose from 41.8% in 2010 to 89.2% in 2015. This Z11 compliant group was more likely to undergo RNI compared to Z11 non-compliant group (36.4% vs 31.3%, $p<.05$), with RNI increasing from 29.6% in 2010, to 43.8% in 2015. Factors associated with use of RNI in this group included later year of diagnosis (OR 1.8, 95%CI 1.6-2.1), HR negative tumor (OR 1.2, 95%CI 1.1-1.4), grade 3 tumor (OR 1.2, 95%CI 1.1-1.3), treatment at non-academic site (OR 1.2, 95%CI 1.1, 1.3) and 2 vs. 1 + SN (OR 2.0, 95%CI 1.8-2.2). In the Z11 non-compliant group, use of RNI increased from 26.9% in 2010 to 44.4% in 2015. In this group, higher use of RNI was associated with age < 50years (OR 1.3, 95%CI 1.1-1.6), later year of diagnosis (OR 2.1, 95%CI

1.7-2.6), grade 3 tumor (OR 1.3, 95%CI 1.1-1.5), and 2 vs. 1 positive node (OR 1.8, 95%CI 1.6-2.0). With a median follow up of 43.3 months, RNI was not significantly associated with overall survival (HR 1.1, p=0.14). Conclusion: Since the publication of Z11, omission of ALND has reached 90%. RNI rates are also increasing but appear quite variable, suggesting that the optimal RT approach for this low nodal burden population warrants further study.



P63

Minimizing Opioid Use and Length of Stay in Patients Undergoing Mastectomy with Reconstruction C. McGugin,* S.B. Coopey, B.L. Smith, B. Kelly, M. Gadd, K.S. Hughes, M.C. Specht. *Massachusetts General Hospital, Boston, MA.*

Introduction Increasingly, patients and clinicians are concerned about postoperative opioid requirements. We sought to determine trends in inpatient opioid requirements in mastectomy patients undergoing immediate reconstruction. Methods A retrospective review of 801 mastectomy patients with immediate tissue expander (TE) or implant reconstruction was performed; 189 patients treated in 2010 (prior to ERAS protocol) compared to 612 patients treated between 2016 and 2018. Patients who required reoperation during the same admission were excluded. Opioid use and LOS were compared over time and stratified by laterality (unilateral or bilateral), mastectomy (skin-sparing or nipple-sparing), and reconstruction (TE or implant). Associations were assessed by univariate and multivariate analyses. Results Over time, more patients underwent bilateral mastectomies (68.1% vs 62.4%), nipple-sparing mastectomy (73.5% vs 26.5%), and direct-to-implant reconstruction (74.7% vs 44.4%). Inpatient IV opioid use decreased over time. In 2010, 180 (95.2%) patients required postoperative IV opioid analgesia compared to 420 (68.6%) patients in 2016-2018. Of those who did require IV opioids, time to last dose decreased from median 17 hours (IQR 10-20) in 2010 to 1.4 hours (IQR 0.8-2.5) in 2016-2018 (p<0.001). In 2016-2018, 84 patients (13.7%) did not require inpatient oral opioids, and 48 (7.8%) did not require inpatient IV or oral opioids. Mean LOS (SD) decreased from 37.0 (+/-14.0) hours with 2.0 (+/-0.6) nights in 2010 to 27.5 (+/-10.1) hours with 1.2 (+/-0.6) nights in 2016-2018 (p<0.001). In logistic regression models adjusting for laterality, mastectomy type, and reconstruction, LOS was associated with year (p<0.001) and IV opioid use (p<0.001). IV opioid use remained significantly associated with year even when adjusting for LOS (p<0.001). Conclusion Compared to 2010, patients undergoing mastectomy with immediate TE or implant reconstruction in 2016-2018 had decreased inpatient opioid requirements and shorter lengths of stay. We attribute this to improved patient expectations, surgical efficiencies, and a shift towards non-opioid analgesics.

P64

Nononcologic Impact of Preoperative Chemotherapy for Early Stage Breast Cancer A.M. Altman,* S. Marmor, E. Jensen, J. Denbo, T. Tuttle, J. Hui. *Surgery, University of Minnesota, Minneapolis, MN.*

Introduction: Women with early stage breast cancer have many clinical decisions regarding care with comparable oncologic outcomes. One of these is the choice to undergo either preoperative or postoperative chemotherapy. Given equivalent outcomes, we sought to further understand if there were differences in the workup, treatment and non-oncologic outcomes between these two groups. Methods: We performed a retrospective hospital-system wide survey study of women who were treated for breast cancer from 2010 to 2015. Eligible women were mailed a study packet with consent as well as a modified Holmes-Rovner (HR) Scale, to evaluate satisfaction with surgery and decision-making, and BCS-DQI, to evaluate the quality of patient's decisions and breast cancer knowledge. We included patients aged <60 years who consented to the study and completed the included surveys. We excluded patients with stage T3/4 or N2. Results: 176 women met inclusion criteria and returned surveys. 146 had no preoperative chemotherapy and 30 had preoperative chemotherapy. Women who underwent preoperative chemotherapy were significantly younger, more likely to have HER2+ tumors, have stage T2 and N1 disease when compared to those who did not. Furthermore, women who underwent preoperative chemotherapy were more likely to be cared for at an academic institution, have a preoperative MRI, preoperative genetic testing and preoperative consultation with medical oncology. While both cohorts had high HR scores, indicating satisfaction with decision making, women who underwent preoperative chemotherapy tended to have slightly higher scores (p=0.08) and felt significantly more comfortable with their surgical decisions (p=0.015). There was no difference in knowledge detected with the DQI between the cohorts. Conclusions: Women with early stage breast cancer are satisfied with their treatment choices. Patients who undergo preoperative chemotherapy have more time to meet with consults and receive additional testing, knowledge scores were similar across both cohorts. Offering patients preoperative chemotherapy may allow more time prior to surgery to process their decisions, thus possibly leading to increased satisfaction.

	No Preoperative Chemotherapy	Preoperative Chemotherapy	p-Value
Pre-Operative Workup			
Hospital type (% Community)	39.7	16.7	0.028
Preoperative MRI (% Yes)	59.6	83.3	0.024
Preoperative genetic testing	33.6	63.3	0.004
Plastics Consultation	39	50	0.403
Medical Oncology Consultation	37	100	<0.001
Radiation Oncology Consultation	6.2	6.7	1
Survey Results	Mean (sd)	Mean (sd)	
Holmes Rovner Score	38.59 (6.61)	40.83(6.11)	0.09
"I wish I would have given more consideration to other surgery options" (1-Strongly Agree, 5-Strongly Disagree)	4.01(1.13)	4.53(0.73)	0.015
DQI Knowledge Score	64.76 (16.55)	58.89 (17.03)	0.8

Table comparing select workup and outcomes between patients who underwent preoperative chemotherapy and those that did not.

P65

The Role of Tumor Phenotype and Histology in the Surgical Treatment of Early Stage Breast Cancer A.M. Gupta,* H.V. Williamson, R.A. Greenup, S.M. Thomas, O.M. Fayanju, J.K. Plichta, L.H. Rosenberger, E. Hwang. *Duke University, Durham, NC.*

BACKGROUND: Among eligible women with breast cancer, surgical treatment decisions are influenced by multiple factors. We sought to investigate if tumor histology and phenotype influence surgical patterns of care for early-stage breast cancer. METHODS: We identified women 18-69 years old diagnosed with early-stage (cT0-2; cN0; cM0), unilateral breast cancer between 2010-2015 in the National Cancer Data Base. Patients were classified as receiving lumpectomy with radiation (BCT), unilateral mastectomy (UM), or bilateral mastectomy (BM). A generalized logit model was used to determine factors associated with surgery type. Unadjusted overall survival (OS) was estimated using the Kaplan-Meier method. Cox proportional hazard modeling was used to estimate the effect of surgery types and tumor subtypes on OS after adjustment. RESULTS: Of the 338,366 patients identified, 59% (N=199,423) underwent BCT, 25% (N=85,194) underwent UM, and 16% (N=53,749) underwent BM. On multivariable analysis, patients with HER2+ and triple-negative (TN) phenotypes were more likely to undergo BCT than UM, compared to those with hormone receptor-positive (HR+) disease (OR 0.92, 95% CI 0.89–0.95; OR 0.5, 95% CI 0.48–0.52). TN patients were also more likely to undergo BCT than BM (OR 0.62, 95% CI 0.59-0.65). Patients with lobular histology were more likely to undergo UM and BM (OR 1.39, 95% CI 1.34-1.45; OR 1.60, 95% CI 1.53 – 1.68) compared to BCT. Intermediate and high-grade tumors were associated with increased rates of UM and BM (OR 1.3, 95% CI 1.27–1.33; OR 1.3, 95% CI 1.23-1.31) compared to low-grade tumors. After adjustment for several factors, including phenotype, patients who underwent UM (HR 1.43, 95% CI 1.28-1.59) or BM (HR 1.33,

95% CI 1.14- 1.54) had worse OS than those who underwent BCT. CONCLUSION: Tumor phenotype and histology influence surgical patterns of care. BCT is increasingly incorporated into the care of women with HER2+ and TN tumors, while lobular histology and high grade tumors are more likely to undergo mastectomy. These results indicate that aggressive phenotypes do not necessitate more extensive surgery; and that anatomy, rather than phenotype, drives surgical decisions.

P66

Use of Neoadjuvant Versus Adjuvant Chemotherapy for Hormone Receptor Positive Breast Cancer: A National Cancer Data Base (NCDB) Study H. Schmidt, J. Alberty-Oller, M. Zeidman, M. Ru, k. pisapati, E. Moshier, S. Ahn, m. mazumdar, E. Port.* *Dubin Breast Center, Mount Sinai Medical Center, New York, NY.*

Introduction: Neoadjuvant chemotherapy (NAC) is a well established therapeutic option for patients with locally advanced disease often allowing downstaging and facilitation of breast conserving therapy. With evolution of better targeted treatment regimens and awareness of improved outcomes for patients with significant response, use of NAC has expanded particularly for triple negative and HER2 positive breast cancer. In this study we explore utility of neoadjuvant chemotherapy for a notoriously resistant subset of hormone receptor positive Her2 negative(HR+Her2-) patients. Methods: Patients with HR+Her2- breast cancer treated with chemotherapy before or after surgery were identified from 2010-2015 in the NCDB. Multivariable regression models adjusted for covariates were used to determine associations within these groups. Overall survival (OS) was computed with Cox proportional hazards model with propensity score adjustment. Results: Among 134,849 patients (clinical stage2A,64%; 2B,21%; 3,15%), 105,510 (78%) had surgery first and 29,339 (22%)received NAC. Use of NAC increased over time (2010 to 2015; 19.7-24.2% and OR=1.34 for 2015; p<.0001). Patients were more likely to receive NAC with cT3, cT4, cN+ disease (OR= 1.86,2.77,1.7). Patients less likely to receive NAC were age>49, lobular carcinoma, increased Charlson-Deyo score, and government insurance (OR= .75, .78, .78, .79). Complete response (CR) was noted in 9.05% of NAC patients. Adjusted OS was improved with primary surgery (hazard ratio 1.24;95% CI, 1.21-1.27). Conclusions: Neoadjuvant chemotherapy use among HR+Her2- breast cancer patients has expanded over time and offers downstaging of disease for some patients, with CR seen in only a small subset. Further analysis is warranted to determine the subgroup of patients with HR+Her2- disease who benefit from this approach.

P67

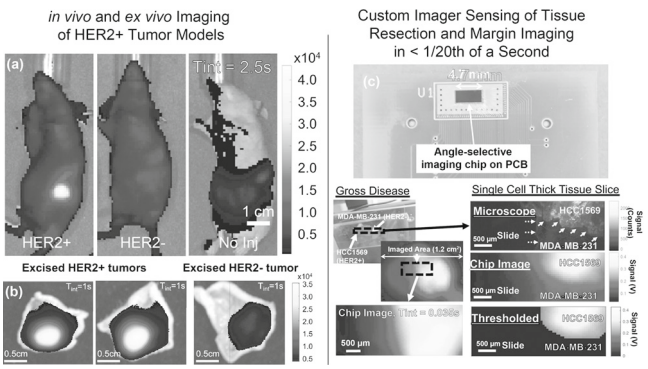
APOBEC3-mediated RNA Editing in Tumor is Associated with Survival in Breast Cancer M. Asaoka,[1]* S.K. Patnaik,[1] T. Ishikawa,[2] K. Takabe.[1] *1. Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY; 2. Tokyo Medical University Hospital, Tokyo, Japan.*

APOBEC3 (A3) enzyme activity is a source of DNA mutations in cancer. Especially in breast cancer, A3B is now well known as an important cause of mutagenesis, and high A3B expression in tumors is associated with poor disease prognosis, whereas the prognostic significance of the other six APOBEC3s (A3A, C-H) is unclear. Our recent studies have brought to light the hitherto unknown RNA editing activity of multiple APOBEC3s. However, the prevalence and significance of such editing in any cancer is unknown. We developed a bioinformatics workflow to determine C-to-U RNA editing levels in 1040 primary breast carcinoma tumors of The Cancer Genome Atlas using whole exome and mRNA sequencing data. Measurements of other molecular/cellular features of the tumors were obtained from TCGA publications. Spearman and Kaplan-Meier methods were respectively used for correlation and survival analyses. A cut-off of 0.05 was used to judge significance of P values. A3B expression had stronger association with both tumor mutation burden and neoantigen load (Spearman r = 0.34 and 0.31, resp.) than the other six APOBEC3s (-0.03-0.08). C-to-U RNA editing with an average level of 6.3% (SD = 4.3) was observed among tumors for 767 genes. RNA editing was most common for GATAD2B (100% of tumors), AMPD3 (80%) and SERPINA1 (78%). Tumor subtype or pathological stage had no association with RNA editing level. Tumors with high editing had 1.4-11x higher gene expression of A3A and C-H (P <0.05) but not A3B (P = 0.33). CD8 T cell infiltration, TCR diversity, and immune cytolytic activity in tumors correlated with RNA editing (r = 0.11, 0.20 and 0.26, resp.) and expression of A3A and C-H (0.13-0.45, 0.26-0.70 and 0.31-0.79, resp.) but not A3B (-0.03, 0.13 and 0.10, resp.). Concordantly, high A3A and C-H expression as well as RNA editing were associated with improved overall or disease-free survival (HR = 0.43-0.66, P <0.05). In conclusion, we have performed the first comprehensive analysis of C-to-U RNA editing in cancer. In breast cancer tumors, RNA editing level correlates with A3A and C-H expression. Editing is more prevalent in tumors with stronger immune response and is associated with a better outcome.

P68

Feasibility of Breast Tumor Imaging in a Mouse Model Using Angle Selective Fluorescence Contact Imaging J.M. Wong,[1]* E.P. Papageorgiou,[2] S. Giverts,[2] C. Park,[1] M. Anwar.[1] *1. Surgery, University of California, San Francisco, San Francisco, CA; 2. University of California, Berkeley, Berkeley, CA.*

Background: Achieving clear margins during the initial partial mastectomy remains a surgical challenge. Intraoperative imagers face the dual challenge of needing to maneuver in tight, irregular cavities while rapidly assessing a large surface area with several hundred cell sensitivity. The development of a small, flexible angle selective fluorescence contact imager with <100-cell sensitivity and a compatible fluorescent imaging agent provides a potential novel method for imaging a partial mastectomy cavity intra-operatively, allowing for real time margin assessment and selective re-excision of a positive margin. Methods: Mice with implanted tumors were injected with a fluorescent imaging agent, a fluorophore conjugated to the antibody Trastuzumab, to specifically target and identify HER2+ tumors. In vivo imaging of the mice and their tumors occurred at 3, 9, 23, 30, and 46 hours after injection using both the fluorescence contact imager and an IVIS Spectrum live animal imaging system. The tumors were excised at 72 hours. Ex vivo images of the excised tumor were taken at 72 hours with both the fluorescence contact imager and the IVIS. Results: Imaging data was obtained in 5 mice – 3 implanted with HER2+ tumors and 2 implanted with HER2(-) tumors. One HER2(-) mouse was not injected with the fluorescent imaging agent to act as a control. Binding of the fluorescent imaging agent to the HER2+ tumors was visible in all 3 HER2+ mice by the fluorescence imager and the IVIS by hour 9. The fluorescence imager visualized all 3 HER2+ tumors at all subsequent in vivo time points and in the excised tumor at 72 hours. Imaging by the fluorescence imager occurred in <100 ms (1.25cm^2/s) for real time imaging. No fluorescence was seen by the fluorescence imager in the HER2(-) tumor or the control mouse tumor both in vivo and in the excised tumor. Imaging by the IVIS confirmed the fluorescence imager's findings. Conclusions: The fluorescence imager synergistically paired with the fluorescent imaging agent readily distinguished between HER2+ and HER2(-) tumors in mice both in vivo and ex vivo in real time, demonstrating applicability in the operating room setting.



P69

Two-Stage Free-Flap Breast Reconstruction Following Mastectomy Diminishes Post-Operative Narcotic Use and Length of Stay: A Single Institution Pilot Study A.M. Mateo,* C. McGreevy, E. Jablonka, D. Sataloff, A. Brooks, S. Kanchwala, L. De La Cruz. *Surgery, University of Pennsylvania, Philadelphia, PA.*

INTRODUCTION: Abdominally-based free-flap breast reconstruction has evolved to provide patients with an acceptable autologous reconstruction while minimizing morbidity at the abdominal donor site. With the aim of reducing surgical morbidity, post-operative narcotic use and hospital length of stay (LOS), the authors introduce a two-staged approach by exploiting the

advantages of two-staged single-perforator free-flap delay (SPFFD). METHODS: A prospective study was conducted of patients undergoing mastectomy opting for autologous reconstruction who were candidates for a two-staged SPFFD. Candidates were selected based on pre-operative CAT scan showing a sizeable, low-positioned perforator, with a short intramuscular course. Post-operatively, patients were managed via nonnarcotic ERAS protocol using a combination of NSAIDs, Gabapentin pre-operatively and added tramadol as needed in the post-operative period. Outcomes of interest were post-operative narcotic use, LOS (days), and flap complication and/or loss. RESULTS: Institutional Review Board (IRB) approval was obtained. We prospectively enrolled patients at our institution from September 2017 to April 2018. A total of 80 patients (108 flaps) had a two-staged SPFFD procedure. None (0%) of the patients required narcotics during either hospitalization (Stage I/II). Average LOS was 1.1 and 2.1-days following Stage-I and II, respectively. Two flaps had venous congestion (1.9%) during Stage II and one (1.0%) flap loss was reported during the study period. CONCLUSION: In the era of over utilization of narcotics and universal healthcare, this pilot study shows the feasibility of the two-staged SPFFD in carefully selected patients with low morbidity and the benefit of decreasing LOS and narcotic use. The second stage of this study is currently underway and future studies will help further elucidate the impact of two-staged SPFFD on previously reported outcomes such as cost, cosmesis, patient satisfaction, and quality of life.

P70

Breast MRI May Identify Patients that Benefit from Oncolytic Therapy in a Novel Phase I Trial Combining Neoadjuvant Talimogene Laherparepvec (TVEC) with ACT Chemotherapy in Patients with Triple Negative Breast Cancer (TNBC)

L.D. Rothermel,* L. Khazai, B. Mooney, H.H. Soliman, B.J. Czerniecki. *Surgical Oncology, Moffitt Cancer Center, Temple Terrace, FL.*

Background: Pathologic complete responses to neoadjuvant chemotherapy (NAC) typically show resolution or significantly decreased tumor size for TNBC patients. In the ongoing investigator-initiated phase I/II trial of TVEC with NAC for TNBC patients, a phenomenon has been observed in certain patients wherein little change is seen in treated breast tumors on post-neoadjuvant MRI despite achievement of a pCR determined at the time of surgery. This report describes the pre- and post-neoadjuvant radiologic and pathologic characteristics for a patient achieving this unusual response Methods: On protocol, TNBC patients receive up to 5 injections of neoadjuvant TVEC at 2-3 week intervals with concurrent weekly paclitaxel (12 weeks) followed by dose-dense doxorubicin/cyclophosphamide (8 weeks). MRI assessment before and after neoadjuvant therapy was performed by a certified breast radiologist. Gross pathology and histology of the pre-treatment core biopsy and operative tumor tissue were evaluated by a certified breast pathologist. Comparative evaluation of MRI and pathologic responses of a separate patient with TNBC who achieved a "typical" pCR with NAC was used as a baseline Results: A patient with T3N0 stage IIIB TNBC was treated on protocol. Pre-treatment MRI showed a 7.5cm mass with diffuse type 3 peripheral rim enhancement. Core biopsy revealed poorly differentiated IDC with patchy necrosis. Post-treatment MRI showed a residual 5.3cm mass with notably decreased and clumped rim enhancement. Mastectomy with a negative sentinel node biopsy was performed. Gross pathology showed a 6x4.5cm necrotic mass. Histology described a centrally necrotic tumor surrounded by fibrosis, inflammation and histiocytes (pCR) Conclusion: The achievement of a pCR without the typical finding of tumor resolution on MRI may represent the impact of neoadjuvant TVEC in TNBC patients whose tumors would not have attained a pCR with chemotherapy alone. Analysis of the MRI features for all patients in the phase I component of this clinical trial is ongoing

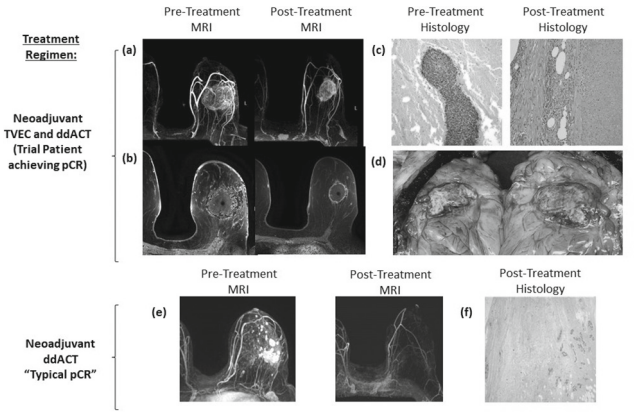


Figure 1. Residual breast mass despite a pathologic complete response (pCR) for a patient treated with neoadjuvant TVEC and ddACT versus a patient with tumor resolution after neoadjuvant ddACT. (a) DCAD-MIP-Rotated Subtraction Axial MRI; (b) DCAD-MIP-Thin Slab DCE Axial MRI; (c) H&E stain, 10x; (d) Gross operative pathology; (e) DCAD-MIP-Rotated Subtraction Axial MRI showing no visible tumor after ddACT alone; (f) H&E stain, 4x, fibrotic stroma with no glands, no viable tumor

P71

Alterations in Breast Cancer Biomarkers Following Neoadjuvant Therapy S. Walcott-Sapp,* M. Lee, M. Srour, S. Kim, F. Amersi, A.E. Giuliano, A. Chung. *Cedars-Sinai Medical Center, Los Angeles, CA.*

Introduction The occurrence and impact of changes in biomarkers (BM) in patients with residual disease (RD) after neoadjuvant systemic chemotherapy, targeted therapy, and/or endocrine therapy (NAT) is unclear. The purpose of this study was to examine the prevalence of BM (hormone receptor (HR) and HER2) change from positive to negative or negative to positive after NAT and the effect of changes on disease free survival (DFS) and overall survival (OS). Methods 303 patients with stage I-III invasive breast cancer treated with NAT from 2008 to 2016 were identified from a prospectively maintained database. BM status of all tumors was determined prior to NAT. Patients with RD after NAT were identified, and BM status was repeated. HR and HER2 positivity was determined by American Society of Clinical Oncology guidelines. DFS and OS were compared using Kaplan-Meier estimates with log-rank test comparisons in four groups: pathologic complete response (pCR; group A), no change in BM (group B), change in either estrogen or progesterone receptor which did not alter HR status (group C), and change in at least one BM with resultant change in HR or HER2 status (group D). Subgroups of those with no change and those with HR change were examined (see Table 1, groups B1, B2, D1, D2). Results 61% of patients had RD after NAT and change in at least one BM occurred in 32.8% of patients with RD (see Table 1). Group A had greater DFS than any of the other three groups (p=0.013 vs. B, <0.001 vs. C, 0.011 vs. D). Group A had greater OS than B (p=0.027) or D (p=0.009). OS was worse in group D1 compared to group B1 (p=0.013). Group D2 had improved OS compared to group B2 (p=0.028). Median follow up was 3.6 years. Conclusion PCR after NAT is associated with improved survival compared to RD independent of changes in BM status. Among those with RD, BM status change overall was common and only impacted survival in specific subgroups of HR+ or TN disease with BM change. Retesting BMs after NAT is important because alteration in BM status may have therapeutic and prognostic implications.

	Number of patients	Estimated 3 year DFS Rate (95% CI)	Estimated 3 year OS Rate (95% CI)
A. pCR	117 (38.6%)	91.7% (8.9, 95.8)	99.1% (93.9, 99.9)
B. No BM change	125 (41.3%)	80.2% (71.3, 86.5)	91.5% (84.2, 95.5)
B1. HR+HER2- unchanged	61 (20.1%)	87.2% (74.9, 93.7)	98.2% (87.8, 99.7)
B2. TN unchanged	41 (13.5%)	64.4% (46.2, 77.8)	76.2% (57.5, 87.5)
C. Change in BM without change in HR or HER2	25 (8.3%)	81.0% (56.9, 92.5)	100% (unable to estimate)
D. Change in HR or HER2 status	36 (11.9%)	67.6% (48.8, 80.7)	84.8% (66.8, 93.4)
D1. HR+HER2- to TN	6 (2.0%)	50.0% (11.1, 80.4)	66.7% (19.5, 90.4)
D2. TN to HR+HER2-	4 (1.3%)	75.0% (12.8, 96.1)	100% (unable to estimate)

P72

Thickened Lymph Node Cortex May Not be Associated with Metastasis in African-Americans with Breast Cancer H. Tran,* C. Mylander, M. Rosman, L. Martino, K. Waite, L. Tafra, D. Pack, T. Sanders, R.S. Jackson. *Anne Arundel Medical Center, Baltimore, MD.*

Introduction: A sonographically thickened lymph node cortex can be a manifestation of inflammation or malignancy. Many breast centers categorize an axillary lymph node (LN) with cortical thickness >3mm as abnormal and recommend core needle biopsies of these LN. Our breast center has an ethnically heterogeneous population, and our radiologists have observed that African American (AA) patients with breast cancer (BC) and a thickened LN cortex often do not have metastasis on LN core biopsy. There has not been a study comparing axillary ultrasound (AxUS) in AA versus non-AA patients. We undertook a study to determine whether false positive (FP) rate of axUS differed by ethnicity, especially for axUS defined as abnormal base on thickened LN cortex. Methods: This was a retrospective analysis of BC patients at a single center with (1) non-suspicious axillary physical exam, (2) a suspicious AxUS, and (3) a LN core biopsy. At our center, AxUS having any of the following is generally considered suspicious: cortical thickness > 3mm, loss of fatty hilum, asymmetrical cortical thickening, cortical bulge or nodule, or asymmetrical enlarged nodes >10mm. We compared AxUS FP rates in AA vs. non-AA. A FP AxUS was defined as a suspicious AxUS with negative core biopsy. BMI was also assessed, as it was thought that obesity-related intertrigo could lead to FP AxUS. Results: 157 patients met the above criteria. 36 were AA and 121 were Non-AA. The FP rate of a suspicious AxUS for all patients was 35.0%, and was similar by race (Table). 12 AA and 36 non-AA had thickened cortex as the only abnormality on AxUS. The FP rate in this subset was 58.3% in AA versus 38.9% in Non-AA (p=0.24). Mean BMI was similar in both groups. Conclusion: Although the FP rate of AxUS was similar by race overall, there was a trend towards higher FP AxUS in AA for the subset of patients with thickened cortex, despite similar BMI in AA vs. non-AA patients. Further research is warranted to determine if this finding holds true in larger cohorts. If validated in a larger cohort, it could be useful to define cortical thickness differently in AA vs. non-AA patients, preventing unnecessary LN biopsies.

Rate of false positive (FP) axillary ultrasound in breast cancer patients, by ethnicity. FP axillary ultrasound was defined as a suspicious axillary ultrasound with negative node needle biopsy. BMI and cortical thickness are also displayed.

All Cases						
	# FP, (%)	p-value	Mean BMI	p-value		
AA (n=36)	12, (33.3%)	.81	32.8	.004		
Non-AA (n=121)	43, (35.5%)		29.1			
Cases with cortical thickening resulting in a core biopsy of a node						
	# FP, (%)	p-value	Mean BMI	p-value	Mean LN Cortex (mm)	p-value
AA (n=12)	7, (58.3%)	.24	28.4	.48	5.00	.92
Non-AA (n=36)	14, (38.9%)		29.6		4.93	

P73

Triple Negative Breast Cancer Patient-Derived Xenografts have better engraftment rate and grow faster by orthotopic approach M. Okano,* M. Oshi, K. Takabe. *Breast Surgery, Roswell Park Cancer Institute, Buffalo, NY.*

Backgrounds: Patient-Derived Xenograft (PDX) has come into the limelight of breast cancer research to be used for pre-clinical studies. Some of its weaknesses are its poor engraftment rates and slow growths so improvement of the models especially in engraftment and tumor growth are in urgent need. We hypothesized that orthotopically implanted tumors (Ortho) engraft better and grow faster compared with subcutaneously implanted PDX (SQ). Methods: A total of 11 tumors from primary breast cancers were xenografted into NSG mice. 6 tumors were ER(+)HER2(-) and 5 tumors were triple negative (TN). Results: The overall engraftment rate was significantly better in Ortho than SQ (70.1% (n=115/164) vs. 32.1% (n=45/140), p<0.01) in TN tumors. Ortho tumors grew remarkably faster than SQ tumors and had more abundant mitotic figures compared with SQ tumors (19.2 vs 7.9, p<0.01). Ortho tumors also had more Ki-67 positive cells than SQ tumors (31.5 vs 21.8, p=0.015). Ortho tumor engraftment rate of 1st generation was low (40% (n=24/60)), but the rate of 2nd (84.6% (n=44/52)) and 3rd (88.9% (n=32/36)) generation was significantly increased (p<0.001). On the other hand, SQ tumor engraftment rate of each generation were 20% (n=12/60), 39.2% (n=11/28) and 52.8% (n=19/36), respectively, and they were significantly low than that of Ortho. The time it took for the 1st generation to grow was the longest between 3 generations (1st; 152days, 2nd; 66days, 3rd; 63days, p<0.01). ER positive cancer xenograft revealed significantly lower engraftment rate (17.8% (n=13/60) vs 70.1% (n=115/164), p<0.01) and slower tumor growth than TN xenograft despite being transplanted in Ortho. Conclusions: Orthotopical implantation showed better engraftment rate and faster growth than heterotopic implantation in triple negative breast cancer PDX.

P74

The Effects of Body Mass Index on Duration of Surgery and Outcomes in Nipple-Sparing Mastectomy C. Webb,* N. Gupta, P. Cronin, C. Stucky, N. Wasif, B. Pockaj, R. Gray. *Surgery, Mayo Clinic Arizona, Phoenix, AZ.*

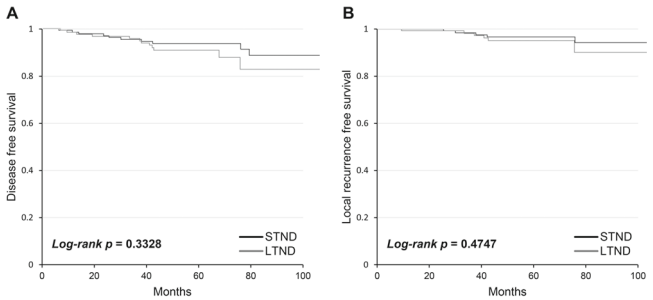
Background. Nipple-sparing mastectomy (NSM) has been shown to be effective and oncologically safe. To date, no study has investigated the relationships between body mass index (BMI), time of surgery (TOS), and nipple-areolar complex (NAC) and mastectomy flap complications. Methods. We performed a retrospective review of patients who had attempted NSM from 2006-2018. TOS was defined as surgery start to stop time by a surgical oncologist and plastic surgeon. Any evidence of NAC or mastectomy flap necrosis (full or partial thickness) was considered an adverse outcome. Data was analyzed by the type of breast reconstruction and laterality by Wilcoxon rank-sum test and logistic regression. Results. A total of 510 NSM were attempted among 294 patients, with 22 converted to skin-sparing mastectomy based on intra-operative pathology (4.3%). Of these, 266 (90.5%) patients had implant/expander reconstruction (200 bilateral, 66 unilateral) and 28 (9.5%) had autologous tissue (primarily free flap) reconstruction (16 bilateral, 12 unilateral). Median BMI for all patients was 23.4 (range 15.8-48.1). Median TOS in the prosthetic group was 266 minutes (215 unilateral, 275 bilateral), and in the autologous tissue group was 529 minutes (387 unilateral, 591 bilateral). Higher BMI correlated with increased TOS (r = 0.33, p<.0001). Median TOS ranged from 236 minutes for patients with BMI <20 to 358 minutes for those with BMI >40. Increasing TOS and BMI were not associated with increased odds for NAC (OR = 1.00, 1.04, CI = 1.00-1.00, 0.99-1.09, respectively) or mastectomy flap complications (OR = 1.00, 0.97, CI = 1.00-1.00, 0.91-1.04, respectively). For patients that had implant/expander reconstruction, a higher ratio of implant size to mastectomy mass was not associated with higher rates of ischemic complications (OR=0.83, CI = 0.58-1.20). Conclusion. In NSM with reconstruction, higher BMI is associated with an up to 50% longer time of surgery, but among properly selected patients was not associated with higher NAC or mastectomy flap complications. Therefore, high BMI is not a contraindication to NSM with reconstruction, but surgeons should recognize the increased time required.

P75

Long Term Outcomes of Nipple-Sparing Mastectomy with Immediate Breast Reconstruction Based on Tumor-Nipple Distance J. Ryu,* J. Lee, E. Alsharif. *Surgery, Samsung Medical Center, Seoul, Korea (the Republic of).*

Background: The nipple-sparing mastectomy (NSM) has gained popularity in the last decade for treating breast cancer patients for it better aesthetic and psychologic outcome in those patients. There is still a debate regarding the oncological safety and outcome in those patients especially with short tumor nipple distance (STND ≤ 2.0 cm) with long term follow up. Our aim in this study to compare the long term oncological outcome between the LTND (define) group > 2.0 cm and STND group ≤ 2.0 cm in preoperative MRI with clear intraoperative frozen biopsy of nipple margin from tumor cells. Materials and Methods: A prospective observational study using retrospectively collected data of Samsung Medical Center that included 245 patients who underwent for NSM followed by immediate breast reconstruction (IBR) between 2008 and 2014. All patients underwent for preoperative breast MRI and intraoperative frozen biopsy and dived into two groups (LTND > 2.0 cm and STND ≤ 2.0 cm). Results: Overall 245 patients were identified and divided LTND (117 patients) and STND (128 patients). Mean age was 42.4 (standard deviation, SD, ±7.6). The overall follow up duration ranges from 15-109 months with mean of 60.5 (±19.9). The mean of follow up duration in LTND group was 63.9 (±20.1) whereas in STND was 56.9 (±19.2). There were no significant differences between the two groups regarding lymphovascular invasion, nuclear grade, multiplicity, nodal status, hormonal status, or

HER2-neu status. The mean TND was 0.6 cm for STND and 3.2 cm LTND. Locoregional recurrence in STND reported in 4 cases (3.1%), 6 cases (5.1 %) in the LTND group. Death occurred in 3 cases (1.2%) under the study 2 cases of STND and 1 case of LTND. There was no significant difference between the two groups regarding disease free survival as well as local recurrence ($p = 0.334$) and ($p = 0.477$) respectively (Figure 1). Conclusion: The long term follow up of patients treated with NSM revealed that the oncological safety is not affected by the TND as much as intraoperative frozen biopsy of nipple margin is free of tumor cells.



P76

ACOSOG Z11 Multimodal Treatment Adherence and Lymphedema Rates J. Gunn,* A. Ferlin, E. Lesser, A. Elder, T. Gibson, L. Vallow, E.M. Gabriel, S.P. Bagaria, S. McLaughlin. *Mayo Clinic, Jacksonville, FL.*

Background: Following the publication of Z0011, many studies have addressed changes in surgical management, but few have quantified adjuvant treatment adherence or lymphedema (LE) rates. We sought to identify patients treated according to Z11, quantify treatment violations, and explore LE rates. Methods: We retrospectively reviewed 504 women with cT1/T2 N0 breast cancer undergoing BCT at our institution between 5/2011 and 6/2016 and stratified patients according to nodal status and axillary management. We collected clinicopathological data and adjuvant therapy adherence. We recorded Z11 treatment violations when no systemic/endocrine therapy or radiation other than whole breast (WB) radiation was given. Two clinicians measured a subset of patients for LE preoperatively, at 6 months, and annually, defining LE as a relative volume change ≥10%. Fisher's Exact test was used to compare proportional differences among Z11 patients based on treatment violations and for LE rates between patient groups with a $p<0.05$ as significant. Results: Overall, 487/504 (97%) patients completed SLNB while 17(3%) proceeded to ALND. Among the SLNB cohort 52/504(10%) patients had 1 or 2 positive nodes and had no further axillary surgery per Z11 eligibility. Only 11/52(21%) received multimodality adjuvant systemic and radiation therapy accordingly to Z11 criteria while the remaining 41(79%) did not. Deviations in radiation therapy accounted for the most violations, $p < 0.001$ (Table 1). No differences existed in patient age, tumor characteristics, hormonal status, or facility of radiation completion among those with or without violations (all p's > 0.087). At 3yrs, LE was diagnosed in 1.8% SLNB, 10% WB+RNI, and 20% ALND patients ($p=0.014$). Conclusion: Although surgeons have widely adopted Z11 minimizing axillary surgery, radiation deviations are common. The addition of RNI significantly increases the risk of LE over SLNB alone.

Matrix of adjuvant systemic and radiation violations in Z11 eligible patients

N=41	No XRT	Partial Breast XRT	WB+RNI
Chemo+endocrine	2(4.9%)	-	18(43.9%)
Chemo only	1(2.4%)	-	4(9.8%)
Endocrine only	-	-	9(22.0%)
Neither	5(12.2%)	1(2.4%)	1(2.4%)

P77

Feasibility of Breast Conserving Therapy (BCT) in Early Stage Breast Cancer Patients (ESBC) with Cosmetic Augmentation L. Kopicky,* B. Pople, N. Dekhne. *Surgery, William Beaumont Hospital, Royal Oak, MI.*

INTRODUCTION BCT in patients with prior implant augmentation is reported to be associated with inferior cosmetic and oncologic outcomes. METHODS Retrospective chart review of patients with prior augmentation who presented with ESBC (Stage 0-IIA) and were treated with BCT between Jan 1, 2007 and Dec 31, 2016 was performed. Patients with a previous cancer history, explanted implant prior to radiation therapy (RT), declined RT following BCT, and missing treatment data were excluded. Age, BMI, smoking history, RT boost, and cosmetic outcome at 6, 12, and 18-months are reported. Cosmetic outcome was determined by physician reporting in EMR. Acceptable cosmetic outcome included "excellent" or "good" description. Descriptive statistics was performed to determine outcomes with respect to cosmesis and local recurrence. RESULTS There were 123 patients with prior breast augmentation who subsequently received BCT for ESBC and 80 patients met selection criteria. Median follow-up was 34.9 months. Seventy-four patients were treated with whole breast irradiation and six patients received accelerated partial breast irradiation. Mean age at diagnosis was 57 years. Acceptable cosmetic outcome was observed in 69 patients (86.25%) at 18-months post-treatment and 54 patients (67.5%) at final follow-up, an average of 34.9 months post-treatment. Patients who had a BMI ≥ 30 kg/m^2 (n=4), prepectoral implants (n=3), or received radiation boost (n=20) were more likely to have cosmetic outcome described as "fair" or "poor" at the 6, 12, or 18-month follow-up. Twenty-seven patients (33.75%) required implant removal or revision, due to capsular contracture (n=20) or implant rupture (n=6); one revision was due to patient preference to decrease breast size. Eight patients (10%) developed local recurrence within an average of 44.9 months. Of these 8 patients, one patient had positive inferior and deep margins but declined re-excision. CONCLUSION Breast conserving surgery with RT produced favorable cosmetic outcome and local control in the majority of patients with prior breast augmentation.

P78

Racial Differences in Tumor Biology: An Explanation for the Hispanic Paradox in Breast Cancer Y. Huang,* D.R. Heller, T. Park, D. Bertoni, M. Pronovost, N. Horowitz, A. Chagpar, B.K. Killelea, D.R. Lannin. *Department of Surgery and Yale Comprehensive Cancer Center, Yale University School of Medicine, New Haven, CT.*

Introduction: There is an abundance of literature suggesting that black women have reduced breast cancer survival secondary to barriers in access to care related to lower socioeconomic status. Hispanic women share similar socioeconomic status but do not demonstrate the same reduced survival. This has been termed the "Hispanic Paradox" and the explanation is unknown. Methods: We identified women in the National Cancer Database (NCDB) who were diagnosed with invasive breast cancer between 2010 and 2015. The distribution of socioeconomic factors, breast cancer survival, molecular tumor type, and Oncotype DX recurrence scores (RS) were compared by racial-ethnic group. Results: Among the 1,040,437 patients with invasive breast cancer, 823,855 (79.2%) were Non-Hispanic White (NHW), 121,645 (11.7%) were Non-Hispanic Black (NHB), and 58,821 (5.7%) were Hispanic. When compared to NHW women, NHB and Hispanics were more likely to have no health insurance or Medicaid (5.8% for NHW vs 17.4% for NHB and 28.7% for Hispanics); more likely to live in areas with poor education (10.3% vs 30.2% and 45.5% respectively); and more likely to live in areas with low income (11.3% vs 37.4% and 24.0%, $p<0.001$ for all comparisons). Despite this, the 6-year overall survival for breast cancer patients under 65 (chosen to reduce non-breast cancer deaths and make the age distribution more similar among groups) was 87% for NHW, 78% for NHB, and 87% for Hispanics. There were large biological differences between the groups. NHB had 23.0% triple negative cancers, compared to 10.8% for NHW and 13.8% for Hispanics. NHB also had 47.1% high grade tumors, compared to 29.4% for NHW and 38.2% for Hispanics ($p<0.001$ for all comparisons). For hormone receptor positive tumors, Oncotype DX RS was available for 24% of patients. As shown in Table 1, NHB, but not Hispanics, had higher RS in comparison to NHW. Conclusion: Breast cancer biology is similar between Hispanic and NHW women. These data do not imply that socioeconomic status is insignificant, but they do suggest that major breast cancer outcome differences between blacks, whites and Hispanics are mediated more by tumor biology than by socioeconomic factors.

Table 1: Oncotype DX Recurrence Score for Women with Hormone Receptor Positive Breast Cancer

Recurrence Score	Non-Hispanic White	Non-Hispanic Black	Hispanic
Low	47,176 (28.6%)	4,076 (26.8%)	2,352 (28.8%)
Intermediate	94,203 (57.1%)	8,133 (53.5%)	4,625 (56.6%)
High	23,503 (14.3%)	2,995 (19.7%)	1,188 (14.5%)

P < 0.001.

P79

The Presence of Immune-Eliminating Cells in Androgen Receptor Low Tumor is a Possible Factor Affecting Patients Outcomes in ER-Positive Breast Cancer M. Okano,* E. Katsuta, M. Asaoka, X. Peng, L. Yan, K. Takabe. *Breast Surgery, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction: The androgen receptor (AR) is expressed in 50–90 % of breast cancers and its role in breast cancer is mechanistically complex and remains controversial. It was demonstrated that high AR expression related with resistance to tamoxifen and aromatase inhibitors. Also, it has been demonstrated that AR supports estradiol-mediated ER activity in ER/AR both positive breast cancer cells. In this study, we investigated the association of AR mRNA expression and patient survival using gene expression data of the publically available large cohort. Methods: Clinical and gene expression data were obtained from The Cancer Genome Atlas (TCGA) and METABRIC through cBioPortal. Disease free survival (DFS), overall survival (OS), gene set enrichment analysis (GSEA) and CIBERSORT analysis were conducted comparing high and low AR expression groups. Results: AR high and low expression group were 817 and 272 patients in TCGA cohort and 1068 and 356 patients in METABRIC cohort, respectively. AR expression was significantly higher in ER+ tumors compared toER- tumors (p<0.001) in both cohorts. The high expression AR group showed significantly worse OS in ER+ patients in TCGA cohort (p=0.007). In METABRIC cohort, AR high group showed significantly worse OS in Luminal B patients (p=0.007). To explore the mechanism of these results, GSEA was conducted. Protein secretion related gene set (Normalized enrichment score; NES=1.76, p=0.01) and estrogen response related gene set (NES=1.67, p=0.02) were significantly enriched with high AR. On the other hand, DNA repair related gene sets was significantly enriched in AR low expressed tumors in ER+ tumors (NES=-1.75, p=0.01). In CIBERSORT analysis, AR high tumors were negatively associated with immune-eliminating cells, such as CD8 T-cells, Gamma-Delta T-cells and memory B-cells (p>0.01). Conclusions: Low expression of AR showed better progress in ER+ breast cancer. Low AR expression tumors in ER+ tumors were enriched DNA repair related gene and it might be associated with patients' survival.

P80

Prediction of Axillary Lymph Node Response Based on Breast Pathologic Complete Response and Breast Cancer Subtype After Neoadjuvant Chemotherapy J. Ryu,* J. Lee, S. Nam, S. Kim, S. Lee, J. Yu. *Surgery, Samsung Medical Center, Seoul, Korea (the Republic of).*

Introduction: In HER2 (+) or triple-negative (TN) breast cancer, pathologic complete response (pCR) have increased with advances in targeted therapy. Recent, two studies reported those of patients with clinically lymph node-negative (cN0) and HER-2 (+) or TN breast cancer underwent neoadjuvant chemotherapy (NAC) showed a breast pCR (BpCR) had highly related to axillary pCR (ApCR). We investigated the factors that predicted ApCR based on BpCR and subtype. **Method** This retrospective study reviewed data from Samsung Medical Center, from 2008 to 2016. Participants included patients with cT1-3, cN0/cN1-3 breast cancer who received NAC followed by surgery. Non-ApCR based on BpCR were compared in cN0 and cN(+). BpCR was defined no invasive disease (ypT0 or ypTis) on permanent pathologic results. **Results** A total of 1,044 patients with cT1-3, cN0/cN(+) breast cancer with NAC followed by surgery were identified. Median age was 45.4 years. Of 52 patients with cN0 HER-2 (+) breast cancer, 20 (38.5%) achieved BpCR and of those, only one patient was non- ApCR (5.0%). In 72 patients with cN0 TNBC, 27 (37.5%) achieved BpCR, and of those, only one patient was non- ApCR (3.7%). Non- ApCR were higher in patients with cN0 and residual disease in the breast; 8 of 34 (23.5%) with HER-2 (+) breast cancer and 13 of 25 (52.0%) with TN breast cancer with non- BpCR (all $p < .001$, respectively). Among 294 patients with cN(+) HER-2 (+) breast cancer, 114 (38.8%) achieved BpCR, with 13 of those (11.4%) were non- ApCR. In 266 patients with cN(+) TNBC, 93 (35.0%) achieved BpCR, of these 26 (28.0%) were non- ApCR. BpCR rates in HR (+)/HER-2(-) disease were 8 of 54 (14.8%) for cN0; 62 of 315 (19.7%), for cN(+). ApCR were 16 of 16 (100.0%) in cN0 and 7 of 31 (77.4%) in cN(+) disease with BpCR. ApCR were 30 of 46 (65.2%) in cN0 disease and 51 of 253 (20.2%) in cN1 disease with non- BpCR. **Conclusion** In patients with cN0 HER-2 positive or TN breast cancer showed high BpCR. Among patients with BpCR, only one patient in each group showed non- ApCR, it might be considered to omit of axillary sentinel lymph node biopsy in these highly selected patients.

P81

Influence of Facility Characteristics and Time Trends in Modality of Breast Reconstruction D. Boczar,[1] D. Restrepo,[1] J. Gunn,[1]* E.M. Gabriel,[1] K. Attwood,[2] S. McLaughlin,[1] S.P. Bagaria,[1] R. Lemini,[1] A. Sisti,[2] A. Forte.[1] *1. Mayo Clinic, Jacksonville, FL; 2. Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Background: The aim of this study was to determine the influence of facility characteristics in determining breast reconstruction. We hypothesized that academic facilities are related to greater access to breast reconstruction, as previously suggested in the literature. Methods: Using the National Cancer Data Base (NCDB) we selected female breast cancer patients <70 who underwent mastectomy from 2004-2015. Facility type and location were summarized by reconstructive modality. Analysis of reconstruction modality was performed over 3-year intervals. Results: A total of 189,213 patients met inclusion criteria. Interestingly, the majority of patients (70%) did not have reconstruction during this study period. However, the proportion of patients who did not have reconstruction steadily decreased from 82% in 2004-2007 to 63.7% in 2013-2015 (p<0.001). Among the remaining 30% of patients who did have reconstruction, approximately 10% had autologous tissue based construction, 10% had tissue expanders, and 10% had combined or unspecified approaches. There were no significant differences in reconstruction approach among treatment facility type. Regarding geographic location, the majority of patients were reconstructed in metropolitan areas (89.3%), followed by urban (9.5%) and, rural areas (1.2%), p<0.01. However, within each location, there were no significant differences in reconstruction approach. Conclusion: Differences in reconstructive rates exist based on facility type and geographic location, but interestingly the approach to reconstruction is similar. More striking, the majority of patients did not opt for reconstruction during the study period. However, we demonstrated a trend in the reduction of patients not receiving reconstruction.

P82

The Effect of Surgeon Gender on Breast Cancer Surgical Practice Patterns and Outcomes H. Vora,[1]* F. Amersi,[1] A. Chung,[1] R. Rajani,[2] A.E. Giuliano.[1] *1. cedars sinai medical center, Los Angeles, CA; 2. USC, Los Angeles, CA.*

Background: Recent studies have demonstrated lower mortality and readmission rates in patients cared for by female internists when compared to male internists. Few studies have looked at the effect of surgeon gender on breast cancer (BC) practice patterns and outcomes. The objective of our study was to determine if there was any difference in surgical management or patient outcomes in BC treatment based on surgeon gender. Methods: We identified BC patients in a prospectively maintained database who underwent surgery from 2009-2016. Variables studied included surgeon gender, patient characteristics, clinical management, and patient outcomes. Results: A total 894 patients met inclusion criteria. 10 male and 4 female surgeons were included in the analysis. Despite the disparity in the number of female surgeons, they performed 358 (40.0%) of the operations compared to 536 (60.0%) procedures performed by male surgeons. Males surgeons treated significantly older patients compared to female surgeons (60.8 vs 57.5 years, p<0.001). There were no differences in stage between each cohort (Table 1). Male surgeons had higher rates of lumpectomies (71.6% vs 58.7%, p<0.001). Female surgeons did more mastectomies than male surgeons (41.6% vs 28.5%, p<0.001) and performed more nipple sparing mastectomies regardless of stage (36.5% vs 17.1%, p<0.001). The rates of axillary dissection did not differ between the two groups (6.7% vs 10.1%, p=0.794). Male surgeons had a significantly lower length of stay than female surgeons (0.8 vs 1.1 days, p=0.001). Both male and female surgeons had overall low post-operative complication rates (2.1% vs 1.7%, p=0.818) and 30-day readmission rates were similar between the two groups (male 1.7% vs female 4.2% surgeons, p=0.836). At a median follow

up of 16.33 months, there was no difference in disease free survival (92.6% vs 95.1%, p=0.879) and overall survival (99.2% vs 99.3%, p=1) between cohorts. Conclusion: Despite similar patient stage, female surgeons performed more mastectomies and nipple sparing mastectomies compared to their male counterparts, without any significant difference in post-operative complications, readmissions, disease free and overall survival.

Table 1: Patient Characteristics, Management, and Outcomes of Female Surgeons Compared to Male Surgeons

	Female Surgeon	Male Surgeon	p Value
Staging n(%)			
Stage 0	61 (17.0)	91 (17.0)	1.000
Receptor Profile			
ER +	54 (88.5)	77 (79.4)	0.633
Her2 +	12 (19.6)	29 (31.9)	0.135
Stage 1	156 (43.6)	265 (49.4)	0.087
Receptor Profile			
ER +	139(89.1)	244(92.4)	0.285
Her2 +	21 (13.6)	21 (7.9%)	0.090
Stage 2	111 (31.0)	151 (28.2)	0.369
Receptor Profile			
ER +	86 (77.5)	127 (84.1)	0.201
Her2 +	34 (30.6)	27 (17.8)	0.018
Stage 3	30 (8.4)	29 (5.4)	0.098
Receptor Profile			
ER +	23 (76.6)	23 (79.3)	1.000
Her2 +	12 (40)	7 (23.3)	0.267
Surgical Management n(%)			
Lumpectomy	210 (58.7)	384 (71.6)	<0.001
Mastectomy	148 (41.6)	152 (28.5)	<0.001
• Nipple Sparing Mastectomy	54 (36.5)	26 (17.1)	<0.001
Sentinel Node Biopsy	282 (78.8)	452 (84.3)	0.598
Axillary Dissection	36 (10.1)	36 (6.7)	0.794
Length of Stay (days)	1.1	0.8	0.001
Rates of Post-Operative Complications n(%)	9 (1.7)	11 (2.1)	0.818
Rates of 30-Day Readmission n(%)	16 (4.2)	9 (1.7)	0.836
Medical Management n(%)			
Chemotherapy	125 (34.9)	128 (23.9)	<0.001
Radiation	184 (51)	323 (60.3)	0.009
Hormone Therapy	261 (86)	425 (90.2)	0.104
Disease Free Survival (n%)	338 (92.6)	510 (95.1)	0.879
Overall Survival n(%)	355(99.2)	534 (99.3)	1.000

P83

Role of Sentinel Lymph Node Biopsy(SLNB) in Prophylactic Contralateral Mastectomy(CPM) or Bilateral Prophylactic Mastectomy(BPM) for BRCA1-2 Genetic Mutation L. Poole,* C. Chen, W.B. Carter, T. Frazier. *Breast, Bryn Mawr Hospital, Havertown, PA.*

Background: Genetically at-risk women can reduce their breast cancer risk from greater than 50% to 2-5% with prophylactic mastectomy. During mastectomy for cancer or prophylaxis, a SLNB is performed to rule out occult metastasis in lymph nodes(LN), which may require a complete axillary node dissection with associated morbidity of 20%. SLNB carries a 1-7% risk of complication, and has a false negative rate of 3-7%. Preoperative MRI is considered standard to evaluate high risk patients undergoing BPM or CPM, with a high sensitivity (>90%) for detection of occult primary cancers. Genetic risk patients have a low risk (<5%) of harboring occult cancer, but there is little data to determine the risk of occult LN metastasis in these patients. The aim of this study was to identify the risk of occult LN metastasis in genetically high-risk patients with negative MRI undergoing BPM for risk reduction or CPM for symmetry. Methods: A retrospective, IRB-approved, single institution study included all patients (1/1/2010 – 2/29/2016) identified with a BRCA genetic mutation who subsequently underwent BPM or CPM for symmetry. Patient demographics, tumor characteristics, genetic mutations, preop MRI and SLNB results were evaluated. The primary endpoint was incidence of occult metastasis in SLN in patients with negative MRI. Results: 120 patients were identified with BRCA1/BRCA2 mutation. Male patients comprised 28/120 and were excluded. Of the remaining 92 female patients, most are still undergoing surveillance, but 27 had 49 mastectomies for BPM or CPM. One patient did not have a documented preoperative MRI and was excluded. Of the 47 evaluable mastectomies, 30 had SLNB. No LN metastasis or occult breast cancer was identified on final pathology in any patient with a negative preoperative MRI. Conclusion: Genetically at-risk patients have a low risk of harboring occult cancer (<5%) not detected by preoperative MRI. Our study supports this data with no occult breast cancer identified on final pathology in breast or LNs. In patients with genetic risk undergoing BPM or CPM with a negative MRI, SLNB can be safely eliminated.

P85

Racial, Ethnic, Socioeconomic and Geographic Disparities in Survival Among Women with Breast Cancer T. Yen,* Z. Garacci, P. Laud, A. Nattinger, L. Pezzin. *Surgery, Medical College of Wisconsin, Milwaukee, WI.*

BACKGROUND: Since 2000, significant efforts have focused on reducing the large disparities in cancer burden by race/ethnicity, socioeconomic status (SES), and geography. We sought to examine current disparities in survival in a nationwide cohort of women with breast cancer. METHODS: Women diagnosed with stage I-III unilateral invasive breast cancer from 2007 to 2012 with survival information through 2015 were identified within the National Cancer Data Base. Multivariable Cox regression models, adjusted for patient demographic factors, disease extent, hospital volume and two composite measures assessing appropriateness of locoregional (margin status and radiation therapy) and systemic (chemotherapy and hormonal therapy) treatment, were estimated to examine the association between race/ethnicity, SES, and geography with survival. RESULTS: Among 623,756 women, the mean age was 60 years (SD 13) and 85% were healthy; 84% were white, 11% black and 5% other races and 5% were of Hispanic ethnicity. The majority (62%) had a median annual income <$63,000; 33%, 6% and 4% had Medicare, Medicaid or unknown/no insurance, respectively; 16% lived in a non-metropolitan county. Nearly half (46%) had Stage II/III tumors; 80% had hormone receptor-positive tumors. Only 31% were treated at high-volume facilities. After controlling for potential confounders, women who were black, non-Hispanic, or of lower SES, as well as those with public or no insurance and those living in the South or Midwest regions had significantly worse survival (Table). For example, compared to women with private insurance, those with Medicaid had a 60% greater risk of death. CONCLUSIONS: Our results, based on a contemporary, nationwide cohort of women with incident breast cancer treated at Commission on Cancer-accredited facilities, indicate that substantial racial/ethnic, SES, and geographic disparities in survival remain, even after controlling for a wide array of patient, tumor and treatment factors. A better understanding of the root causes of persistent disparities is critical for the development and implementation of policies and interventions aimed at reducing, if not eliminating, cancer disparities.

Racial/ethnic, socioeconomic, and geographic factors	Hazard ratio (95% CI) of death
Race (white=ref)	-
Black	1.14 (1.11-1.17)
Other	0.79 (0.75-0.83)
Hispanic ethnicity (no=ref)	-
Yes	0.79 (0.75-0.82)
Unknown	1.02 (0.98-1.05)
Median annual household income (>= $63,000=ref)	-
$48,000-$62,999	1.11 (1.09-1.14)
$38,000-$47,999	1.20 (1.17-1.23)
< $38,000	1.26 (1.22-1.29)
Insurance (private or other government=ref)	-
Medicare	1.44 (1.40-1.48)
Medicaid	1.60 (1.55-1.66)
Not insured/unknown	1.36 (1.30-1.43)
Geographic region (West=ref)	-
Northeast	1.01 (0.98-1.04)
South	1.07 (1.04-1.09)
Midwest	1.10 (1.07-1.13)
Multivariable Cox regression model adjusted for patient age, Charlson-Deyo comorbidity score, tumor size, grade, nodal and hormone receptor status, appropriateness of locoregional and systemic treatment (Yen TW. Cancer 2017;123:957-66), hospital volume, urbanicity and year of diagnosis.	
All p-values <0.0001.	

P86

A Prospective Assessment of Postoperative Quality of Life After Axillary Lymph Node Dissection A. Barrio,* E. Zabor, S. Thomas, M. Stempel, B. Mehrara, M. Morrow. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction Axillary lymph node dissection (ALND) is associated with subjective and objective lymphedema symptoms, which can negatively impact quality of life (QOL). We sought to evaluate arm volume and QOL in the early postoperative (PO) period after ALND and identify factors associated with worse QOL. Methods Breast cancer patients treated with ALND were prospectively evaluated with arm volume measurements (perometer) and QOL questionnaires at baseline and post-operatively. QOL was measured using the Upper Limb Lymphedema (ULL)-27 questionnaire, which assesses subjective arm swelling and its impact on daily functioning in 3 dimensions (physical, psychological and social). The ULL-27 scores were analyzed as a continuous variable adjusting for baseline scores, with higher scores indicating fewer arm symptoms; specifically, a decrease in the physical dimension score correlated with an increase in subjective arm swelling. Results From 12/2016-8/2018,

108 patients had an ALND with baseline and PO assessments, performed at a median of 15 days after ALND. Median patient age was 47 years and median BMI was 25.8, with 73% receiving neoadjuvant chemotherapy and 77% undergoing mastectomy. Following surgery, most patients experienced a modest increase in measured arm volume (median relative volume change 0.7%; interquartile range [IQR] -0.7, 2.8). In contrast, PO QOL significantly decreased in the physical (change -33; IQR -47.1, -20; p<0.001), psychological (change -10.7; IQR -28.6, 0; p<0.001) and social dimensions (change -20; IQR -35, 0; p<0.001)(Fig.). Younger age (p=0.02) and reconstruction after mastectomy (p=0.002) were associated with worse PO physical dimension scores, while objective arm swelling showed no correlation (p=0.25). Mastectomy (p=0.047) and reconstruction (p=0.005) resulted in worse psychological dimension scores; no factors were associated with social dimension scores. Conclusions Decrease in QOL after ALND in the PO period is due to symptoms of perceived arm swelling, with only a modest measurable increase in arm volume. Further studies are needed to determine the impact of early subjective lymphedema symptoms on long-term lymphedema risk.

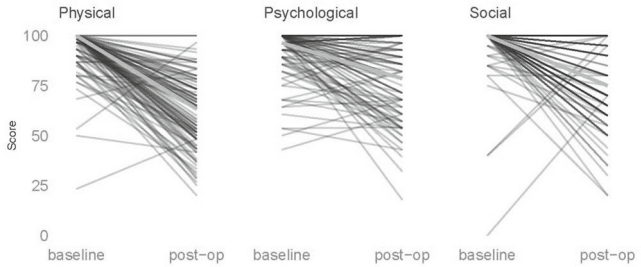


Fig. Median change in quality of life in the physical, psychological and social dimensions in the postoperative period after adjusting for baseline

P87

Surgeon-Specific Performance on Breast Care Metrics: Results from a Large Integrated Cancer Network R.L. White, Jr,[2]* P. Palmer,[1] D. Sarma,[2] T. Sarantou,[2] M. Robinson,[1] S. Trufan.[1]
1. Levine Cancer Institute, Charlotte, NC; 2. Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC.

Introduction Site-based quality metrics have become a common and integral part of clinical care (CoC, NAPBC, CQIP). Within the breast surgery program. We sought to analyze surgeon-specific performance on 22 breast care metrics. Some metrics were related to quality, others were related to surveillance. Methods Retrospective review of breast surgery procedures performed at the Levine Cancer Institute between July 1, 2015 through December, 31, 2017. The breast cancer surgery program consists of 26 surgeons and 9 facilities. Exclusion criteria included patients who received treatment at an outside facility, those with substantial co-morbidities, and those > 90 years. Each breast care metric was summarized for each surgeon as either a proportion or a mean. For surgeons with an adequate number of cases, 95% confidence intervals were calculated for each metric. Data for breast care metrics were reported in 6 month intervals. Trends over time (means) were assessed for each metric to show improvement or decline in performance. After forming a steering committee to review and evaluate the results, individualized surgeon-specific reports were created and distributed to the respective surgeon at 6 month intervals. Although 22 metrics were included in the overall report, this abstract reports on 10 metrics only. Results 3056 breast surgery procedures were performed. From this cohort, 22 breast care metrics from 26 surgeons were analyzed. Table 1 shows the individual surgeon performance on 10 metrics, including means over time for the entire cohort. Four metrics showed improvements: 1) likelihood of pre-operative discussion of sentinel node biopsy in preference to axillary dissections; 2) discussion of reconstruction options; 3) the orientation of lumpectomy specimens; and 4) a decrease in the mastectomy positive margin rate. Some metrics that showed consistent and exceptional adherence were retired. Conclusion As we move toward a value-based payment model, metrics for performance will be an increasing part of practice. The process of developing surgeon-specific reports on breast care metrics and integrating the results into practice led to improved individual performance.

Metric Name (Source)	Date Range	# of surgeons analyzed[1]	# of cases analyzed	Overall Proportion	Trend Over Time	p value for trend over time
Core biopsy rates (NAPBC)[2]	7/1/2015 - 12/31/2016	26	1586	99%	99% (7/2015) to 100% (12/2016)	p = 0.32
Axillary sentinel lymph node biopsy is considered or performed for patients with invasive malignancy (NAPBC)[3]	7/1/2015 - 12/31/2017	20	369	88%	76% (7/2015) to 98% (12/2017)	p = 0.007
All appropriate patients undergoing mastectomy are offered a preoperative referral to a reconstructive/plastic surgeon. (NAPBC)	7/1/2015 - 12/31/2017	18	528	90%	91% (7/2015) to 97% (12/2017)	p=0.007
Discussion of subsequent breast cancer risk as well as discussion of need for excisional biopsy in patients with ADH and ALH (NAPBC)	7/1/2015 - 12/31/2016	17	263	100%	100% (7/2015) to 100% (12/2016)	-
Breast-conservation surgery rate for women with Stage 0, I, or II breast cancer. (NAPBC)[4]	7/1/2015 - 12/31/2017	19	2525	67%	68% (7/2015) to 71% (12/2017)	p = 0.99
Referral to Medical Oncology[5]	7/1/2015 - 12/31/2016	19	322	100%	100% (7/2015) to 100% (12/2016)	-
Referral to Genetics[6]	7/1/2015 - 12/31/2016	13	98	97%	98% (7/2015) to 95% (12/2016)	p= 0.27
Positive Margin Rate - Lumpectomy	7/1/2015 - 12/31/2017	19	1730	14%	16% (7/2015) to 13% (12/2017)	p= 0.9
Positive Margin Rate - Mastectomy	7/1/2015 - 12/31/2017	19	536	4%	5% (7/2015) to 3% (12/2017)	p= 0.04
Orientation of Lumpectomy Specimens	1/1/2016 – 12/31/2017	19	1400	99%	97% (1/2016) to 99% (12/2017)	p = 0.05

1 Not all physicians have analyzable cases.
2 Palpation guided or image guided needle biopsy was the initial diagnostic approach rather than open biopsy.
3 Patients undergoing neoadjuvant chemotherapy were excluded.
4 A target rate of at least 50 percent of all eligible patients diagnosed with early-stage breast cancer (Stage 0, I, II) is treated with breast-conserving surgery.
5 For all N1 patients and all T2 or T3 patients if HER2 positive or triple negative.
6 All patients under 50 years and all triple negative patients under 60 years.

P88

Therapeutic Nipple-Sparing Mastectomy: Surgical Outcomes for High-risk Cases at Two Academic Cancer Centers E. Parvez,* D. Morency, A.N. Meguerditchian, S. Dumitra, M. Basik, S. Meterissian, K. Martel, J. Boileau. *Department of Surgery and Oncology, McGill University, Montreal, ON, Canada.*

Background: A growing body of literature is examining the surgical and oncologic safety of nipple-sparing mastectomy (NSM) in patients with high-risk features. The objective of this study is to assess institutional experience with NSM in high-risk patients and resultant surgical outcomes. Methods: All patients undergoing NSM for invasive or in-situ breast cancer at two academic cancer centers (CC1 and CC2) between January 2013-August 2018 were identified from administrative health records. Clinicopathologic characteristics and perioperative events were retrospectively collected from medical charts. High-risk features were: locally-advanced breast cancer (LABC)(≥T3 or ≥N2), and treatment with neoadjuvant chemotherapy(NAT) or radiation (RT). Descriptive statistical analysis and multivariate regression was performed. Results: Of 175 NSM (143 CC1, 33 CC2) performed in 164 patients, 12(6.9%) were for LABC, 51(29.1%) were following NAT, 20(11.4%) received pre-op RT and 42(24.0%) received post-mastectomy RT(PMRT). Proportions of patients with high-risk features were similar between hospitals. Median follow-up was 11 months. Nipple/skin necrosis requiring re-operation occurred in 12(6.9%) cases. No association between nipple/skin necrosis and LABC(OR 1.26,p=0.586), NAT(OR 1.23,p=0.748), pre-op RT(OR 2.87,p=0.143) or PMRT(OR 0.62,p=0.733) was observed. Smoking was the only significant predictor of nipple/skin necrosis on multivariate analysis. Implant loss, hematoma, and infection occurred in 8(4.6%), 3(1.7%) and 8(4.6%) of cases respectively, and were not associated with any high-risk features. A positive margin

occurred in 5 cases for invasive disease and 8 cases for DCIS (3 involving the nipple-areolar complex margin). There was no significant association between a positive surgical margin and LABC or NAT. Conclusion: In our series, NSM in patients with LABC, NAT and RT was not associated with an increased risk of perioperative complications. However, this study is limited by its retrospective nature, small sample size and low event rate. Prospective, multi-centric studies with long-term follow-up are needed.

P89

A Prospective Study of Opioid Use for Postoperative Pain Management After Breast Surgery K.E. Limbach,* S.J. Pommier, R.F. Pommier, A.M. Naik. *General Surgery, Oregon Health & Science University, Portland, OR.*

Background: The opioid epidemic has led to increased attention to prescribing practices across surgical specialties, but many studies are limited by their retrospective nature and exclusion of patients with chronic pain. This study seeks to quantify the postoperative opioid use of patients undergoing breast operations prospectively. Methods: Consecutive patients undergoing breast operation at a single institution prospectively tracked each dose of postoperative pain medication. Logs were collected at follow up or via telephone, and a survey was conducted of patient perceptions regarding their opioid prescription. Results: Of 100 patients included, 88 completed the medication log, survey, or both. Those lost to follow up were more likely to have depression or anxiety (p=0.05) but were not more likely to require a refill (p=0.367). The median number and interquartile range (IQR) of tabs taken were: Partial mastectomy (PM) 0 (IQR 0-4), PM with sentinel lymph node biopsy (SNLB) 3 (IQR 0-6), PM with bilateral reduction (R) 6.5 (IQR 3-13), total mastectomy (TM) 16 (IQR 2-31.25), and bilateral total mastectomy (BM) 27 (IQR 25.25-73). The number of tabs required to fulfill the needs of 80% of patients was: PM 3, PM+SLNB 6, PM+R 8, TM 34, and BM 47. For patients who had undergone PM, there was no significant difference in the number of tabs taken for surgical pain between those with chronic pain and those without (p=0.956) or those with history of mental illness and those without (p=0.902). There was no decrease for those who used ice (p=0.596), regular dosing of acetaminophen (p=0.877), or marijuana products (p=1.00). Of survey respondents, 50.6% felt they had been prescribed too much pain medication. Most (81.9%) had leftover tabs, and 67.9% indicated they kept them in their home. If initial prescriptions had been written to fulfill the needs of 80% of patients, an estimated 954 fewer tabs (43.3%, p<0.001) would have been prescribed. Conclusions: The majority of patients were overprescribed opioids after breast operation, but a reduction in opioid prescription could be achieved by targeting the needs of 80% of the population.

P90

Impact of the Extent of Pathologic Complete Response (pCR) on Outcomes After Neoadjuvant Chemotherapy (NAC) M. Lee,* M. Srour, S. Walcott-Sapp, G. Cook-Wiens, F. Amersi, A.E. Giuliano, A. Chung. *Surgery, Cedars-Sinai Medical Center, Beverly Hills, CA.*

Introduction With advances in systemic therapies for breast cancer (BC), responses to NAC have dramatically increased. pCR after NAC is an independent prognostic factor. The objective of this study was to examine the impact of breast and/or nodal pCR on survival. Methods From a prospectively maintained database, 202 women were identified with T1-4, lymph node (LN) positive BC diagnosed from 2008-2016 who underwent NAC followed by an operation. Clinical and pathologic factors were compared between 4 groups: pCR in both breast/LNs, node-only pCR, breast-only pCR, and residual disease (RD) in both breast/LNs. Disease-free survival (DFS) and overall survival (OS) were compared among groups. Results Forty-eight (23.8%) patients had pCR in both breast/LNs, 43 (21.3%) node-only pCR, 5 (2.5%) breast-only pCR, and 106 (52.5%) had RD. Compared to patients with pCR in both breast/LNs, those with node-only pCR were more likely to have estrogen receptor positive (63.4% vs 35.4%, p=0.008) and HER2 negative (63.4% vs 33.3%, p=0.005) tumors. There was no difference in age, clinical stage, or type of breast operation between groups. RD patients were more likely to have axillary lymph node dissection compared to those with pCR in both breast/LNs and node-only pCR (92.5% vs 62.8% vs 73.0%, p<0.0001). No patient with breast-only pCR had a local or distant recurrence. For locoregional recurrences, 1 patient with node-only pCR had an in-breast recurrence and 1 with pCR in both had an axillary recurrence. With a median follow-up of 48.2 months, patients with any pCR had improved DFS (HR 0.3; 95% CI 0.157-0.572) and OS (HR 0.192; 95% CI 0.057-0.652) compared with patients who had RD. There were no significant differences in DFS (log-rank p=0.18) and OS (log-rank p=0.12) between patients with node-only pCR, breast-only pCR, and pCR in both breast/LNs. Conclusion In patients with node positive BC who received NAC, any pCR was associated with improved survival compared to those with RD. However, the anatomic site of pCR did not appear to impact survival. This suggests that any favorable response to NAC may have more prognostic value than whether the pCR is in the LNs or breast.

P91

Resource Utilization After MRI in Patients Diagnosed with Breast Cancer E.A. Elder,* A. Ferlin, Z. Li, T. Gibson, E.M. Gabriel, S.P. Bagaria, S. McLaughlin. *Mayo Clinic Florida, Jacksonville, FL.*

Introduction: Breast MRI after the diagnosis of breast cancer frequently identifies additional MR abnormalities requiring workup in the ipsilateral or contralateral breast. To avoid significant delays in surgery and maximize radiology scheduling, choosing the correct biopsy method is critical. We sought to evaluate MR abnormalities and determine accuracy and downstream utilization of MR and US resources Methods: We performed a retrospective review of 1348 women with newly diagnosed breast cancer undergoing preoperative MR at our institution from 2007-2017. We identified 539/1348 (39%) breasts with an additional MR abnormality. We collected clinical, radiographic and pathologic data to categorize subsequent recommended and performed interventions. Results: In total, 539 women had 706 breasts with ipsilateral or contralateral additional abnormalities classified as enhancing mass (436/706, 62%), clumped/cobblestone enhancement (187, 26%), or nonmass enhancement (NME) in 83 (12%). Overall, 662/706 (94%) required additional evaluation. Definitive biopsy (bx) recommendations were made based on MRI findings in 268/662 (40%) and unknown in 20 (4%) breasts. Of the remaining 374/662 (56%), 2nd look US was deemed necessary to guide appropriate additional intervention. The US was completed for 316/374 abnormalities and resulted in the following further workup recommendations: US bx 139/316 (44%), MR bx 88 (28%), and no bx needed 85 (27%). In total, MR resulted in the recommendation for one additional test in 85/662 (13%), one additional bx in 268/662 (40%) and 2 additional procedures (2ndUS+bx) in 227/662 (35%) breasts. Patients needing MR bx after 2nd look US were more likely to have mass findings (not NME) on initial MRI than those recommended for MR bx without 2ndUS (mass: 70% vs 35%). When performed, bx confirmed additional cancer in 151/432 (35%) breasts with 106 being IDC/ILC. Conclusions: Working up MRI abnormalities is labor intensive. 2nd look US spared bx in only 13% but was needed to determine bx modality in an additional third of abnormalities. Patients with NME or clumped enhancement should preferentially be recommended for MR biopsy without 2ndUS. 2nd look US cannot be eliminated.

P92

Reducing Low-Value Surgical Care in Breast Cancer M.E. Smith,* S.P. Shubeck, C.A. Vitous, T.M. Hughes, L.A. Dossett. *General Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: To address overtreatment of early stage breast cancer, the Society for Surgical Oncology and the American Society of Breast Surgeons participated in the Choosing Wisely campaign aimed at identifying low-value practices. Four surgical practices were identified as low value: (1) re-excision for close but negative margins, (2) completion axillary lymph node dissection (cALND) for pts meeting Z0011 criteria, (3) sentinel lymph node biopsy (SLNB) in pts over 70 with hormone receptor positive cancer and (4) contralateral prophylactic mastectomy (CPM) in the absence of a hereditary breast cancer syndrome. Preliminary data suggest re-excision and cALND rapidly decreased, while SLNB remains high and CPM rates are increasing. We sought to assess providers' practices, knowledge, and beliefs regarding these procedures. Methods: We conducted semi-structured interviews with breast surgeons across the US beyond thematic saturation (n=20). Clinical vignettes were designed to capture surgical decision making and barriers to guideline concordant care for practices identified in Choosing Wisely. Using thematic analysis, the interviews were coded through an iterative process with comparative analysis to identify emerging themes. Results: Three major themes emerged which varied among targeted practices. (1) Regarding re-excision and cALND, surgeons described clinical factors (e.g. the number of close margins) as drivers of guideline discordant care. (2) Surgeons frequently described attitudes of skepticism toward avoiding SLNB and uncertainty of data supporting this guideline. This skepticism was used to justify guideline discordant care. (3) Surgeons consistently deemed CPM as low-value, yet

reported continued utilization due to patient factors such autonomy and preference (Table). Conclusions: Clinical factors are the primary driver of guideline discordant care in practices that have been rapidly de-implemented. Conversely for procedures with persistent high use, doubts on the strength of the evidence base and pts preferences are significant barriers to reducing use of low-value care. Future interventions focused on these factors may improve de-implementation of low-value breast cancer care.

Barriers to Guideline Concordant Care	Sample Quotes
Clinical Factors	[Myself and my partners] do not routinely re-operate on close margins anymore after the release of the guidelines, but we also believe there are still patients with close margins who may benefit from re-excision. We base that [decision] on how broad the margin is, whether it's a close margin by the primary or this [close but negative margin] is a small satellite area, etc. I think the scenarios we [consider re-excision in] is when it's multiple, like six out of six [close margins]. In a younger patient, you might want to be a little more aggressive in terms of trying to get a better margin, or if there was extensive intraductal component to the pathology [I] worry about a close margin not being really adequate enough.
Uncertainty of Data and Skepticism	Guidelines suggests that patients over 70 [years] shouldn't have sentinel lymph node biopsies routinely, although I don't necessarily agree to that. I will mention [to the patient] that there are some evolving practices that suggest a lymph node biopsy may or may not benefit them. The problem is, I don't think there is so much compelling data specifically regarding age [of the patient] to support forgoing a sentinel lymph node biopsy uniformly in patients. [Age of 70] is not my particular cut off [for sentinel lymph node biopsy] even though I know that is the recommendation from a lot of governing bodies. I use overall health status because, as you know, not all 70 year olds are created equal.
Patient Autonomy and Preferences	I think the data is very clear on this, that those patients... do not benefit from removal of a normal breast. I will still offer a CPM [contralateral prophylactic mastectomy] to the patient because it's [the patient's] decision making really. I kind of let [the patient] decide. I just try to tell them that unfortunately there's always going to be anxiety about a breast cancer coming back... [but] if a women is insistent that [contralateral prophylactic mastectomy] is what she wants to do, then it is what I end up doing. Some patients you're never going to talk off the cliff regardless of how many good reasons you have to tell them and I ultimately do what the patient wants. Sometimes it's patient anxiety and like I said, you can talk to them about the lack of survival benefit and you can talk to them about a one percent per year chance of developing a second cancer. It doesn't matter, none of the data matters if their anxiety trumps all the data and they want [a contralateral prophylactic mastectomy].

Thematic Analysis of Factors Influencing Guideline Discordant Breast Cancer Care

P93

The Additional Value of Gene Expression Profile in cT1-2N0 Breast Cancer Patients in Whom the Recommendation for Adjuvant Chemotherapy Could be Missed in Absence of Pathological Lymph Node Status M.L.G. Vane,[1]* L. van Roozendaal,[2] S. Siesling,[3] M. Smidt.[1] *1. Surgical Oncology, Maastricht UMC+, Maastricht, Netherlands; 2. Zuyderland MC, Heerlen, Netherlands; 3. Netherlands Comprehensive Cancer Organization, Utrecht, Netherlands.*

Introduction Several trials investigate whether the sentinel lymph node biopsy (SLNB) can be safely omitted in cT1-2N0 breast cancer patients treated with breast conserving therapy (BCT). A consequence of omitting the SLNB is the absence of pathological lymph node status information for the recommendation of adjuvant chemotherapy. The aim of this study was to determine the additional value of a gene expression profile (GEP) in cT1-2N0 breast cancer patients treated with BCTin whom the recommendation for adjuvantchemotherapy could be missed in absence of pathological lymph node status. Methods All cT1-2N0 breast cancerpatients treated with BCT and SLNB were included from the Netherlands Comprehensive Cancer Organization between 2011-2017, if a GEP was performed. Patients were excluded in case of neoadjuvant treatment and age >70 years. For each patient, recommendation based on the Dutch breast cancer guideline was determined, first for patients' true pathological lymph node status (clinical high versus low risk) and second pretending the SLNB was not performed (considered as negative SLN) compared to GEP (genomic high versus low risk). Results In 3.803 of the patients, a gene expression profile was used for the recommendation of adjuvant chemotherapy (see Table 1). Pretending that SLNB was not performed, the pathological lymph node status changed in 736 of the patients. In 510 patients the recommendation for chemotherapy remained, based on other risk factors. In 226 patients, the recommendation changed from chemotherapy to no chemotherapy (116 contained micrometastases). Of these, 190 patients had a genomic low and 36 genomic high risk. Conclusion If pathological lymph node status is absent, recommendation of adjuvant chemotherapy is missed in 226 of the 3.803 patients (5.9%). GEP showed agenomic low risk in 190 (84.1%) and genomic high risk in 36 of these patients (15.9%).

Table 1. Clinical versus genomic risk in all patients (n=3.803)

	Genomic low risk	Genomic high risk	Total
Clinical high risk	1.372	2.183	3.555
Clinical low risk	75	173	248
Total	1.447	2.356	3.803

P94

Is Nipple-Sparing Mastectomy Associated with Increased Complications, Readmission, and Length of Stay Compared to Skin-Sparing Mastectomy? M. Wang, J. Huang, A. Chagpar.* *Surgery, Yale University, New Haven, CT.*

Introduction: Nipple sparing mastectomy (NSM) is a key part of the breast surgeon's armamentarium, but may be technically challenging. Some have questioned whether this increases the rate of complications, readmission, and length of stay (LOS) compared to skin sparing mastectomy (SSM). Methods: All patients undergoing NSM or SSM at our institution between January 1, 2010 and December 31, 2017 were reviewed. Non-parametric statistical comparisons were made using SPSS Version 24. Results: There were 798 patients in this cohort: 217 (27.2%) underwent NSM, 581 (72.8%) underwent SSM. Clinicopathologic and sociodemographic differences between the two groups are shown in the table below. There was no difference in complication rate between the two groups with 20.7% of NSM and 22.5% of SSM having at least one complication (p=0.632). In particular, there was no difference between NSM and SSM, respectively, in terms of bleeding (2.8% vs. 4.5%, p=0.317), infection (6.0% vs. 7.1%, p=0.639), thrombosis/necrosis of flap (4.6% vs. 4.0%, p=0.691), skin breakdown (4.1% vs. 7.7%, p=0.082), seromas (1.4% vs. 2.2%, p=0.577), and implant rupture (0.5% vs. 0.9%, p=1.000). Further, there was no difference in the need for readmission (8.3 vs. 10.3%, p=0.424) between NSM and SSM, respectively. The median LOS was 2 days (range; 0-13). NSM patients were less likely to have a LOS > 2 d than SSM patients (69.1% vs. 79.7%, p=0.002). Complications did not predispose to having a LOS > 2 d (23.4% vs. 17.8%, p=0.129). After controlling for the factors differentiating NSM from SSM (see table below), NSM was no longer a predictor of LOS > 2 d (OR: 0.65; 95% CI: 0.41-1.03, p=0.071). Significant predictors of LOS > 2 d included type of reconstruction (p<0.001), presence of DCIS (p=0.010), AJCC stage (p=0.002), and her2 status (p<0.001). Conclusion: While NSM may be more technically challenging than SSM, it is not associated with a higher rate of complications, readmissions, nor LOS when taking into account type of reconstruction, presence of DCIS, AJCC stage and her2 status.

Factor	NSM (n = 217)	SSM (n = 581)	p-value
Median age (yrs)	47	51	<0.001
Race White Black Asian Other	- 183 (84.3) 15 (6.9) 8 (3.7) 11 (5.1)	- 452 (77.8) 69 (11.9) 19 (3.3) 41 (7.1)	0.114
Hispanic	14 (6.5)	51 (8.8)	0.312
Insurance type Uninsured Medicaid Medicare Military Private	- 0 (0) 23 (10.6) 5 (2.3) 7 (3.2) 182 (83.9)	- 6 (1.0) 81 (13.9) 56 (9.6) 11 (1.9) 427 (73.5)	<0.001
Current smoker	12 (5.5)	39 (6.7)	0.627
Diabetes	4 (1.9)	46 (7.9)	0.001
Median BMI	25.6	27.6	<0.001
Number of sides Unilateral Bilateral	- 51 (23.5) 166 (76.5)	- 187 (32.2) 394 (67.8)	0.019
Indication Prophylactic Cancer	- 43 (19.9) 173 (80.1)	- 32 (5.6) 543 (94.4)	<0.001
BRCA+	55 (25.3)	65 (11.2)	<0.001
Neoadjuvant chemotherapy	21 (9.7)	127 (21.9)	<0.001
AJCC Stage 0 I II III IV	- 81 (43.5) 64 (34.4) 33 (17.7) 8 (4.3) 0 (0)	- 192 (35.4) 157 (28.9) 133 (24.5) 57 (10.5) 4 (0.7)	0.003
Multifocality/Multicentricity	37 (17.3)	127 (22.2)	0.140
DCIS	126 (58.1)	413 (71.1)	0.001
ER+	130 (60.2)	428 (74.2)	<0.001
PR+	114 (52.8)	360 (62.4)	<0.001
Her2+	23 (10.6)	80 (13.9)	0.005
Reconstruction type Implants Autologous	- 143 (65.9) 74 (34.1)	- 324 (55.8) 257 (44.2)	0.010
Median weight of breast (g)	375	548	<0.001

P95

Breast Conservation Therapy Confers Survival and Distant Recurrence Advantage Over Mastectomy for Stage II Triple Negative Breast Cancer Patients R. Macfie,[2]* K. Panwala,[1] C. Aks,[1] N. Johnson,[1] J.R. Garreau.[1] *1. surgical oncology, Legacy Cancer Institute, Portland, OR; 2. OHSU, Portland, OR.*

Introduction: Recent studies suggest survival benefit of breast conservation over mastectomy. We evaluated distant recurrence (DR) rates after breast-conservation therapy (BCT) versus mastectomy in our community- based cancer institute. Methods: A retrospective review of patients undergoing treatment of Stage 0 to 3 breast cancer from January, 2002 to December, 2011 was performed. We evaluated outcomes between those having BCT versus mastectomy. Results: We reviewed 4,866 patients. There was no significant difference in DR between patients undergoing BCT versus mastectomy in DCIS (n=904; BCS 521, mastectomy 383; DR=1/521 vs 1/383; p=0.09), Stage I (n=2202; BCT 1505, mastectomy 697; DR=6/1505 vs 17/697; p=0.98) or Stage III cancer (n=417; BCT 87, mastectomy 330; DR=17/87 vs 59/330; p=0.50). There was significantly less DR in Stage II patients (n=1353) undergoing BCT vs mastectomy (32/645 vs 64/708; p=0.003). Subgroup analysis of Stage II TNBC (n=198) showed 104 mastectomy and 94 BCT patients. Those in the BCT group had significantly lower rates of DR (6/94 vs 16/104; p= 0.03) and significantly higher overall survival (OS)(81/94 vs 69/104; p=0.007) than those undergoing mastectomy. (Clinical data summarized in Table 1.) This was not true for other Stage II subtypes (luminal A, luminal B, Her 2-neu positive) Of Stage II TNBC patients with DR there was no difference in age, lymph node status or tumor size (p>0.05 for all) in BCT versus mastectomy groups; there was a significant difference in radiation status (94/94 vs. 28/104; p<0.0001). Radiation was associated with worse outcomes in the mastectomy group (HR 2.32; p=0.04). Conclusions: We found significantly less DR and improved OS in Stage II TNBC patients undergoing BCT vs mastectomy. An explanatory factor was not able to be identified. Until the difference is better understood, eligible patients with TNBC should be encouraged to undergo BCT.

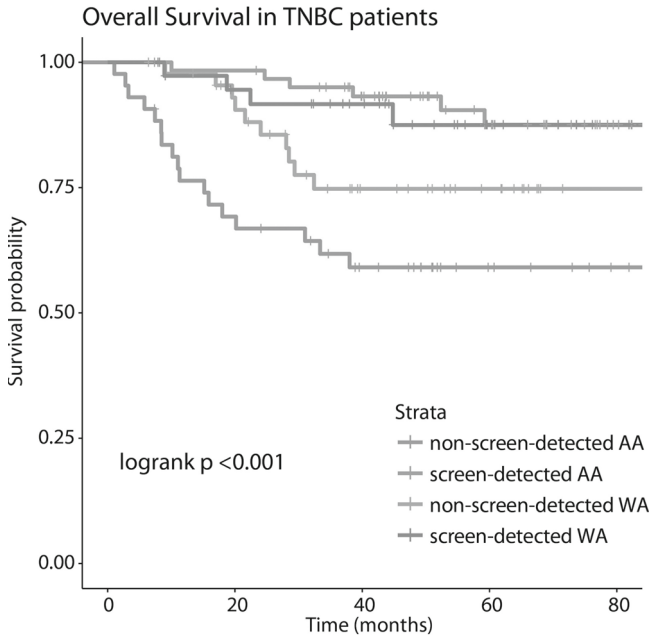
Clinical and Pathological Features of Stage IIA/B Triple Negative Breast Cancer Patients

	Mastectomy	Breast Conservation Therapy	p-value
N	104	47	
Age at Diagnosis (years)	56.9+/-0.8	53.7+/-0.1	0.12
Median Stage at Diagnosis	IIA	IIA	0.08
Tumor Size	3.27	3.26	0.09
>2+LNs	12.1%	11.8%	0.95
Neoadjuvant chemotherapy	29.2%	15%	0.02
Adjuvant chemotherapy	67.7%	78.5%	0.04
Radiation	27%	100%	<0.0001
Local Recurrence	3.3%	3.2%	0.96
Distant Recurrence	15.4%	6.5%	0.001
Years Follow-up	4.94+/-0.0	5.3+/-0.03	0.14
Overall survival	66.3%	86.1%	0.007

P96

Screening Mammography Reduces Disparities by Improving Triple Negative Breast Cancer (TNBC) Early Detection and Outcomes J.A. Burns,[1]* J. Bensenhaver,[1] Y. Chen,[1] L.L. Susick,[1] L. Petersen,[1] E. Proctor,[1] S.D. Nathanson,[1] S. Mandava,[1] M. Davis,[2] L.A. Newman.[2] *1. Multidisciplinary Breast Surgery, Henry Ford Health System, Monroe, MI; 2. Weill Cornell Medicine, New York, NY.*

Introduction: TNBC is more common in African American (AA) compared to White American (WA) women, thereby contributing to higher breast cancer mortality in the AA population. The extent to which screening can reduce breast cancer disparities is uncertain, as TNBC (compared to non-TNBC) is more likely to present as an interval breast cancer detected following a normal screening mammogram. Methods: We compared 106 AA (median follow-up 50.3 months) and 87 WA (median follow-up 47.5 months) patients (pts) with TNBC managed 2010-2015 in an urban hospital system. Results: Mean age at diagnosis was 61 yrs for both AA and WA pts. Mean tumor size was also similar (2.2 and 2.7cm, respectively; p=0.3); 23.6% of AA and 19.5% of WA pts had node-positive TNBC (p=0.6). Disease was detected by screening mammography in 58.5% of AA and 44.8% of WA pts (p=0.13). Surgical and systemic therapy patterns were comparable. Compared to non-screen-detected disease, screen-detected TNBC was more likely to be T1 for AA (79% versus 32%; p<0.001) and WA pts (80% versus 42%; p=0.001); and also more likely to be node-negative (92% versus 54% for AA pts; p<0.0001 and 92% versus 68% for WA pts; p=0.017). Distant metastasis developed in 16% of both AA and WA pts. AA pts with screen-detected TNBC had longer 4-year overall survival (OS)- 93% (95% CI 87.0-99.9%) compared to those with non-screen-detected TNBC- 59.1% (95% CI 45.8-76.2%). Similar patterns were seen for WA pts: 4-year OS for screen-detected TNBC 87.5% (95% CI 76.5%-100%) versus 74.8% (95% CI 62.3-89.7%). Other univariate predictors of better survival included age <50 years; small tumor size; non-high-grade disease; absence of lymphovascular invasion; and node-negative disease, but not race/ethnicity. On multivariate analysis, mammography screen-detected disease remained associated with overall survival; mortality hazard 0.21 (95% CI 0.10-0.45; p<0.0001). Conclusions: Screening mammography is effective for early detection of TNBC in AA and WA pts, resulting in improved survival. It can therefore minimize breast cancer disparities related to the disproportionate burden of TNBC in the AA population.



P97

Neoadjuvant Chemotherapy for Metaplastic Breast Cancer: A National Cancer Data Base Review K.H. Dinh,* E.J. Diego, J.G. Steiman, A. Soran, D. Keenan, R. Johnson, P.F. McAuliffe. *Surgery, University of Pittsburgh Medical Center, Pittsburgh, MA.*

INTRODUCTION: Metaplastic breast cancer (MBC) is rare and aggressive. This study examines national trends of timing of chemotherapy for MBC and its associated overall survival (OS). METHODS: Women who underwent surgery for stage I-III MBC, diagnosed 2010-2014, were identified in the National Cancer Database. Demographic and clinical characteristics were retrospectively reviewed. Chemotherapy administration was classified as neoadjuvant (NAC), adjuvant (AC), or none (NC). Univariate analysis was used to associate chemotherapy treatments with patient (pt) characteristics. Multivariate survival analysis was used to estimate the relationship between OS and chemotherapy timing, adjusting for demographic, tumor, and treatment factors. RESULTS: 2769 pts with MBC were identified. 1981 (74%) of tumors were triple-negative (TN), 143 (5%) were HER2+, and 549 (21%) were luminal. 576 (21%) received NAC, 1504 (54%) AC, and 689 (25%) NC. Of the luminal MBCs, 382 (63%) received endocrine therapy, and the rate of this treatment was similar between the NAC and AC groups. Compared with AC and NC, pts receiving NAC were more likely to be black (20% vs. 16% and 14%, p<0.001), have larger tumors (median 4.3 cm vs. 2.6 cm and 2.8 cm, p<0.001), undergo mastectomy (71% vs. 54% and 61%, p<0.001), undergo axillary lymph node dissection (48% vs. 32% and 27%, p<0.001), and receive radiation (65% vs. 56% and 38%, p<0.001). Complete pathologic response (pCR) was achieved in 7.1% of patients receiving NAC (5.4% of TN, 18.2% of HER2+, and 8.3% of luminal). Compared with NAC, pts who received AC had improved adjusted OS [hazard ratio (HR) 0.55, 95% confidence interval (CI) 0.44-0.69], while NC patients had similar OS (HR 1.02, 95% CI 0.78-1.34). CONCLUSION: In MBC, treatment

with NAC was associated with a worse OS compared to AC and a similar OS to NC. While the pts treated with NAC tended to have more advanced disease, this OS trend persists after adjustment for demographic, tumor, and treatment factors. Information about chemotherapy regimens utilized was not available in this database. However, prolonged time to surgery in the setting of chemoresistance may have contributed to these findings.

P98

Disparities Influence Pathologic Complete Response Rates After Neoadjuvant Chemotherapy In Triple Negative Breast Cancer

C. Calvo,* A. Colton, C.A. Hester, X. Xu, H. Zhu, N.S. Partain, R. Wooldridge, D. Farr, J. Huth, M. Leitch. *University of Texas Southwestern, Dallas, TX.*

Background: Pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC) has become a predictive measure for disease-free and overall survival in triple negative breast cancer (TNBC). The goal of this study was to evaluate if differences exist in pCR rates in TNBC patients treated at a safety-net hospital compared to a university hospital. Methods: 875 women who received NAC for newly diagnosed breast cancer from 2005 to 2017 were identified from tumor registries at a safety-net and university hospital. Patients at both hospitals are managed by the same group of university physicians. Univariable and multivariable logistic regression analyses were used to investigate how demographic, tumor pathologic features, time from diagnosis to NAC, compliance, and time from NAC completion to surgery were associated with pCR rates among the 294 women with TNBC treated at both hospitals. Results: pCR was achieved in 101 patients in the entire TNBC cohort (34%). The presence of lymphovascular invasion (LVI) (p=0.0005) and premature NAC cessation (p=0.04) were independently associated with decreased pCR rates on multivariable analysis. Patients with TNBC treated at the safety-net hospital (n= 165) had significantly lower rates of pCR compared to those treated at the university hospital (n= 129) (29% vs. 41%, p=0.03). Safety-net hospital patients were more likely to be uninsured (40% vs. 2.33%, p=<0.0001), Hispanic (50% vs. 14%, p=<0.0001), higher stage at diagnosis (45.6% vs. 25.5%, p=0.0004), and have longer time from diagnosis to NAC initiation (median of 47 days vs. 33 days, p=<0.0001). Lack of insurance and delays from diagnosis to NAC in turn significantly influenced pCR rates. Conclusion: Lack of insurance, LVI, and premature NAC cessation adversely affected pCR rates among TNBC patients treated at both hospitals. Disparities in socioeconomic status and longer time from diagnosis to NAC initiation adversely affected pCR rates in TNBC patients treated at the safety-net hospital despite uniform physicians and treatment algorithms. Reducing delays to NAC may lead to improved pCR rates and outcomes in low socioeconomic TNBC patients.

Pathologic Complete Response Variables in Triple Negative Cohort (n=294)

	pCR	No pCR	Univariable Odds Ratio (95% CI)	Univariable P-value	Multivariable Odds Ratio (95% CI)	Multivariable P-value
Hospital						
Safety-net	48 (29.09%)	117 (70.91%)	0.588 (0.362, 0.956)	**0.0323**	0.886 (0.401, 1.957)	0.7645
Private	53 (41.09%)	76 (58.91%)	1.000 (reference)			
Age						
≤ 45 years old	44 (35.48%)	80 (64.52%)	1.000 (reference)			
46-55 years old	31 (32.98%)	63 (67.02%)	0.895 (0.508, 1.575)	0.6998		
>55 years old	26 (34.21%)	50 (65.79%)	0.945 (0.519, 1.723)	0.8546		
Race						
African American	34 (38.20%)	55 (61.80%)	0.971 (0.532, 1.774)	0.9248		
Hispanic	28 (28.00%)	72 (72.00%)	0.611 (0.333, 1.123)	0.1127		
Caucasian	35 (38.89%)	55 (61.11%)	1.000 (reference)			
Other	3 (23.08%)	10 (76.92%)	0.472 (0.121, 1.834)	0.2782		
Insurance Status						
Medicare/Medicaid	29 (40.85%)	42 (59.15%)	1.096 (0.601, 1.997)	0.7652	1.146 (0.545, 2.411)	0.7190
Safety-net	12 (35.29%)	22 (64.71%)	0.866 (0.391, 1.915)	0.7217	0.777 (0.281, 2.153)	0.6280
Private	46 (38.66%)	73 (61.34%)	1.000 (reference)			
None	14 (20.29%)	55 (79.71%)	0.404 (0.202, 0.808)	**0.0104**	0.372 (0.141, 1.984)	**0.0464**
Tumor Grade						
Grade 1	0	1 (100.00%)	0.594 (0.006, 55.459)	0.8221		
Grade 2	5 (19.23%)	21 (80.77%)	0.457 (0.169, 1.232)	0.1216		
Grade 3	81 (35.84%)	145 (64.16%)	1.000 (reference)			
LVI						
Absent	89 (39.73%)	135 (60.27%)	1.000 (reference)			
Present	9 (16.07%)	47 (83.93%)	0.290 (0.136, 0.622)	**0.0015**	0.207 (0.086, 0.500)	**0.0005**
Ki67						
≤50	13 (23.64%)	42 (76.36%)	0.534 (0.270, 1.054)	**0.0706**	0.515 (0.245, 1.081)	0.0793
>50	80 (36.70%)	138 (63.30%)	1.000 (reference)			
Stage at Diagnosis						
Stage 1	8 (44.44%)	10 (55.56%)	1.377 (0.516, 3.676)	0.5230		
Stage 2	61 (36.75%)	105 (63.25%)	1.000 (reference)			
Stage 3	29 (29.90%)	68 (70.10%)	0.734 (0.429, 1.256)	0.2593		
Stage 4	1 (10.00%)	9 (90.00%)	0.191 (0.024, 1.546)	0.1208		
Time from Diagnosis to NAC						
< 40 days	54 (41.86%)	75 (58.14%)	1.777 (1.092, 2.892)	**0.0207**	1.472 (0.780, 2.777)	0.2324
≥ 40 days	47 (28.83%)	116 (71.17%)	1.000 (reference)			
Premature Cessation of NAC						
No	92 (36.22%)	162 (63.78%)	1.000 (reference)			
Yes	6 (19.4%)	25 (80.6%)	0.423 (0.167, 1.068)	**0.0686**	0.328 (0.112, 0.955)	**0.0410**
Time from NAC Completion to Surgery						
< 40 days	66 (36.87%)	113 (63.13%)	1.000 (reference)			
≥ 40 days	32 (33.68%)	63 (66.32%)	0.870 (0.516, 1.467)	0.6005		

P99

Chemotherapy Trends for Triple Negative Metaplastic Versus Invasive Ductal Breast Cancer: A National Cancer Data Base Review K.H. Dinh,* P.F. McAuliffe, J.G. Steiman, A. Soran, D. Keenan, R. Johnson, E.J. Diego. *Surgery, University of Pittsburgh Medical Center, Pittsburgh, MA.*

INTRODUCTION: Triple-negative (TN) metaplastic breast cancer (MBC) is a rare subtype which may have higher rates of chemoresistance compared to the more common TN invasive ductal cancer (IDC). This study evaluates national trends of systemic treatment of TN MBC versus TN IDC, with respect to pathologic complete response (pCR) and overall survival (OS). METHODS: Women who underwent surgery for stage I-III TN MBC and IDC, diagnosed 2010-2014, were identified in the National Cancer Database, and demographic and clinical characteristics were retrospectively reviewed. Chemotherapy administration was classified as neoadjuvant (NAC), adjuvant (AC), or none (NC). Multivariate survival analysis was used to estimate the relationship between chemotherapy and OS, adjusting for demographic, tumor, and treatment factors. RESULTS: 66,025 patients with TN breast cancer were identified, 1981 (3%) with MBC and 64,044 (97%) with IDC. 17,960 (27%) received NAC, 36,071 (55%) AC, and 11,994 (18%) NC. NAC was administered in 426 (21.5%) and 17,534 (27%) in patients with MBC and IDC respectively (p<0.001). Compared to patients with IDC, patients with MBC were more likely to be white (72% vs. 67%, p<0.001), have larger tumors (median 3.0 cm vs. 2.1 cm, p<0.001), be clinically node negative (84% vs. 75%, p<0.001), and undergo mastectomy (59% vs. 49%, p<0.001). pCR was achieved in 5.4% of patients with MBC and 21.6% with IDC (p<0.001). For MBC, OS adjusted for tumor characteristics was lower for NAC than for AC (hazard ratio [HR] 1.88, 95% CI 1.45-2.42), and this effect was not as pronounced for IDC (HR 1.43, 95% CI 1.36-1.51). CONCLUSION: In this study, the treatment of TN breast cancer with NAC was associated with a worse OS compared with AC, even after adjustment for demographic, tumor, and treatment factors. This effect was stronger in MBC than in IDC, although information about specific regimens was not available in the database. MBC was also associated with a decreased pCR. These findings suggest that NAC is less effective in treating TN MBC than TN IDC, and there may be a consideration for multidisciplinary treatment planning in this subset.

Pathologic Response to Neoadjuvant Chemotherapy in Triple-Negative Breast Cancer

	Invasive Ductal Cancer (N=17,534)	Metaplastic Breast Cancer (N=426)	p
Pathologic complete response	3,484 (21.6%)	22 (5.4%)	<0.001
Downstage from cT stage to ypT stage	10,501 (63.3%)	176 (42.3%)	<0.001
Conversion from clinical node positive to ypN0	3,191/8,681 (36.8%)	45/153 (29.4%)	0.06

Percentage calculations did not include patients with missing data.

P100

Patient Decision Role Preference is Associated with Clinical Stage of Breast Cancer L.A. Gutnik,[1]* C. Allen,[2] A.P. Presson,[2] C.B. Matsen.[1] *1. Huntsman Cancer Institute at the University of Utah, SALT LAKE CITY, UT; 2. University of Utah, SALT LAKE CITY, UT.*

Introduction: Breast cancer patients prefer different levels of involvement in decision making about surgery. There are very few studies that have attempted to study this prospectively and little data exists about how disease factors might contribute to role preference. These factors and preferences could influence the type of surgery chosen. Methods: 100 newly diagnosed breast cancer patients identified their preferred role in decision-making prior to the first meeting with their surgeon using the Patient Preference Scale (five roles: 1-most active, 2-active, 3-collaborative, 4-passive, 5-most passive). Chart review captured the type of initial surgery and clinical stage. The Kruskal Wallis test was used to analyze patient role preference by clinical stage. Type of initial surgery was analyzed across clinical stage using Fisher tests. Results: There were 11 patients with Stage 0, 43 with Stage I, 31 with Stage II, and 15 with Stage III breast cancer. There were significant differences in patient role preference according to stage (p=0.024). The majority of Stage 0 (64%) and Stage III (60%) patients preferred active roles. The majority of Stage I (60%) and Stage II (52%) preferred a collaborative role. Few patients at any stage chose a passive decision-making role. There were significant differences in surgery choice based on clinical stage (p<0.001). Stages 0 (60%) and I (91%) had more lumpectomies than mastectomies. Stage II (62%) and III (85%)

patients favored mastectomy. Within mastectomy patients, there were no statistically significant differences between unilateral vs bilateral mastectomy among stages, but Stage II patients represented the largest proportion opting for bilateral procedures. Table 1 summarizes the findings. Conclusion: Decision role preferences vary by clinical stage, though most patients prefer some level of involvement in decision-making. A larger proportion than expected of Stage II patients had more aggressive surgery. Further study is necessary to elucidate how stage affects patient decision role preference and how this impacts the type of surgery chosen, so that surgeons can provide optimal patient-centered care and participate in shared decision making.

Table 1. Type of Surgery and Role Preference by Clinical Stage

Variable*	Type/Level	Stage 0: N=11	Stage 1: N=43	Stage 2: N=31	Stage 3: N=15	P-value
Type of Initial Surgery	Lumpectomy	6 (60%)	39 (91%)	11 (38%)	2 (15%)	<0.001
	Mastectomy	4 (40%)	4 (9%)	18 (62%)	11 (85%)	
Type of Mastectomy	Bilateral	0 (0%)	1 (25%)	11 (61%)	5 (45%)	0.14
	Unilateral	4 (100%)	3 (75%)	7 (39%)	6 (55%)	
Patient Role Preference	[median (IQR)]	2 (2, 3)	3 (2, 3)	3 (2, 3)	2 (2, 3)	0.024
	1-Most active: Patient decides	0 (0%)	1 (2%)	0 (0%)	1 (7%)	
	2-Active: Patient decides with some input from provider	7 (64%)	12 (28%)	10 (32%)	9 (60%)	
	3-Collaborative: Patient and provider decide together	3 (27%)	26 (60%)	16 (52%)	5 (33%)	
	4-Passive: Provider decides with some input from patient	1 (9%)	3 (7%)	5 (16%)	0 (0%)	
	5-Most Passive: Provider decides	0 (0%)	1 (2%)	0 (0%)	0 (0%)	

*Missing values: Type of Initial Surgery = 5
Note: There are 0 mastectomies missing the type of mastectomy. Other missing values are the lumpectomies or are missing the type of initial surgery.

P101

Comparison of the 21-Gene Recurrence Score Assay in Women and Men with Early Stage Breast Cancer A. Allen, D. Kwon, E. Avisar, N. Goel, S.B. Kesmodel.* *University of Miami, Miami, FL.*

Introduction: The 21-gene recurrence score (RS) assay is a prognostic and predictive test which provides information on risk of distant recurrence and benefit from adjuvant chemotherapy (CTX). This test has been validated in women with estrogen receptor positive (ER+), human epidermal growth factor receptor-2 negative (HER2-), early stage breast cancer (ESBC). We compare 21-gene RS testing in women and men with ESBC, including RS distribution and impact on treatment. Methods: Patients with ESBC (T1/2 N1/2 M0), ER+/HER2- were selected from the National Cancer Database (2010-2015). RS testing, RS distribution (low <18, intermediate 18-30, high >30) and treatment were compared between women and men. Logistic regression was performed to identify factors associated with RS testing. Results: We identified 478,271 patients with ER+/HER2- ESBC; 473,554 women (99%) and 4,717 men (1%). RS testing was performed in 37% of patients, 38.4% with N0 and 31.5% with N1 disease. Utilization of RS testing increased from 2010 to 2015 in both women (29.4% to 42.2%,p<.001) and men (22.6% to 34.4%,p<.001). RS testing was associated with female sex, younger age, non-Hispanic white patients, private insurance, treatment in the northeast, treatment at a high/intermediate volume center, poorly-/un-differentiated tumors, progesterone receptor + tumors, negative nodes, lobular/mixed histology, and year of diagnosis. RS distribution differed for women and men (p<.001, Table 1). Differences in RS distribution were observed for patients with positive nodes (T1N1 p<.001;T2N1 p<.005) and within treatment groups (hormone therapy (HT) p<.001;CTX+HT p=.003). The majority of patients with low RS received HT only (women 89.0%;men 86.5%). Within each RS risk group, significant differences in treatment were seen among women and men (low p<.001;intermediate p<.001;high p=.03). Conclusion: RS testing increased in both women and men over time. RS distribution differed between women and men as did treatment within RS risk groups. The difference in RS distribution for women and men with N1 disease may indicate different tumor biology. Given the increasing use of RS testing in men, validation studies are necessary.

Distribution of Recurrence Scores for Women and Men with Early Stage Breast Cancer

	Women			Men			
Recurrence Score	Low (<18) N (%)	Intermediate (18-30) N (%)	High (>30) N (%)	Low (<18) N (%)	Intermediate (18-30) N (%)	High (>30) N (%)	p-value
All Patients	90,626 (59.9)	48,940 (32.3)	11,734 (7.8)	743 (60.4)	359 (29.2)	129 (10.5)	<.001
TN Stage							
T1N0	60,122 (61.0)	31,772 (32.2)	6,635 (6.7)	392 (62.2)	189 (30.0)	49 (7.8)	0.343
T2N0	14,950 (54.0)	9,236 (33.3)	3,509 (12.7)	191 (56.7)	102 (30.3)	44 (13.1)	0.488
T1N1	10,422 (64.7)	4,919 (30.5)	774 (4.8)	101 (69.7)	29 (20.0)	15 (10.3)	0.001
T2N1	5,132 (57.3)	3,013 (33.6)	816 (9.1)	59 (49.6)	39 (32.8)	21 (17.6)	0.005
Treatment[a]							
HT[b] only	78,184 (72.3)	28,320 (26.2)	1,560 (1.4)	615 (73.0)	200 (23.7)	28 (3.3)	<.001
CTX[c] + HT	4,621 (15.6)	16,461 (55.5)	8,556 (28.9)	30 (14.4)	96 (46.2)	82 (39.4)	0.003
CTX only	215 (11.3)	871 (45.7)	818 (43.0)	6 (21.4)	12 (42.9)	10 (35.7)	0.238
None	4,807 (68.0)	1,856 (26.3)	404 (5.7)	60 (68.2)	25 (28.4)	3 (3.4)	0.617

[a]Treatment type known in 146,673 women and 1167 men; [b]HT = hormone therapy; [c]CTX = Chemotherapy

P102

Neoadjuvant Chemotherapy Modulates Breast Tumor Microbiota A. Chiba,* C. Velazquez, M. Howard-McNatt, E. Levine, K.L. Cook. *surgical oncology, Wake Forest School of Medicine, Winston Salem, NC.*

Background: Previous studies in breast cancer patients indicate altered microbiota composition when compared with non-diseased control patients, supporting the role of the microbiome in breast cancer. Published findings demonstrate that the breast microbiome may contribute to cancer development, progression, and recurrence. The aim of our study was to evaluate the differences in breast tumor microbiota in patients undergoing neoadjuvant chemotherapy compared to patients who underwent surgical excision as their initial treatment. Methods: Subjects were retrospectively identified using our institutional surgical outcomes database who were female and diagnosed with invasive ductal carcinoma. We evaluated microbiomes of breast tumor collected during definitive surgery. DNA was isolated from 23 snap-frozen tumor tissue (n=9 neoadjuvant chemotherapy; n=14 surgical treatment first). We sequenced 16S genes. Patient demographics, preoperative variables, surgical details and clinical outcomes were collected. Results: A total of 115 bacterial genus was identified. Overall, proportional abundance of Pseudomonas was 47%, Acinetobacter was 12%, Stenotrophomonas was 3.5%, and Prevotella was 3.3%. Approximately 25% of total tumor microbiota comprised of 105 genus level with less than 1% proportional abundance. Patients that were treated with neoadjuvant chemotherapy had significantly modulated tumor microbiota when compared with tumor tissue from patients who underwent definitive surgery first. Pseudomonas proportional abundance was significantly elevated in neoadjuvant chemotherapy group compared to surgery first group (64.6% vs. 29.4%, p=0.011), and the relative abundance of Streptococcus was significantly lower in neoadjuvant chemotherapy group compared to surgery first group (0.2% vs. 1.6% p=0.015). There were no significant differences between the two groups in terms of age, receptor subtypes, or BMI. Conclusion: Breast tumor microbiome populations differed significantly between patients who underwent neoadjuvant chemotherapy compared to patients who underwent surgical excision first. The modulation in tumor microbiome may represent potential target to improve response to chemotherapy.

P103

Extended Indications for Nipple-Sparing Mastectomy: Comparative Oncological Outcomes of Nipple Preservation in All Stages Breast Cancer at a Single Academic Center K. Martel,[1]* D. Morency,[1] S.M. Wong,[2] E. Parvez,[1] S. Dumitra,[3] S. Meterissian,[4] T. Hijal,[4] M. Basik,[3] J. Boileau.[3] *1. surgical oncology, McGill University, St-Jerome, QC, Canada; 2. Dana Farber/Brigham and Women's Cancer Center, Boston, MA; 3. Jewish General Hospital, Montreal, QC, Canada; 4. Royal Victoria Hospital, Montreal, QC, Canada.*

BACKGROUND Nipple-sparing mastectomy (NSM) with immediate reconstruction is often denied to patients with unfavorable tumor phenotype or locoregional extension. At our institution, NSM is considered in any esthetically suitable patient regardless of cancer stage (except T4d). Tumor related exclusion criteria for NSM is clinical or radiological involvement of nipple areolar complex or positive pathological margin at nipple. We report a comparative analysis of oncological outcomes between NSM and SSM (skin-sparing

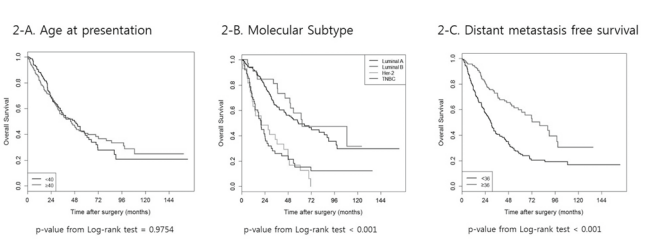
mastectomy) for breast cancer patients. METHOD Using a Health Ministry prospectively maintained database we performed a retrospective review of all NSM or SSM with immediate reconstruction done at a single academic center between January 2013 and December 2017. Patient characteristics, recurrence rates, and overall survival were compared between NSM and SSM groups. RESULTS 216 procedures (118 NSM and 98 SSM) were performed on 204 patients for stage 0-3 breast cancer, including 28% for locally advanced disease (stage IIb-III). Preoperative MRI was done in 23% of the NSM case. Neoadjuvant systemic treatment was given to 33% of the patients with a corresponding pCR of 30%. There was no difference in positive margin rate between the surgical approaches (4.2% (NSM) vs 6.1% (SSM) p=0.54). Immediate reconstruction was done using direct-to-implant prepectoral approach (44%), retropectoral approach (55%) or autologous tissue (1%). 34% of the reconstructed breasts were treated with adjuvant radiation, and 33% of patients received adjuvant chemotherapy. At a median follow up of 30 months, comparative oncological outcomes between SSM and NSM showed no difference in locoregional recurrence rate (3.4% vs 3.1% p=0.90), distant recurrence rate (4.4% vs 6.6% p=0.49) or breast cancer related death (0.9% vs 1.1% p=0.89). None of the local recurrence occurred in the retained NAC. Disease-free survival estimates were similar between the 2 groups (p=0.26). CONCLUSION Nipple preservation is not associated with a higher risk of locoregional or distant recurrence and can be considered in all breast cancer stages.

P104

Age is Not an Independent Prognostic Factor in Young Breast Cancer Patients with Distant Metastasis J. Seung,* J. Ryu, S. Nam, J. Lee, J. Yu, S. Lee, I. Kim, H. Choi, S. Kim. *Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea (the Republic of).*

Background Several studies reported that the survival after distant metastasis of young breast cancer patients was not different from that of older patients. Few studies have identified survival after distant metastasis within young breast cancer. We aimed to identifying the factors that affect the prognosis after distant metastasis among the young breast cancer patients. Methods A total of 7,157 patients were reviewed who underwent primary cancer surgery between January 2003 and December 2013 at Samsung Medical center. Three hundred and thirty two premenopausal patients ≤ 50 years with distant metastasis and were included in the analysis. For analysis, the patients were divided into 2 groups based on age of 40. Results There were no demographic differences in clinical stage, nuclear grade, lymphovascular invasion, distant metastasis site, distant metastasis free survival(DMFS) except for ER/PR status, histopathology, and molecular subtype in both group (respectively p-value=0.0229, 0.035, 0.0157, 0.0457). Median follow-up period was 79.4 month. There was no significant difference in the overall survival between the groups under 40 years old and those over 40 years old(Log rank p-value = 0.9754). On the other hand, Luminal A, luminal B group patients showed longer overall survival than Her-2 positive, TNBC group (Log-rank p-value<0.001). Patients who developed distant metastasis within 36 months after operation had worse overall survival than those who developed distant metastases after 36 months from operation (Log-rank p-value<0.001). Age did not make a significant difference in survival(p-value=0.5468), but the molecular subtype, DMFS, and distant metastasis sites produced significant differences (respectively p-value< 0.001). Conclusion In young breast cancer patients who developed distant metastasis, while the age is not related to mortality, the molecular subtype, DMFS, and distant metastasis sites are useful predictors of prognosis.

Figure 2. Survival curve



P105

Comparison of Partial Mastectomy Specimen Volume and Tumor Volume Following Neoadjuvant Chemotherapy in Breast Cancer A.K. Bazzarelli,* F. Angarita, K. Carpenter, R. Au, M. Elmi, T. Cil. *University of Toronto, Toronto, ON, Canada.*

Background: Neoadjuvant chemotherapy (NAC) increases breast conservation rates. Breast conserving surgery (BCS) after NAC yields acceptable rates of locoregional recurrence (LRR), even in those patients in whom BCS was not possible at presentation. However, little data exists regarding the volume of tissue excised in this scenario. The aim of this study was to compare the volume of breast tissue resected in BCS to the disease volume based on pre-operative imaging and pathological tumour size in the post-NAC setting. Methods: A prospectively maintained database was used to identify patients who underwent NAC for breast cancer with curative intent followed by BCS across three academic high-volume hospitals in Toronto, Canada from January 2006 to July 2016. Clinicopathologic data were extracted. Tumour burden was measured on pre-operative, pre-NAC as well as post-NAC MRI using the volume calculation: $4/3\pi$*radius(height)*radius(length)*radius(width). Comparison was performed between imaging measurements of tumors and volume of pathologic tumors and specimens. Results: A total of 152 patients underwent BCS following NAC. The median age was 47 years old (IQR: 39-55 years old). The most common histology was invasive ductal carcinoma (93.4%). Tumors were frequently grade 2 (41.7%). The distribution of clinical T-stage was as follows: 0 (19.1%), 1 (49.3%), 2 (23.7%) and 3 (5.9%). The majority of tumors were estrogen receptor positive (54.6%), progesterone receptor negative (51%), and HER2 negative (55.9%). Imaging tumor volume on MRI diminished significantly with NAC (5.9cm^3 to 1.9cm^3, p=0.0001). Pathologic tumor volume corresponded to post-NAC MRI imaging volume (1.0cm^3 vs. 1.9cm^3, p=0.1). However, mean specimen volume was much greater at 17.7cm^3. Conclusions: This study demonstrated significantly lower tumor volumes on imaging and pathologically following NAC. However, volume of resected tissue remained high. Therefore, potentially lower specimen volumes may be achievable than was found in our sample. Future studies are needed to determine effects of tumor and patient factors on volume of resected tissue and compare to oncologic outcomes.

P106

Fighting the Opioid Epidemic: Pectoral Blocks and Their Role in Decreasing Post-Operative Narcotic Use After Breast Surgery F. Perez,* S. Nolano, D. Goodman. *Abington Memorial Hospital, Abington, PA.*

Introduction In the current opioid epidemic alternative analgesic strategies are being investigated to reduce the need for post-operative narcotic medications. Regional anesthetic techniques are prevalent in clinical practice for multiple procedures. In breast surgery, pectoral plane (PECs) blocks are recently described as part of a multifactorial approach. This strategy has been used to promote good immediate and early post-operative analgesia that prevents patient from needing more intense pain medications like opioids and can be linked with fewer side effects. At our center, a number of procedures including breast lumpectomies are being anesthetized in this fashion with good acceptance by the patients and faculty. Methods Patients were identified after a retrospective chart review of those who underwent breast lumpectomies and were anesthetized using PEC Block at Abington Jefferson Health system Surgery center. All patients got a routine follow up call as part of the hospital protocol that included information on post operative analgesia. Data was the gathered from the Electronic Medical Records. Results A total of 185 patients were identified from 2014-2017 operated at Abingthon Memoral Hospita, underwent lumpectomies and where discharged home on the same day. All patients identified got a Pectoral plane block. Sixty seven (36%) recieved intraopoperative opioids, 21 (11%) patients asked for narcotics in post-anesthesia care unit. All 185 patients were contacted with a follow up phone call on post operative day one. Not all patients, 46 (25%) were discharged home with a narcotic prescription. On that day, 64 (35%) patients refered to have had no pain at all; 60 (32%) patients had minimal pain not requiring medication, 18 (10%) patients had moderate pain that they treated with non-narcotic medication (over the counter Nonsteroidal Anti-inflammatory Drugs; finally 3 (2%) patients required narcotic for pain control. Forty patients (22%) did not respond to the call back. Conclusion Pectoral plane block is a safe and effective procedure that reduces post operative pain and the need for oral opioids post operatively after same day breast procedures.

P107

Can Magee Equations be Used to Predict Response to Neoadjuvant Chemotherapy (NAC)? J.C. Gooch,* B. Turner, L. Bell, D. Hicks, K.A. Skinner. *University of Rochester Medical Center, Rochester, NY.*

Introduction: OncotypeDX (ODX) results are rarely available to guide NAC decision making. Magee equations (ME) are a series of linear regression models that use standard histologic variables to calculate a score (MS) that reliably predicts the ODX recurrence score. We applied a modified ME using pretreatment(PreTX) variables to examine whether the MS predicted response to NAC. Methods: A prospective database was reviewed for patients receiving NAC for core-biopsy proven, ER/PR positive, Her2 negative locally advanced breast cancer who underwent surgery at our institution. Clinicopathologic variables including PreTX ER/PR/Her2 status and grade, and tumor size and node status, before and after treatment were collected. PreTX tumor size was calculated as the mean of tumor sizes found on physical exam and diagnostic imaging. Residual cancer burden(RCB) score and class was assessed by a breast pathologist. Tumors were considered good responders(GR) if they had an RCB class of 0-1, had a 50% decrease in tumor size from pre-treatment, or the remaining tumor bed had less than 50% cellularity. Nodal response was considered separately. Groups were compared using chi-square and t-test analysis. Results: Forty-nine patients were identified and 73.5% were GRs. The only significant differences identified between GRs and nonresponders were higher ER and PR H Scores in the GRs which may explain why GRs were not more likely to have MS ≥26 (Table 1). There was a trend towards higher MS with lower RCB class (p=0.079). Thirty-one patients had biopsy proven positive nodes (pN+) prior to NAC; 18% of needle biopsy proven pN+ achieved a nodal pCR, and all were in the GR group. The mean MS for nodal pCR was 31.68, compared to 24.35 in the nodal non-responders (p=0.05). There were no RCB 0-1 with a MS <18, and no nodal pCRs were observed with a MS <22. Conclusions: Modified MEs generate scores that are predictive of axillary responses in ER/PR positive, HER2 negative breast cancer. They may be a useful tool when evaluating which patients are more likely to derive substantial benefit from NAC. These findings are hypothesis-generating, and need to be validated in a larger dataset.

Table 1

Variable	Good Responders (n=36)	Non Responders (n=13)	p-value
Age at diagnosis (mean; range)	51 years (30 - 67)	53 years (36 - 82)	NS
PreTX tumor size (mean; range)	4.4cm (1.0 - 11.4cm)	4.5cm (1.3 - 10.0cm)	NS
RCB Score (mean; range)	2.390 (0.0 - 4.36)	3.637 (2.345 - 4.591)	NA
RCB Class			NA
0 or 1	8 (22.3%)	0 (0%)	
2	17 (47.2%)	4 (30.8%)	
3	11 (30.6%)	9 (69.2%)	
Post-treatment tumor bed cellularity (mean; range)	15% (0 - 40%)	67 (5 - 100%)	NA
Magee Score			NS
<26	23 (66.7%)	7 (53.8%)	
≥26	13 (33.3%)	6 (46.2%)	
Pre-treatment node status (pN+)	20 (56%)	11 (84.6%)	
Needle Biopsy	14 (38.9%)	9 (69.2%)	0.06
Surgical Biopsy	6 (16.7%)	2 (15.4%)	
ER H Score (mean; range)	236 (30 - 300)	202 (1 - 285)	0.01
PR H Score (mean; range)	124 (0 - 285)	97 (0 - 270)	0.004

P109

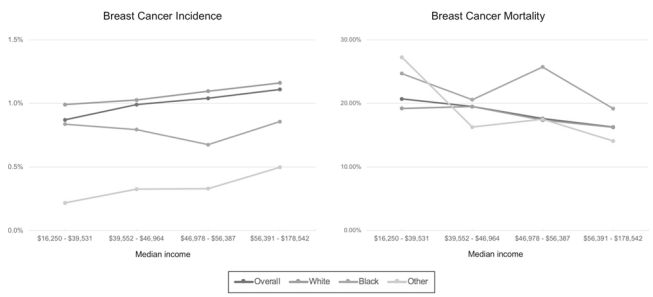
Local Recurrence and Survival in Patients Treated with Accelerated Partial Breast Irradiation (APBI) Therapy J.S. Kennedy,[1]* K. Brandon.[2] *1. Surgery, Emory Decatur Hospital, Decatur, GA; 2. University of Maryland, Baltimore, MD.*

APBI has been reported to yield low local recurrence rates comparable to external beam therapy (EBRT) in early breast cancer, though there are limited published reports for recurrence rates of 5 years or more. We reviewed our general surgical group practice APBI experience in patients with more than 5 years of followup. A retrospective review was done of all APBI patients treated within our group practice from 2006 through 2012. Patients were offered APBI, generally according to ASBS guidelines: age >45, < 3 cm, clear margins, negative nodes, unifocal. Data was obtained from office, hospital, and registry records. All included patients were either deceased or were followed for at least 5 years. All PBI balloons were inserted in the office setting postoperatively under ultrasound guidance. Oral antibiotics were routinely administered while the balloon was in place. APBI was administered twice daily for a total of 10 fractions. There were 135 women, 64% Caucasian, 34% African American, and 2% Asian. Average followup was 8.4 years. Average age was 69. There were 70% invasive (85% ER+), and 30% DCIS (92% ER+). For the invasive cancers, average tumor size was 1.2 cm. Of the 29 deceased patients, only one had a recurrence of cancer (distant). Five year survival was 93%. The local recurrence rate at 5 years was 3.0%. Overall the local recurrence rate was 5.9%. There were 2% regional and 2% distant recurrences at 5 years, and overall 2% and 3% respectively. Seromas developed in 17%. Infections occurred in 1.2%, both responded to oral antibiotics. Conclusions Use of APBI for women within the ASBS Consensus guidelines in this group practice resulted in a low 5 year local recurrence rate of 3.0% which compares favorably with recurrence rates for EBRT. Complications of infection and seroma were deemed acceptable.

P110

Racial and Economic Disparities in Breast Cancer Incidence and Mortality in Pennsylvania A.D. Williams,* M. Buckley, R.M. Ciocca, J.L. Sabol, S.L. Larson, N. Carp. *Lankenau Medical Center, Wynnewood, PA.*

Many studies have demonstrated disparities in breast cancer (BC) mortality among Black women and have shown an association with differences in tumor and socioeconomic factors. We hypothesized that in Pennsylvania (PA), a large economically diverse state, BC mortality would be similar among races when stratified by a municipality's median income. We collected the frequencies of female BC diagnoses and mortalities for years 2011-2016 in each PA municipality from the Pennsylvania Cancer Registry. We also collected demographics (population by age, gender, and race, and median income) for each municipality from the 2010 U.S. Census. We analyzed BC diagnoses and mortalities when municipalities were stratified by to median income (as a proxy of neighborhood socioeconomic status) and race using chi square and Cochran-Mantel-Haenszel tests. In this cohort of 5,398,893 women there were 54,111 BC diagnoses (1.0% incidence) and 9,837 BC mortalities (18.2% mortality rate). BC incidence was highest among White women (p<0.001), whose odds for developing breast cancer were 1.69x higher than non-White women when controlling for income (p>0.001). BC incidence increased with median income (p<0.001) in all races except for Black women whose incidence was highest and equivalent for the top and bottom income groups. BC mortality was highest in Black women (p<0.001) and varied significantly across income groups for all races (all p £0.008). Black women had the highest rate of mortality across income groups except in the lowest income where women of other races had the highest mortality. When controlling for income, odds of BC mortality in non-White women 1.29x higher than for White women (p<0.001). We found that in PA, a municipality's median income is associated with the rate at which women are diagnosed with and die from BC regardless of race. This likely represents differences in exposure to risk factors, the rates of BC screening and differential access to care. The fact that BC mortality for poor non-White women is disproportionately higher highlights that, in addition to presenting with different tumor characteristics, income and race remain important factors related to BC survival.



Rates of breast cancer incidence and mortality in Pennsylvania from 2011-2016 stratified by municipality's median income

P111

Barriers to Breast Reconstruction for Women with Lower Socioeconomic Status T. Stankowski-Drengler,* J. Schumacher, B. Hanlon, J. Tucholka, A. Amessoudji, M. Venkatesh, D. Yang, H.B. Neuman. *General Surgery, University of Wisconsin Hospital and Clinics, Madison, WI.*

Introduction: Disparities in post-mastectomy breast reconstruction exist for women with lower socioeconomic status (SES). Understanding factors that influence reconstruction may identify actionable changes to reduce disparities. Key informants have suggested that finding surgeons that accept Medicaid and travel time to a plastic surgeon are key factors. Our objective was to assess the relationship between these factors and reconstruction for low SES women in Wisconsin. Methods: We identified women <75 years of age with stage 0-III breast cancer who underwent mastectomy between 2009-2014 using the Wisconsin Cancer Reporting System. Area deprivation index, a census block-based composite measure, was calculated as a surrogate for SES. Women were categorized by tertiles and the lowest tertile comprised our cohort. Geocoding determined turn-by-turn drive time from a woman's home to the nearest accredited Commission on Cancer or National Accreditation Program for Breast Centers. Multivariable logistic regression determined the relationship between reconstruction and Medicaid and travel time, controlling for variables known to impact receipt of reconstruction. Results: Our cohort consisted of 1756 primarily white women (82%) with early stage breast cancer (52% stage 0/I). The median age was 55 and 18% had Medicaid. 37% of women underwent reconstruction. On multivariable regression (Table), low SES women with Medicaid vs. any other insurance were significantly less likely to receive reconstruction (OR 0.56, 95% CI 0.4-0.7). Longer travel time was also significantly associated with lower odds of reconstruction (OR 0.99, 95% CI 0.99-1.0). This translates to an adjusted predicted probability of 38% vs. 33%, depending on whether a woman lives within 10 vs. 50 minutes of an accredited center. Conclusion: In our cohort of low SES women living in Wisconsin, having Medicaid and living further from an accredited center remain important predictors of reconstruction, even after controlling for clinical variables. Further work will explore opportunities to improve access to reconstruction for women with Medicaid. This is particularly challenging and may require low SES women to travel further to receive care.

Table: Likelihood of Breast Reconstruction Attributable to Patient and Clinical Variables

	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Medicaid	0.56	0.42-0.74	<0.0005
Travel time to accredited center	0.99	0.99-1.00	0.007
Age <40 40-50 50-60 60-70	Reference 0.72 0.30 0.11	-- 0.54-0.96 0.22-0.41 0.07-0.16	<0.0005
Stage 0 1 2 3	Reference 0.70 0.50 0.31	-- 0.44-1.11 0.31-0.83 0.16-0.60	0.002
Bilateral mastectomy	2.13	1.68-2.70	<0.0005
Radiation	0.90	0.66-1.23	0.53
Chemotherapy	0.84	0.62-1.14	0.26

*Also controlled for Estrogen/Progesterone receptor, Her2neu status, and Year of diagnosis

P112

Identifying Factors Associated with Slow Adoption of Oncotype DX Utilization: Analysis Using the National Cancer Data Base C. McGreevy,* A.D. Williams, S.M. Nazarian, D. Anderson, L. De La Cruz, J. Tchou. *Endocrine and Oncologic Surgery, University of Pennsylvania, Philadelphia, PA.*

Introduction Oncotype DXTM (oDX) is a 21 gene recurrence score assay aimed to help guide adjuvant chemotherapy decisions in women with node negative estrogen/progesterone receptor (HR) positive, Her-2/neu (Her2) negative breast cancer (BC). We have previously noted a slow adoption of oDX testing of 14% to 35% in 2009 to 2014 respectively in oDX eligible patients. We sought to identify factors that influenced the utilization of oDX in the entire study period and compared with individual years, specifically 2009 vs. 2014, to understand trend change in oDX utilization. Methods Using the National Cancer Database (NCDB), we identified women with T1/T2, node negative, HR positive BC from 2009 to 2015. Demographics, tumor characteristics, and oDX utilization were collected, and we analyzed factors associated with the utilization of oDX. Results Over 430,000 patients were included and oDX testing was performed on 37% of patients. In 2009 only 30% of eligible patients had oDX testing, while in 2015 41% had testing performed. In univariate analysis being white, having a lower comorbidity score, being treated at an academic institution, and having private insurance all were associated with oDX testing. Also having a tumor > 2 cm, moderately or poorly differentiated and no lymphovascular invasion (LVI) were associated with oDX testing. In multivariate analaysis being white, having a lower comorbidity score, being treated at an academic institution or cancer network, having private insurance, a tumor > 2cm, moderately or poorly differentiated and not having LVI were independent predictors of oDX testing. Conclusion Since ASCO and the NCCN endorsed oDX in 2007 and 2008 respectively, the use of oDX has been steadily rising in the US. However, our results showed that a large proportion of oDX eligible patients did not undergo oDX testing. The rising adoption of oDX was partly driven by oDX utilization in those with T2 tumors. The disparity in oDX testing may translate into worse clinical outcomes, but future studies involving other datasets which provide disease specific outcomes not available in the NCDB are necessary to identify these outcomes.

P113

Neoadjuvant Chemotherapy is Not Associated with Decreased Rates of Breast Cancer Recurrence S.M. Nazarian, M. Pomponio, C. Huang, A.D. Williams, A. Doucette, C. McGreevy, L. De La Cruz, D. Anderson, J. Tchou.* *Surgery, University of Pennsylvania, Bryn Mawr, PA.*

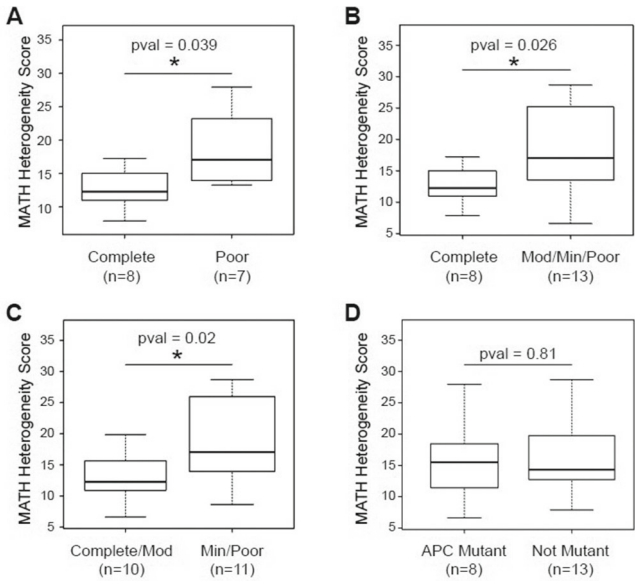
Introduction Whether the use of neoadjuvant chemotherapy (NAC) is associated with better clinical outcomes in breast cancer is unclear. Methods We queried our IRB-approved, single institution series for breast cancer diagnosed between 1/1/09 and 12/31/15. Chi-squared analyses were used to compare use of NAC and outcomes across subtypes (ER-, PR-, HER2- (TNBC); ER+ or PR+, HER2-; HER2+) and clinical stage of breast cancer. Multivariate logistic regression was used to predict risk of recurrence by cancer subtype. StataMP 14.2 (StataCorp, College Station, TX) was used for all analyses. Results 4,635 patients were diagnosed with breast cancer during the study period, including 605 TNBC, 3,369 ER+ or PR+, HER2- and 661 HER2+. NAC was administered for 26.9%, 7.6% and 28.3% of these patients, respectively. Response to NAC differed significantly by subtype ($P < 0.001$), with higher rates of complete response for TNBC (43.1%) and HER2+ (49.1%) compared to ER+ or PR+, HER2- (9.5%). Response to NAC did not differ by stage for TNBC and HER2+ but did show decreasing rates of complete response as stage increased for ER+ or PR+, HER2- ($P = 0.024$). Subgroup analyses according to clinical stage and subtype demonstrated that the use of NAC was not associated with improved rates of recurrence. Within TNBC, rates of recurrence were only statistically different by receipt of NAC for stage 1 tumors, with recurrence seen in 42.9% for NAC compared with 7.6% for no NAC ($P < 0.001$). Similar findings were seen in stage 2 ER+ or PR+, HER2- as well as stage 1 HER2+ patients, with significantly higher rates of recurrence seen for those who received NAC. In multivariate models for risk of recurrence, controlling for age at diagnosis, race, presenting stage and response to NAC, TNBC patients with complete pathologic response had 0.057 the odds of recurrence versus those with no response, $P = 0.026$. Conclusions In our 7-year, single institution series, NAC use was not associated with lower rates of recurrence when stratified by cancer subtype and presenting stage. Of those with complete pathologic response, improved clinical outcomes were seen in those with TNBC but not other subtypes.

P114

Characterization of Tumor Heterogeneity as a Predictor of Response to Neoadjuvant Chemotherapy in Locally-Advanced Rectal Cancer A. Greenbaum,[1]* D. Martin,[1] T. Bocklage,[4] J. Lee,[3] S. Ness,[2] A. Rajput.[2] *1. Surgery, University of New Mexico Health Sciences Center, Albuquerque, NM; 2. University of New Mexico Comprehensive Cancer Center, Albuquerque, NM; 3. University of Florida College of Medicine, Gainesville, FL; 4. University of Kentucky, Lexington, KY.*

Introduction: Neoadjuvant chemoradiation therapy (nCRT) is the standard of care for locally advanced adenocarcinoma of the rectum, but it is currently unknown which patients will respond. This study tested the correlation between response to nCRT and intratumoral heterogeneity, measured using next-generation sequencing assays. Methods: DNA was extracted from

formalin-fixed, paraffin-embedded biopsy samples from a cohort of patients with locally advanced rectal adenocarcinoma (AJCC 7th edition stage T3/4 or N1/2) who received nCRT. High read-depth sequencing of >400 cancer-relevant genes was performed using the Ion Ampliseq Comprehensive Cancer Panel™ assay. Tumor mutations and variant allele frequencies were used to calculate Mutant Allele Tumor Heterogeneity (MATH) scores as measures of intratumoral heterogeneity. Response to nCRT was determined by primary surgical resection pathology report. Results: Biopsy samples from 21 patient tumors were analyzed. No correlations between response and either the presence of specific mutations or the number of acquired mutations were identified. 8 patients were noted to have complete response, 2 were moderate, 4 minimal and 7 demonstrated poor response. Higher MATH scores correlated with poorer response to treatment, demonstrating significantly increased tumor heterogeneity compared to those with complete response (Figure 1, panel A, p=0.039). A similar difference was observed when comparing complete response to samples in all other categories (moderate, minimal or poor, P = 0.026, panel B) or when comparing complete plus moderate response to minimal plus poor response (P = 0.02, panel C). In contrast, there was no difference in MATH scores when comparing samples that did or did not harbor mutations in APC (panel D) or other common mutations (not shown). Conclusion: The application of MATH scores as a measure of tumor heterogeneity may provide a useful biomarker for treatment response in locally advanced rectal cancer.



P115

Ki67 Does Not Predict Recurrence for Low-Grade Appendiceal Mucinous Neoplasms with Peritoneal Dissemination After Cytoreductive Surgery and HIPEC E.P. Ward,* L. Okamuro, M. Valasek, K.J. Kelly, J. Veerapong, A.M. Lowy, J. Baumgartner. *Surgery, UCSD, San Diego, CA.*

Introduction Low grade appendiceal mucinous neoplasms can disseminate to become low grade mucinous carcinoma peritonei (LGMCP), which is optimally treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC). Approximately half of patients with LGMCP recur despite complete cytoreduction, and risk factors for recurrence are unknown. We sought to evaluate if the proliferation marker Ki67 predicts progression of LGMCP after CRS/HIPEC. Methods A retrospective review of a prospectively-maintained institutional database was performed to identify patients treated with CRS/HIPEC for appendiceal cancer with LGMCP from 2008-2018 with Ki67 assessed. Patient characteristics, histologic data, average and focally high ("hotspot") Ki67 index, perioperative data, and progression-free survival (PFS) were collected. Results Forty-nine patients with LGCMP (51% male, median age 61, range 27-86) with a median CEA of 6.8 ng/mL (range 27-86) and median PFS of 15 (0.59-82) months were identified. The median peritoneal carcinoma index (PCI) was 16 (8-34) and the majority had a completeness of cytoreductive (CC) score of 1 (CC-0: n=32 66%, CC-1: n=15, 31%). The median Ki67 score and hotspot Ki67 score was 15% (1-70) and 50% (1-90); respectively. On univariate analysis, average Ki67 and hotspot Ki67 were not predictive of PFS when analyzed as continuous normalized values (HR 0.97, p=0.82 and HR 1.67, p=0.59; respectively) or as categorical values when stratified by the median (HR 0.85, p=0.85 and HR 0.79, p=0.72, respectively) (Figure 1) or by quartile (p=0.25, p=0.90, respectively). CEA did not significantly correlate with PFS (p=0.317), although CC score did (HR 6.26 and HR 8.8, for CC-1 and CC-2 vs. CC-0, respectively, p=0.014). CC score remained an independent predictor of PFS when adjusted for CEA and Ki67 (p=0.047). Conclusion Although Ki67 index has been found to be useful for predicting clinically relevant outcomes for other malignancies, it did not predict recurrence for patients with LGMCP in this cohort. Further investigation into other histologic variables to help predict PFS is needed.

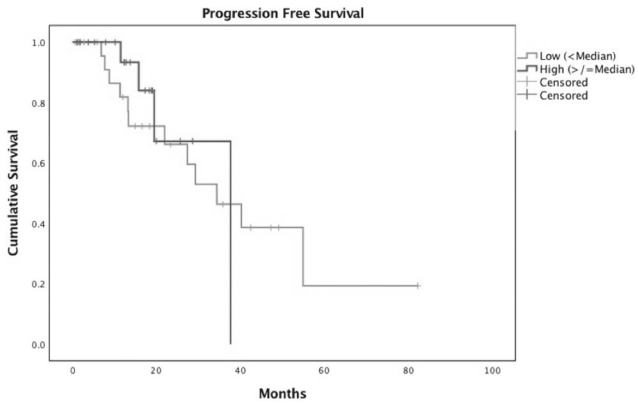


Figure 1. Disease Free Survival For Low Grade Mucinous Carcinoma Peritoneal Disease Stratified by Ki67 Median (p=0.785)

P116

Perioperative and Oncological Outcomes of the Abdominoperineal Resection in the Prone Position versus the Classic Lithotomy Position: A Systematic Review with Meta-analysis J.B. Mesquita Neto,[1]* F. Macedo,[2] S. Kim,[1] D. Weaver.[1] *1. Karmanos Cancer Center/ Wayne State University, Detroit, MI; 2. Sylvester Comprehensive Cancer Cancer, Miami, FL.*

BACKGROUND: This study is a systematic review with meta-analysis designed to compare the perioperative and oncological outcomes of the abdominoperineal resection (APR) carried out in the prone jack-knife position (P-APR) versus the classic lithotomy position (C-APR). METHODS: We established two PICO questions at the beginning of the study: i) for patients undergoing an APR, should the prone or the lithotomy position be used to achieve better immediate perioperative outcomes?; and ii) in patients with rectal cancer undergoing an APR, should the prone or the lithotomy approach be used to decrease recurrence rates and increase survival? We conducted an electronic search through the PubMed according the PRISMA guidelines and included all the randomized or nonrandomized studies which allowed us a comparative analysis between the two groups. Pooled variables and number of events were analyzed using the random-effect model. RESULTS: Seven studies, all nonrandomized retrospective cohorts, encompassing 1,663 patients were included in the final analysis. Prone position was associated with decreased operative time (OT) (DM, -43.8min; 95% CI [-61.94, -25.66], p <0.01) and blood loss (EBL) (DM, 86.9ml; 95%CI [98.88, 75.9], p < 0.01). There were no observed differences regarding the following outcomes: perineal wound infections (PWI) (OR 0.36 [0.08-1.61]; p=0.18), intraoperative perforation of rectum (IOP) (OR 0.98 [0.37-0.97]; p=0.97), circumferential resection margin (CRM) positivity (OR 1.02; [0.34-3.00]; p=0.98) and 5-year local recurrence rate (OR 1.00 [0.61-1.66];p=0.99). CONCLUSION: The prone approach for APR leads to decreased EBL and OT, although it does not change the incidence of PWI or intraoperative rectal perforation. Moreover, surgical positioning per se does not affect the CRM positivity rates or the 5-year local recurrence rate.

Fig. 1A) Operative time: P-APR *versus* C-APR

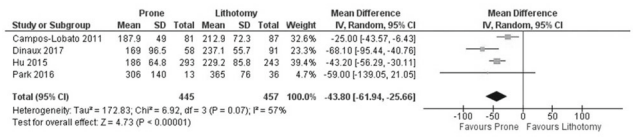


Fig. 1B: 5-year local recurrence: P-APR *versus* C-APR

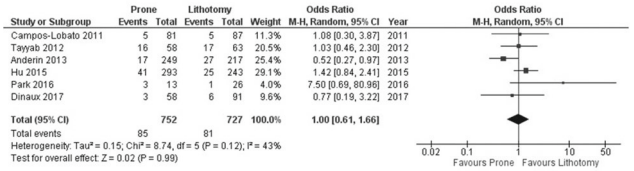


Figure 1: Forest plot comparing pooled outcomes in the P-APR versus the C-APR group

P117

Systematic Implementation of a Colon Bundle Significantly Decreases Surgical Site Infections E. Bianchi,* T. Adegboyega, S. Shih, C. Zhang, D. Rivadeneira. *Colon & Rectal Surgery, Huntington Hospital-Northwell Health, Woodbury, NY.*

Purpose: Surgical site infections (SSIs) represent significant morbidity and financial implications post colon surgery. The objective of this prospective study is to compare clinical outcomes pre- and post- implementation of a dedicated colon surgery bundle to reduce SSIs in our health system. Methods: A prospective study was conducted in which a dedicated colon surgery bundle and interdisciplinary team for its implementation was established. Consecutive patients who underwent a colorectal procedure between January 2015 and January 2016. SSIs were recorded and subdivided by surgical wound class. Twenty-five components of the colon surgery bundle were divided into pre-hospital, pre, intra, and post-operative measures. These included standardized pre-operative mechanical bowel preparation and oral antibiotics and body wash skin cleansing, alcohol-based skin preparation, intra- and peri-operative maintenance of normothermia, therapeutic levels of antimicrobial prophylaxis and optimal tissue oxygenation, glucose control, and the introduction of a clean standardized fascial closure process, and negative pressure wound therapy. Specific enhanced pre-operative patient education was also provided. Results: SSIs where identified in 11/198 patients (7%) eligible for colon bundle implementation. When compared to the year prior to implementation of the colon bundle, SSIs where identified in 26/175 (15%). Implementation of the colon bundle led to a significant decrease in SSIs 7% vs. 15%, ($p < 0.05$).. Additionally, SSIs observed in clean-contaminated and contaminated procedures decreased from 34.6% to 14.3% and 38.5% to 14.3%, respectively ($p<0.05\%$). Conclusions: We demonstrate in this prospective study that the implementation of a specific colon bundle resulted in a 54% decrease in post-operative surgical site infections. These results are particularly seen in wound class II and III. We also show a very high adoption and compliance of the colon bundle with a dedicated implementation of an interdisciplinary team. An approach to incorporating an advanced surgery bundle for colon and rectal procedures can provide an effective strategy to reduce surgical site infections.

P118

Effects of Operative Approach on Oncologic and Perioperative Outcomes in Low Anterior Resection for Colorectal Cancer M.I. Orloff,* J. Lu, S. Kolakowski, D. Vyas, A. Dayama. *Surgery, San Joaquin General Hospital, French Camp, CA.*

Introduction: Surgical resection is the cornerstone of treatment of colorectal cancer. This study sought to compare oncologic and 30-day perioperative outcomes following open, laparoscopic and robotic low anterior resection (LAR) for colorectral cancer. Methods: We reviewed the ACS-NSQIP targeted colectomy database from 2014-2016 to identify patients who underwent LAR. We excluded non-cancerous pathology, LAR with diverting ostomy, hybrid operative approaches, and patients with missing data on anastomotic leak or lymph nodes harvested. Primary outcomes were margin status, number of lymph nodes harvested, anastomotic leak and 30-day mortality. Multivariate analysis was used to determine the association between operation approach, anastomotic leak, and mortality. Results: A total of 5,367 patients met our inclusion criteria – 2119 underwent open LAR, 2432 underwent laparoscopic LAR and 816 underwent robotic LAR. There was no difference in the average number of nodes harvested (19.1 open, 19.7 laparoscopic, 20.0 robotic, P 0.06) (Table 1A). None of the patients had positive margins. Operative time was greater in robotic LAR compared to laparoscopic and open surgeries (open 215 minutes (mins), laparoscopic, 219 mins, robotic 266 mins, $P < 0.01$). Length of stay was greater in open LAR (open 7.9 days (d), laparoscopic 5.1 d, robotic 5.0 d, $P < 0.01$). There was no difference in rates of anastomotic leak (open 4.7%, laparoscopic 3.7%, robotic 5.4%, P 0.06) (Table 1B). Laparoscopic and robotic LAR were associated with lower mortality, compared to open (open 1.4%, laparoscopic 0.5%, robotic 0.1%, $p < 0.01$). On multivariate analysis, there was no association between operative technique and anastomotic leak (Table 1c). Multivariate analysis showed that laparoscopic LAR was associated with a statistically lower mortality compared to open LAR (OR 0.42, CI 0.20 – 0.87). Conclusions: Review of a national database reveals equivalent oncologic outcomes among patients who undergo open, laparoscopic and robotic LAR for colorectal cancer. However, laparoscopic and robotic LAR are associated with less postoperative morbidity, shorter length of stay and lower mortality.

Table 1. Outcomes of open, laparoscopic and robotic low anterior resection without diverting ostomy for colorectal cancer.

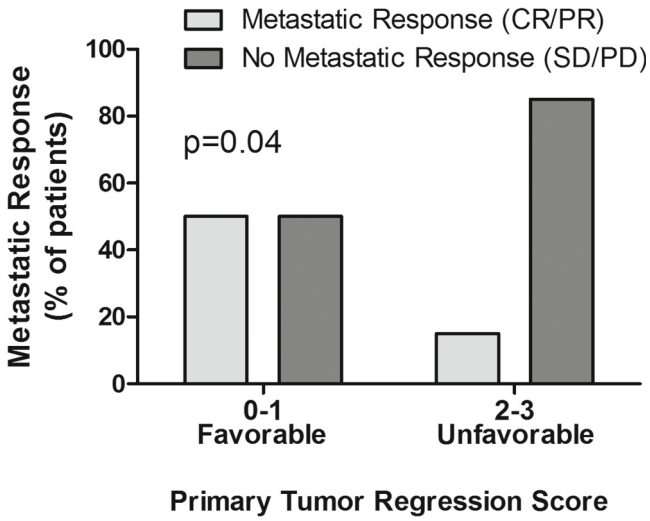
Variable	Open (2119) N (%)	Laparoscopic (2432) N (%)	Robotic (816) N (%)	P value
Table 1a. Outcomes				
Positive Margins	0 (0)	0 (0)	0 (0)	N/A
Number of lymph nodes	19.1 ± 10.6	19.7 ± 10.0	20.0 ± 10.0	0.06
Operative time	215.1 ± 113.8	219.3 ± 93.9	266.2 ± 103. 6	< 0.01
Length of stay	7.9 ± 6.4	5.1 ± 4.8	5.0 ± 5.8	< 0.01
Table 1b. Complications				
Anastomotic leak	100 (4.7)	89 (3.7)	44 (5.4)	0.06
Mortality	29 (1.4)	11 (0.5)	1 (0.1)	< 0.01
Superficial surgical site infection	120 (5.7)	46 (1.9)	19 (2.3)	< 0.01
Postoperative ileus	386 (18.2)	206 (8.5)	97 (11.9)	< 0.01
Table 1c. Multivariate Analysis – adjusted associations between operative technique and primary outcomes. Open as compared to laparoscopic and robotic LAR				
Outcome		Odds ratio	95% Confidence Interval	P value
Anastomotic leak				
➢ Open (reference)		1		
➢ Laparoscopic		0.90	0.67 – 1.23	0.51
➢ Robotic		1.31	0.90 – 1.92	0.15
Mortality				
➢ Open (reference)		1		
➢ Laparoscopic		0.42	0.20 – 0.87	0.02
➢ Robotic		0.15	0.02 – 1.13	0.06

P119

Rectal Cancer Pathologic Response After Neoadjuvant Chemoradiation Predicts Chemotherapy Response for Metastatic Lesions G. Karagkounis,* D. Liska, M.F. Kalady. *Colorectal Surgery, Cleveland Clinic, Cleveland, OH.*

Introduction Tumor regression scores after neoadjuvant chemoradiation (nCRT) are prognostic in rectal cancer. However, as response likely reflects tumor biology, we hypothesized that response of the primary tumor would predict distant tumor response to subsequent chemotherapy. This study analyzes the relationship between rectal cancer primary tumor regression score after nCRT and the subsequent chemotherapy response of metastatic disease. Methods A single institution rectal cancer database of patients treated with long course nCRT and proctectomy was queried, and those who presented with synchronous or metachronous liver or lung metastases treated with chemotherapy were included. Primary tumor regression scores were assessed according to AJCC guidelines (0-3), and grouped as favorable (0-1) or unfavorable (2-3). Response of metastatic lesions was graded as response (complete or partial), or no response (stable or progressive disease), using RECIST criteria. The groups were compared using Fisher's exact test. Results 37 patients met the inclusion criteria and were further analyzed (mean age 53.8 years, 21.6% female). Metastases were synchronous in 17 patients (46%). Twenty-four patients had metastatic disease in the liver, 10 in the lungs and 3 in both sites. Ten patients (27%) had favorable primary tumor response and 27 (73%) had unfavorable. Chemotherapy regimens were FOLFOX in 30 patients (81%),

5-FU/capecitibine in 5 (13.5%), and FOLFIRI in 2 (5.5%). Additional bevacizumab or cetuximab was administered in 17 patients (49%). Patients with favorable primary tumor response were more likely to exhibit response in the metastatic lesions than those without (50% [5/10] vs 15% [4/27], p=0.04). No difference in the response patterns between synchronous and metachronous metastatic cases was noted. Conclusions Primary rectal cancer response to nCRT is associated with metastases' response to chemotherapy. An unfavorable primary tumor response portends poor chemotherapy response for metastatic disease. This information is useful for patient conversations about treatment expectations and may expedite therapy changes from regimens that are not being effective.



P120

Clinical Stage and Response to Neoadjuvant Chemoradiation in Rectal Cancer: Implications for Organ Preservation Strategies G. Karagkounis,* D. Liska, M.F. Kalady. *Colorectal Surgery, Cleveland Clinic, Cleveland, OH.*

Objective Neoadjuvant chemoradiation (nCRT) is recommended for locally advanced rectal cancer, with pathologic response predicting long-term oncologic outcomes. However, as organ preservation protocols are gaining popularity, there is interest in offering nCRT for early stage tumors, though the expected response of these tumors remains unclear. The purpose of this study was to investigate the pathologic response of rectal cancer depending on clinical stage. Methods Patient demographics, tumor characteristics, and nCRT regression scores (based on the AJCC Manual, 7thEdition; scores 0-3) were assessed from rectal cancer patients treated by nCRT followed by surgery at a single institution between 1992 and 2012. Clinical stage was determined by magnetic resonance imaging or, early in the study period, endorectal ultrasound. Groups were compared using Fisher's exact test, and survival analyses performed using Cox proportional hazards models. Results 491 patients were included (median age 58 years, range 26-86, 28.7% female). Clinical stage was I in 72 (15%), II in 202 (41%), III in 184 (37%), and IV in 33 (7%) patients. 59 (12%) patients had clinical T1 (cT1) tumors, 36 (8%) cT2, 340 (69%) cT3, and 56 (11%) cT4. 210 patients (43%) had clinically positive lymph nodes. Pathologic complete response (pCR, score 0) rates for the primary tumor varied by clinical stage (33%, 21%, 20%, and 9%, for stages I, II, III and IV, respectively, p=0.028). Similarly, lower cT classification was associated with greater pCR rates (29%, 33%, 21%, and 11%, for cT1, cT2, cT3, and cT4, respectively, p=0.027). Interestingly, even among clinical Stage I tumors, response to nCRT remained a powerful, independent, predictor of overall survival (Hazard Ratio 2.02, 95% Confidence interval 1.38-2.95). Conclusion Early stage rectal cancers exhibit improved response to nCRT with higher pCR rates. In the context of organ preservation strategies, offering nCRT to early stage rectal cancers, which are generally not given nCRT, may have clinical benefit by achieving a higher rate of complete response.

P121

Impact of Time to Surgery on Oncological Outcomes of Patients with Colon Cancer L.S. Lino-Silva,* R.A. Salcedo-Hernández, C. Zepeda-Najar, J.C. Guzmán-López, A. Meneses-García. *Instituto Nacional de Cancerología, Mexico City, Mexico.*

Background. The waiting-time from cancer diagnosis to surgery (WTTS) is a worry for the healthcare system, healthcare providers, and patients; especially increases anxiety and fear around cancer progression during the waiting interval. WTTS has been suggested to impact treatment outcomes in several different tumor sites and quality of life. Despite there is non-strong evidence about the idea WTTS, several health systems or big centers had stated 6 weeks as a good WTTS. Our aim was to identify if a delayed WTTS in patients with surgically resected colon cancer is associated with worse overall survival (OS). Methods. Retrospective population-based cohort study of 266 patients receiving elective colonic resection after diagnosis of colon cancer in Mexico City from 2005 to 2015 followed until august 2018. For the analysis, we defined a delayed WTTS a time higher than 75th percentile (60 days) and we repeated the analysis with a WTTS of 42 days (6 weeks, as stated by previous literature). The association between WTTS and OS were examined using multivariate Cox regression. Results. The median age was 57 years, there was no predominance of sex, 58.3% of cases they presented with invasion to the subserosa layer (pT3), about half of the patients had lymph node disease (stage III). Of the total, 70% of the cases corresponded to adenocarcinomas of conventional type. The median time to surgery was 38 days, with 75% of the cases operated before 60 days. Regarding the influence of WTTS on OS, the baseline characteristics of the groups are shown in Table 1. As observed, the baseline characteristics of both groups are comparable and survival was not statistically different (median OS of 116 months in the group <60 days vs. 95.6 months in the group > 60 days; p=.717). The analysis with a WTTS of 42 days showed similar (non-significant) results. Conclusion. We found no association between a WTTS of 60 days (75th percentile) and long-term survival. The results from this study can be used by providers to patients who are interested in optimizing cancer health system performance.

Baseline characteristics of 266 cases of colon cancer collected consecutively and surgically treated at the National Institute of Cancerology (2005-2015) grouped according to the time to surgery.

Variable	Group with waitnig time less than 60 days (n=199)	Group with waiting time of 60 days ormore (n=67)	p-value
Age - Median (interquairtile Range), years	56 (45-67)	61 (49-69)	.090
Sex - Count (%) Male Female	. 99 (49.7) 100 (50.3)	. 31 (46.3) 36 (53.7)	.243
Tumoral stage - Count (%) pT1 pT2 pT3 pT4	. 3 (1.5) 25 (12.6) 122 (61.3) 49 (24.6)	. 2 (3) 10 (14.9) 33 (49.3) 22 (32.8)	.499
Nodal stage - Count (%) pN0 pN1-2	. 108 (54.3) 91 (45.7)	. 37 (55.2) 30 (44.8)	.892
Histologic grade - Count (%) G1 G2 G3	. 33 (16.6) 102 (51.3) 64 (32.2)	. 14 (20.9) 27 (40.3) 26 (38.8)	.356
Lymphovascular invasion - Count (%) Absent Present	. . 132 (66.3) 67 (33.7)	. . 43 (64.2) 24 (35.8)	.748
Perineural invasion - Count (%) Absent Present	. . 167 (83.9) 32 (16.1)	. . 57 (85.1) 10 (14.9)	.822
Clinical stage - Count (%) I II III	. 18 (9) 84 (42.3) 97 (48.7)	. 14 (20.9) 18 (26.9) 35 (52.2)	.012
Tumor type - Count (%) Conventional Non-conventional	. 144 (72.4) 55 (27.6)	. 42 (62.7) 25 (37.3)	.135
Tumor size - Median (IQR), mm	57 (40-80)	55 (40-78)	.604
Adjuvant treatment - Count (%) No Yes	. . 91 (45.7) 108 (54.3)	. . 35 (52.2) 32 (47.8)	.356
Outcome - Count (%) Alive Dead	. 173 (87) 26 (13)	. 61 (91) 6 (9)	.371
Survival median time (95% confidence intervale), month	116 (109.6-124)	95.6 (70.5–120.7)	.717
p-values are based on Chi-square test for categorical variables, U-Mann-Whytney test for numerical variables and Log-rank test for survival comparisons.			

P122

Increased Mortality in Younger Patients with Inflammatory Bowel Disease Associated Colorectal Cancer: A Population-Based Cohort Study J. Bogach,* C. Eskicioglu, G. Pond, H. Seow. *Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada.*

Introduction: Inflammatory Bowel Disease (IBD) is a known risk factor for colorectal cancer (CRC). The reported oncologic outcomes for IBD associated CRC are inconsistent in the literature. We aimed to compare survival outcomes in patients with IBD-associated CRC to those with sporadic CRC using a population-based cohort and to explore prognostic factors associated with survival Methods: Population-based administrative data from the Institute of Clinical Evaluative Sciences was used to perform a retrospective cohort study. All adult (>18 years old) patients diagnosed with colorectal cancer from 2007-2015 were included. The validated Ontario Crohn's and Colitis Cohort was used to identify patients with a diagnosis of IBD. The primary outcome measure was overall survival from time of CRC diagnosis until the date of death. Kaplan-Meier method and Cox regression models were used. Secondary outcome measures included treatments received and publicly-provided health care costs. Results: Colorectal cancer was diagnosed in 67,137 people between 2007-2015. IBD was present in 783 (1.2%). The IBD-associated CRC patients were diagnosed at a younger age (median range 55-59 vs 70-74, p<0.001) and were more frequently T4 (27% vs 19%) and N2-3 (23% vs 11%) at diagnosis. Five-year survival in IBD associated CRC patients was 56.4% (95%CI 52.6, 59.9) and 57.0% (95% CI 56.6, 57.4) in those with sporadic CRC (p=0.8). In the multivariable model, the presence of IBD was a significant predictor of death (HR=1.50, 95% CI=1.35 to 1.62, p<0.001) after adjusting for other variables. An interaction was observed between the presence of IBD and age (p<0.001) and neared significance between IBD and stage (p-0.13). Age specific 5-year survival for IBD-associated vs sporadic CRC patients was 56.8 vs 71.4 (<50 years old, p<0.001), 61.8 vs 69.6 (50-64, p<0.001), 59.0 vs 59.5 (65-80, p=0.71) and 33.9 vs 34.6 (80+, p=0.78). Conclusion: Young patients (<65) with IBD associated CRC have worse survival outcomes than young (<65) patients with sporadic CRC. These findings inform prognostication and may direct research on treatment for this high-risk population.

P123

Feasibility of Using a Fitness Tracker to Assess Activity Level and Toxicity in Colorectal Cancer Patients W.H. Ward,[1]* C. Meeker,[2] M. Hill,[2] E. Handorf,[2] M.J. Hall,[2] E.R. Sigurdson,[2] I. Astsaturov,[2] C. Denlinger,[2] S. Reddy,[2] J.E. Meyer,[2] M. Zibelman,[2] D. Madnick,[3] M. Moccia,[3] E. Dotan,[2] J. Farma,[2] N. Vijayvergia.[2] *1. Naval Medical Center, Portsmouth, VA; 2. Fox Chase Cancer Center, Philadelphia, PA; 3. Temple University, Philadelphia, PA.*

INTRODUCTION: Performance status (PS) is traditionally used to predict tolerance and morbidity associated with colorectal cancer (CRC) treatment. Monitoring activity level at the start of therapy using a wearable fitness tracker (Fitbit) may provide a more accurate estimate of overall patient (pt) PS and help predict treatment-related toxicity. METHODS: With IRB approval, we prospectively enrolled CRC pts undergoing therapy into 2 cohorts, medical (M) and surgical (S). Our primary aim was to assess the feasibility of using Fitbit to assess activity level and toxicity. After documenting baseline ECOG PS, M and S pts wore Fitbit for 4 days while receiving chemotherapy or prior to surgery, respectively. Pts' mean steps per day (SPD) were calculated, excluding days Fitbit was worn < 12 hours. To stratify the prediction of toxicity risk, a cutoff of 5000 SPD was selected and any post-operative complication (S pts) or ≥ grade 3 toxicity (M pts) was counted as toxicity. The study is ongoing to accrue 80 pts. RESULTS: On interim analysis, 43 pts were evaluated for the primary aim. Seventy nine percent (34/43) of pts had at least 3 days with ≥ 12 hours of Fitbit usage, meeting the 75% feasibility endpoint. Forty pts (25 M, 15 S) had at least 1 day with ≥ 12 hours of Fitbit usage and had data available for analysis. Mean SPD for PS 0 and PS 1 pts was 7183 and 3214, respectively (p=0.01), and overall was 6290 (SD 4416). Eight M pts and 2 S pts experienced toxicity (Table). The rate of toxicity was 23% (7/30) in pts with PS 0 and 33% (3/10) in pts with PS 1. With SPD as cutoff, the toxicity rate was 11% (2/19) in pts with > 5000, compared to 38% (8/21) in pts with < 5000. CONCLUSION: We observed high rates of compliance with a fitness tracker in CRC pts. SPD serves as a useful identifier for toxicity and may be a better predictor than traditional PS. These findings provide rationale to study SPD in lieu of PS for risk stratification of patients undergoing therapy and possibly incorporate pre-habilitation programs in high risk groups, though validation in larger studies is needed.

Toxicity (T) Rates by PS and SPD [N (%)]

	M (n=25)		S (n=15)	
	T	No T	T	No T
PS 0	6 (38)	10 (63)	1 (7)	13 (93)
PS 1	2 (22)	7 (78)	1 (100)	0 (0)
>5000 SPD	2 (20)	8 (80)	0 (0)	9 (100)
<5000 SPD	6 (40)	9 (60)	2 (33)	4 (67)

P124

Benefits of Laparoscopic Surgery for Sigmoid and Rectal Cancer in Older Adults Compared with Younger Adults T.R. Chesney,* H. Quereshy, A. Draginov, S.A. Chadi, F.A. Quereshy. *Department of Surgery, University of Toronto, Toronto, ON, Canada.*

Background: Initial safety concerns of laparoscopy were more pronounced for older adults. Randomized clinical trials demonstrated oncologic safety and short-term benefits of laparoscopy. It is not clear if these results are similar in older adults. This study investigated short-term outcomes of laparoscopic (LS) and open (OS) surgery for sigmoid and rectal cancer in younger and older adults. Methods: We identified all older adults (70 years or older) and younger adults (<70) with primary sigmoid and rectal cancer treated with resection between 2002 and 2018 from an institutional database. Thirty-day postoperative outcomes were compared after LS and OS between older and younger adults using multivariable logistic regression with interactions. Primary outcomes were mortality, major complications (Clavien-Dindo III-IV), and length of stay (LOS). Results: We identified 792 patients, 293 (37%) older and 499 (63%) younger. Use of laparoscopy was similar between age groups (120/293 (41%) older, 204/499 (41%) younger, p=0.98). All patients had 30-day follow-up. Compared with younger adults, for older adults LS was associated with larger reduction in mortality compared with OS (older LS vs OS, n=2/120 vs 15/173, risk difference (rd) 7.0%; younger LS vs OS, n=2/204 vs 9/295, rd 2.1%; interaction p=0.01). Similarly, compared with younger adults, for older adults LS was associated with larger decrease in major complications compared with OS (older LS vs OS, n=11/120 vs 27/173, rd 6.4%; younger LS vs OS, n=13/204 v 26/295, rd 2.4%; interaction OR 0.52 (95%CI 0.29-0.93), p=0.03). There was no difference in LOS between groups (p=0.48). There were no differences in the magnitude of difference in secondary 3o-day outcomes. Conclusion: Older adults experience greater benefit from LS in mortality and major complications compared with younger adults for treatment of sigmoid and rectal cancer. Indeed, not only do older adults experience short-term benefits of LS, but for important outcomes of mortality and major complications the magnitude of this benefit is greater for older adults.

P125

Utility of Restaging Patients with Stage II/III Rectal Cancer Following Neoadjuvant Chemo/XRT: A Systematic Review L. Hendrick,* R.L. Levesque, D. Shibata, N.M. Hinkle, J.J. Monroe, E. Glazer, J.L. Deneve, P.V. Dickson. *Surgery, University of Tennessee Health Science Center, Memphis, TN.*

Background: In the US, patients with clinical stage II/III rectal cancer typically receive neoadjuvant chemoradiation (chemo/XRT) over 5-6 weeks followed by a 6-10 week break before proctectomy. As this chemotherapy is delivered at radio-sensitizing doses, there is essentially a 3-month window during which potential systemic disease is untreated. Evidence regarding the utility of restaging patients prior to proctectomy is limited. Methods: PubMed, Scopus, Web of Science, and the Cochrane Library were searched for studies evaluating the utility of restaging patients with locally advanced rectal cancer after completion of long course chemo/XRT, and reporting changes in management after restaging. Studies that were non-English, included <50 patients, or examining the diagnostic accuracy of specific imaging modalities were excluded. Study quality was evaluated using the modified Newcastle Ottawa Scale. Results: Eight studies were identified including a total of 1251 patients restaged between completion of chemo/XRT and proctectomy. All studies were retrospective (6 single institution, 2 multi-institution). Restaging identified new metastatic disease in 72 (6.0%) patients, with 4 studies reporting specific sites: liver (n=28), lung (n=8), adrenal (n=1), bone (n=1), and multiple sites (n=7). Overall, progression (distant or local) was detected in 85 (6.8%) patients and resulted in a reported change in management in 71 (5.7%) patients. One study identified an association of high-grade tumors with progression (p=<0.05), however, this was not reported in any other study. Moreover, tumor-related prognostic characteristics were inconsistently reported among studies, precluding

meta-analysis. Conclusions: Although restaging between completion of neoadjuvant chemo/XRT and proctectomy detects disease progression in only a small percentage of patients, findings may alter the treatment plan. A multi-institutional collaboration with analysis of well-defined prognostic variables may better identify a group of patients most likely to benefit from restaging.

Characteristics of included studies

Study	Country	Study Type	Restaging Modality	Patients (n)	Male (%)	Definition of LARC	Grade	New Metastatic Disease (n)	Overall Progression	Location of Metastases	Change in Management (n)	Quality (modified NOS): scale = 0-7
Ayez et al., 2013	Netherlands	Retrospective Cohort	CT CA	153	61	Clinical stage II/III	NR	15	15	Liver (9), Lung (2), Liver/Lung (3)	18	7
Jaffe et al., 2013	United States	Retrospective Cohort	CT CAP or PET/CT	88	58	T2, T3, or T4	NR	0	0	n/a	0	7
Davids et al., 2014	United States	Retrospective Cohort	CT CAP	83	61	Clinical stage II/III	NR	4	4	Liver (2), Lung (2)	0	7
Hanly et al., 2014	United Kingdom	Retrospective Cohort (multi-institutional)	CT CAP and MRI Pelvis	285	69	Clinical stage II/III	NR	18	18	NR	18	7
Bisschop et al., 2015	Netherlands	Retrospective Cohort (multi-institutional)	CT CA	153	59.5	Clinical stage II/III	NR	19	19	Liver (9), Lung (4), Liver/Lung (4), Adrenal (1), Bone (1)	17	7
McBrearty et al., 2016	Ireland	Retrospective Cohort	CT CAP and MRI	59	51	Any receiving neoadjuvant chemoradiation	NR	NR	9	NR	9	7
Schneider et al., 2016	Australia	Retrospective Cohort	CT CAP, MRI, or PET/CT	199	68.8	T2 or greater, any N, any M	NR	8	12	NR	1	7
Park et al., 2018	South Korea	Retrospective Cohort	CT AP	231	63.2	Clinical stage II/III	Low (1,2)= 42.2% High (3,4)= 57.8%	8	8	Liver (8)	8	7

Legend: LARC=locally advanced rectal cancer, NOS=Newcastle Ottawa Scale, CA=chest/abdomen, CAP=chest/abdomen/pelvis, AP=abdomen/pelvis, NR=not reported

P126

Identification of Factors Associated with Delay in Colorectal Cancer Diagnosis at a Major Safety Net Hospital in San Antonio
L. Chodroff,* S. Mitchell, A. Buazza, S. Valek, L. Bailey, M. Trejo, B. Choi, M. Kitano. *Surgery, UT Health at San Antonio, San Antonio, TX.*

Introduction: Colorectal cancer is a common malignancy and cause of significant cancer-related morbidity and mortality. It is potentially curable when diagnosed early; however, 5-year survival is significantly reduced in patients with advanced disease. Patients present with more advanced disease to a major safety net hospital in San Antonio compared to the national average. Our study aims to identify factors associated with patients presenting with more advanced disease. Methods: A retrospective chart review was performed in patients who were treated with colorectal cancer at our hospital between 2010 and 2014. Patients were divided into two cohorts: early disease (Stage I and II) and advanced disease (Stage III and IV). Univariate and multivariate logistical regression analyses were performed. Results: 644 patients were identified. 58.1% were male with median age of 57 years. On univariate analysis, presence of symptoms at diagnosis and not having a primary care physician (PCP), and lack of insurance, were significantly associated with advanced disease with p-value of <0.001 and 0.009, respectively. On multivariate analysis, the presence of symptoms at diagnosis and not having a PCP at diagnosis remained significant with an odds ratio of 0.53 (CI95 0.33-0.85), however, insurance status was not significant on logistical regression with an OR of 0.73 (CI95 0.47-1.15). Discussion: Our study demonstrated lack of having a PCP is significantly associated with patients presenting with more advanced colorectal cancer. This emphasizes the importance of PCPs who provide health maintenance and offer basic cancer screening. Although not significant on multivariate analysis, lack of insurance was also associated with more advanced disease. Nationally, Texas has the largest number of uninsured patients, and our findings demonstrate correlation between lack of access to healthcare and patients presenting with advanced cancer. Improved access to healthcare via affordable insurance may lead to earlier detection of colorectal cancer in our community, which may translate to decreased cancer-related morbidity and mortality.

P127

Evaluating the Prognostic Significance of Lymphovascular Invasion in Stage II and III Colon Cancer
D. Mutabdzic,* S.B. O'Brien, E. Handorf, K. Devarajan, S. Reddy, E.R. Sigurdson, C. Denlinger, J.E. Meyer, J. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Presence of lymphovascular invasion (LVI) is known to be a predictor of lymph node involvement in colon adenocarcinoma (CA). Lymph node involvement is associated with poorer prognosis necessitating adjuvant therapy. While some studies have suggested that LVI is a predictor of worse survival in early stage colon cancer, the significance of LVI on prognosis has not been tested in a comprehensive North American data set. Methods: Patients with stage II and III CA with LVI data available and those who received predefined standard of care treatment were identified in the National Cancer Data Base from 2011 to 2015. The relationship between LVI and overall survival was tested using Kaplan-Meier survival curves and Cox proportional hazards regression analysis after adjusting for relevant clinical and demographic variables. Hazard ratios and 95% confidence intervals are reported along with median overall survival (OS) where available. Results: The dataset included 93,070 patients with stage II and 66,701 patients with stage III CA. The proportion of patients with LVI was 13% in stage II and 47% in stage III CA. After adjusting for age, sex, gender, race, comorbidities, socioeconomic status, T, and N stage, LVI was associated with worse OS in stage II, HR 1.2 (1.15-1.25, p<0.001), and in stage III, HR 1.25 (1.21-1.30, p<0.001), CA. Median OS was 6.51 years with LVI vs. 6.85 years without LVI in stage II compared with 6.57 years with LVI vs. not reached without LVI in stage III CA. Of the stage II patients with LVI, 20% received adjuvant chemotherapy and median OS was 6.91 years for those who did vs. 6.07 years for those who did not receive chemotherapy. Conclusion: Our data suggest that LVI is an important predictor of OS in stage II and III CA. Despite some uncertainty as to the benefit of adjuvant chemotherapy in stage II CA, guidelines suggest consideration of adjuvant chemotherapy in patients with high risk stage II disease. Our data support the recommendation that LVI be considered a high risk feature in stage II disease. Further studies are necessary to examine whether the type or duration of chemotherapy should differ for patients with CA and LVI.

P128

Peritoneal Metastases have a Distinct Molecular Profile from Primary Colorectal Adenocarcinoma
M. Tsao,[1]* F.W. Williard,[1] M.K. Stein,[2] M.G. Martin,[2] E. Glazer,[1] P.V. Dickson,[1] J.L. Deneve.[1] *1. Surgery, University of Tennessee Health Science Center, Memphis, TN; 2. West Cancer Center, Memphis, TN.*

Background: Peritoneal metastases (PM) from colorectal cancer (pCRC) are associated with poor outcomes; however, molecular differences are not well-defined. Methods: We compared tumor profiles of pCRC and PM patients (pts) from Caris Life Sciences. Testing included next-generation sequencing (NGS) of 592 genes, immunohistochemistry (IHC), copy number variants (CNV), microsatellite instability (MSI) and tumor mutational burden (TMB). Mutations were termed pathogenic (PATH) or variants of unknown significance (VUS). TMB was compared in mutations/Mb (MMb). Results: 617 pCRC and 348 PM pts had similar gender (55% male) and age (median 59). 232 pCRC were left-sided (LS), 189 right-sided (RS), 147 rectum (R) and 49 not otherwise specified (NOS); PM were 45 RS, 29 LS, 22 R and 252 NOS. IHC expression in PM was increased in TOPO1 (62% v. 52%, p<0.01), ERCC1 (27% v. 18%, p<0.01) and MLH1 (96% v. 92%, p<0.05) and decreased in PD-1 (36% v. 65%, p<0.01), TOP2A (76% v. 100%, p<0.01) and PTEN (64% v. 72%, p<0.05). By sidedness, LS PM were more frequently TOPO1 and PD-L1 positive. PTEN IHC was higher in R pCRC. 7 PM CNVs were increased (ADGR2A2, CCND1, ELL, FGF3, FGF4, JAK3 and PDGFRB) and FLT3 CNVs were decreased. MYC CNVs were more common in RS PM compared to pCRC. No difference was seen in PM and pCRC PATHs in KRAS, BRAF, SMAD2, SMAD4, PTEN. PM had more PATHs in GNAS (8% v. 1%, p<0.01) while pCRC PATHs were increased in APC (76% v. 48%, p<0.01), TP53 (72% v. 53%, p<0.01), ARID1A (29% v. 12%, p<0.05), PIK3CA (22% v. 15%, p<0.05) and FBXW7 (13% v. 7%, p<0.01). LS PM had increased FLCN PATHs (12% v. 2%, p<0.01); R PM had more PATHs in KMT2D (20% v. 1%, p<0.01) and RNF43 (13% vs. 3%, p<0.05). VUS were increased in 39/592 (7%) genes for PM compared to pCRC. No MSI or fusion difference was seen. 53% pCRC (median = 8) pts had TMB ≥8 MMB compared to 43% PMs (median = 7; p = 0.03); no TMB difference was seen

for LS, RS or R subgroups. Conclusions: Compared to pCRC, PM had more PATHs in GNAS and less in classic CRC markers APC and TP53. While TMB was generally lower in PM, differences in IHC expression, CNV and VUSs may serve as biomarkers for PM requiring further study.

P129

Geographic Variability in Colorectal Cancer Care: Limitations of a Universal Healthcare System? M. Delisle,* R. Helewa, J. Park, D. Hochman, A. McKay. *Surgery, University of Manitoba, Boston, MA.*

Introduction: Access to colorectal cancer (CRC) care may be improved in a universal healthcare system, but inequities can still exist due to variations in access to high quality care due to geography. This study aims to determine variations in access and quality of CRC care in a geographically dispersed universal healthcare system. Methods: All patients diagnosed with stage I-IV CRC in Manitoba, Canada between 2004 and 2014 were included. Data were obtained from provincial administrative claims and cancer registry. Published quality indicators were assessed based on availability of data. Primary predictors included distance from Winnipeg, the major urban city with the highest volume centers in Manitoba, and hospital volume. Multivariable logistic regression, expressed as adjusted odds ratios (aOR), and Poisson regression, expressed as adjusted incidence rate ratios (aIRR), were used to assess impact of geography. Confounders included age, sex, year of diagnosis, socioeconomic status, Charlson Co-Morbidity Index and stage. Results: A total of 8,113 patients were included. Significant variations in access to care were found. Patients living most remotely (>500 km) had significantly lower odds of undergoing curative resection (aOR 0.6, 95% CI 0.37-0.99, p=0.05). Patients living >500km who underwent curative resection had an increased odds of receiving surgery in a lower volume hospital (aIRR 2.05, 95% 1.92-2.18, p<0.01). Significant variations in care were found between hospitals. Lower volume hospitals had higher odds of open surgery (aOR 1.02, 95% CI 0.99-1.04, p=0.05), incomplete lymph node harvests (aOR 1.02, 95% CI 1.0-1.04, p=0.03) and anastomotic leaks (aOR 1.06, 95% CI 1.01-1.12, p=0.02). There was no significant differences in odds of 30-day mortality, preoperative colonoscopy or readmission. Conclusion: Geography was found to be associated with variability in CRC care with the greatest impact among the most remote. This has been observed across similar settings and likely reflects the inherent limitations of a universal healthcare system that are due to geography rather than ability to pay.

P130

Stage II and III Rectal Adenocarcinoma Outcomes Related to Lymphovascular Invasion S. O'Brien,* D. Mutabdzic, E. Handorf, K. Devarajan, S. Reddy, E.R. Sigurdson, C. Denlinger, J.E. Meyer, J. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Background: Lymphovascular invasion (LVI) is associated with nodal involvement and local recurrence in rectal cancer. In some smaller, single institution studies studies, the presence of LVI has also been associated with worse survival. Our goal was to examine the effect of LVI on rectal cancer prognosis in a large, inclusive database. Methods: Outcomes of patients with clinical stage II and stage III rectal cancer in the National Cancer Data Base (NCDB) from 2011 to 2015, in whom LVI data was available, were evaluated. Overall survival was compared in patients with and without LVI using Kaplan-Meier survival curves and Cox proportional hazards regression analysis. Median overall survival and hazard ratios with 95% confidence intervals are reported where available. Results: The dataset included 9206 patients with stage II and 12640 patients with stage III rectal adenocarcinoma for which LVI data were available and who received neoadjuvant radiation or chemoradiation and adjuvant chemotherapy. The proportion of patients with LVI was 11% in stage II and 16% in stage III rectal cancer. After adjusting for age, sex, race, T and N stage, comorbidities, and other clinical and demographic variables, LVI was associated with worse overall survival in stage II HR 1.87 (1.62-2.16, p<0.001) and in stage III HR 1.8 (1.61-2.02, p<0.001) rectal cancer. The median overall survival was not reached in stage II rectal cancer patients without LVI vs. 5.73 years with LVI. In stage III rectal cancer, the median overall survival was 6.91 years without LVI vs. 6.21 years with LVI. Conclusions: Lymphovascular invasion is an independent risk factor for mortality in stage II and III rectal cancer. Stage II rectal cancer patients without LVI have the best survival of the groups studied, potentially identifying patients that may benefit from de-escalated therapy. Further studies will be guided at identifying if benefits with chemotherapy are associated with LVI.

P132

Genital Necrosis After Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy with Mitomycin-C C. Velez-Mejia,[1]* A. Sardi,[1] J. Spililotis,[2] M. Sittig,[1] V. Gushchin.[1] *1. Surgical Oncology, Mercy Medical Center, Baltimore, MD; 2. Athens Medical Center, Athens, Greece.*

Background: Mitomycin-C (MMC) is a common perfusion agent in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) for treatment of gastrointestinal malignancies. Regional adverse effects are rare and not fully studied. We report seven patients (5 male, 2 female) who developed genital necrosis after CRS/HIPEC with MMC. Methods: Peri-/post-operative data of patients presenting with genital necrosis from global peritoneal surface malignancy centers (n=2, North America and Europe) was reviewed. Results: Median age was 60 years and onset of symptoms ranged from 40-176 days after MMC exposure (mean 89 days). All patients had stage IV disease with mean preoperative PCI of 25 (range 14-39) and 100% complete cytoreduction (CC-0-1) rate. Five patients received a total intraperitoneal dose of 40mg and two received 28mg. Three patients had splenectomy; however, hematological changes (anemia and thrombocytosis/-penia) were observed in all patients that persisted until symptoms of genital necrosis occurred: erythema, uncontrolled pain, and genital ulceration. Predisposing hematological conditions were ruled out. Histological report showed necrotic tissue and thrombosis of local vasculature in biopsy confirmed cases. MMC was used in 54% (639/1174) CRS/HIPEC procedures with 7/639 patients developing genital necrosis yielding a 1.1% incidence. Conclusion: We propose a mechanism of thrombotic microangiopathy combined with local factors resulting in local inflammation and necrosis of the genital area after MMC perfusion. Initial therapy for genital necrosis after CRS/HIPEC with MMC should focus on conservative treatment and considered as a differential diagnosis of delayed soft tissue lesions following this surgical procedure.

P133

Outcomes in Peritoneal Carcinomatosis from Appendiceal Goblet Cell Carcinoid Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC) K. Zambrano-Vera,* A. Sardi, K. Studeman, C. Nieroda, M. Sittig, C.A. Munoz-Zuluaga, A. Sipok, V. Gushchin. *Surgical Oncology, Mercy Medical Center, Baltimore, MD.*

Background: Appendiceal goblet cell carcinoma (GCC) is considered an aggressive tumor that is often misclassified due to controversial microscopic features. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is standard of care for appendiceal peritoneal carcinomatosis (PC), however; some studies report no survival benefit in peritoneal carcinomatosis (PC) from GCC, concluding these patients should not be treated aggressively. We analyzed outcomes in PC from GCC treated with CRS/HIPEC. Methods: A prospective institutional database of patients who underwent CRS/HIPEC between 1995-2017 was reviewed. Twenty-three patients with histopathologic diagnosis of known goblet cell carcinoid arising in the appendix were included. Perioperative variables were analyzed including previous surgeries, neoadjuvant chemotherapy, Peritoneal Cancer Index (PCI), and completeness of cytoreduction (CC score). Overall survival (OS) and progression-free survival (PFS) were calculated. Log-rank test compared survival outcomes between subgroups Results: Twenty-three patients underwent 28 CRS/HIPEC procedures. Twenty (87%) patients had previous surgery and 3 (13%) received systemic chemotherapy before HIPEC. Median pre-operative PCI was 14 (range 1-39). CC score of 0/1/2/3 after 23 procedures was achieved in 17 (61%), 4 (14%), 2 (7%), 4 (14%), and 1 (4%) not reported, respectively. Median follow-up was 82 months. PFS at 1, 3, and 5 years was 94%, 67%, and 60%, respectively. Median PFS in CC-0/1 (<0.25cm residual disease) was 96 months. OS at 1, 3, and 5 years was 100%, 73%, and 67%, respectively. Median OS was not reached in CC-0 patients but was significantly longer than CC-1/ 2/ 3 patients (p=0.001). OS in PCI<20 at 1, 3, and 5 years was 100%, 90%, and 90%, respectively; median OS was not reached. OS in PCI ≥20 at 1, 3, and 5 years was 100%, 67%, and 50%, respectively (p=0.013) with median OS of 50 months. Conclusion: Patients with PC from appendiceal GCC should not be excluded from CRS/HIPEC only based on the aggressive biological behavior of goblet cell carcinoma.

P134

Management of Low-Grade Appendiceal Mucinous Neoplasms (LAMN): An International Survey of HIPEC Surgeons M. Gage,[2]* A. Istl,[2] J. Esquivel,[1] N. Ahuja,[3] F.M. Johnston.[2] *1. Frederick Regional Health System, Frederick, MD; 2. Johns Hopkins Hospital, Baltimore, MD; 3. Yale School of Medicine, New Haven, CT.*

LAMNs are rare tumors and preferred pre-referral management is unestablished. We determined to assess the current consensus amongst HIPEC surgeons on preferred pre-referral and definitive management of mucinous appendiceal lesions. Methods An online survey was sent to 106 HIPEC surgeons internationally. The survey assessed common presentations and work up, and preferred pre-operative and operative management of LAMN. Results The response rate was 40% with 33% located internationally and 67% within the USA. Surgeons performed an average of 27 (range 1-200) HIPEC cases in the last year, with 17 (range 1-150) of them for LAMN. The majority (>90%) of surgeons reported half or more of their LAMN cases underwent surgery prior to referral. Of these, an average of 49% underwent appendectomy, while 25% underwent right hemicolectomy. The majority of surgeons reported that preferred management for suspected LAMN prior to referral was appendectomy (60%) or biopsy of mucin (43%) if mucin was present (Figure). For definitive management of LAMN confined to the appendix, 86% of surgeons reported treating with appendectomy only. If present with mucinous implants, 24% of surgeons reported they surveille after appendectomy, while 76% would proceed with HIPEC. However, if the mucinous implants contained malignant cells, 100% would proceed with HIPEC. Conclusion Pre-referral management of LAMN is diverse with 25% of patients referred after potentially avoidable hemicolectomy. Management of LAMN with non-malignant mucinous deposits is also diverse with 24% of HIPEC surgeons recommending observation and the rest cytoreduction with HIPEC. Identification of prognostic indicators are needed to refine management approaches.

P135

Minimally Invasive Versus Open Surgery for T4-Colon Cancer: A Propensity-Matched Analysis K.J. Lafaro,* I. Konstantinidis, L.G. Melstrom, L. Lai, K. Melstrom, S. Sentovich, B. Lee, M. Raoof. *Surgery, City of Hope, Pasadena, CA.*

Background: Minimally invasive colectomy (MC) has improved perioperative outcomes over open colectomy (OC) with comparable oncologic outcomes in randomized clinical trials. Patients with T4 cancers are either excluded or under-represented in these trials. Methods: Using the National Cancer Database (NCDB), we analyzed patients undergoing surgery for T4 colon cancer over a four-year period (2010-2014). Propensity score nearest-neighbor 1:1 matching (PSM) was performed between MC and OC patients based on year of diagnosis, tumor site and size, zone of extension, grade, lympho-vascular invasion, comorbidities, extent of surgery, race/ ethnicity, insurance status, socioeconomic indicators, facility type and hospital colectomy volume using an intention to treat analysis. Primary outcome was overall survival. Stratified analyses by zone of extension were performed: Zone 0 (T4a); Zone 1 (adherence without invasion); Zone 2 (anatomically adjacent organ); Zone 3 (abdominal wall); Zone 4 (anatomically non-adjacent organ) Results: Of the 19,178 eligible patients, 6,564 (34%) underwent MC. After PSM two well-balanced groups of 5,099 patients each were analyzed. Despite matching, minimally invasive approach was associated with improved overall survival (HR: 0.71, 95% CI 0.67-0.76; Median OS 59 vs. 42 months, p<0.001). Compared to MC patients undergoing OC had: a higher margin positive rate (20.5% vs. 18.4%, p-value=0.009); lower median nodes examined (20 vs. 21, p-value<0.001); a lower rate of adjuvant chemotherapy (46.8% vs. 54.2%, p-value<0.001); and a longer median time to chemotherapy (47 vs. 44 days, p-value<0.001). Overall conversion rate was 22.3%. Stratified survival analyses demonstrated that MC was associated with improved overall survival compared to OC in all zones except zone 3 and 4. For zone 3 and 4 extension, the overall survival was similar between the two groups. Conclusion: In this analysis of a large nationally representative cohort, after matching for tumor biology, socioeconomic factors and institutional factors, MC for T4 colon cancer is associated with improved oncologic outcomes compared to OC.

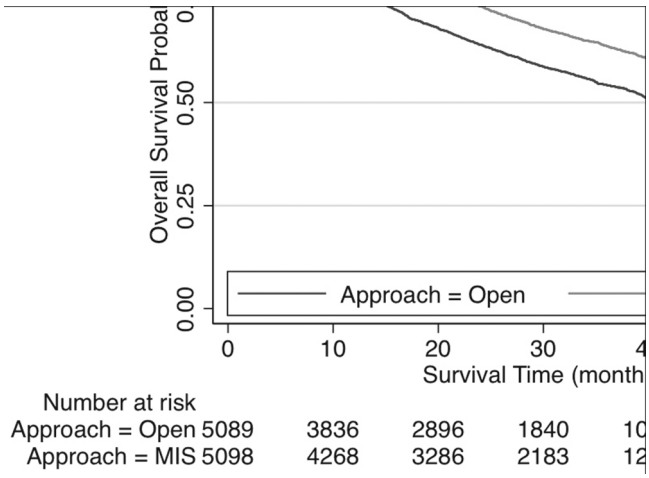


Figure 1. Kaplan-Meier Overall Survival Estimates of patients undergoing MC vs.OC in a propensity-matched, national cohort. (Log-rank p-value <0.001)

P136

KRAS Mutation is Associated with Upregulation of Integrin β4 and Colorectal Cancer Invasiveness S. Choi,[1]* M. Marco,[1] C. Chen,[1] R. Pelossof,[1] K. O'Rourke,[2] J.J. Smith,[1] J. Garcia-Aguilar.[1] *1. Surgery, Memorial Sloan Kettering, New York, NY; 2. Weill Cornell / Sloan Kettering / Rockefeller University Tri-Institutional MD-PhD Program, New York, NY.*

Background: KRAS mutation ($KRAS^{mut}$) has been shown to be associated with reduced expression of extracellular matrix (ECM) genes and with resistance to chemoradiotherapy in colorectal cancer (CRC). Here, we investigated the impact of $KRAS^{mut}$ on integrins, receptors for ECM proteins, expression and CRC phenotype. Methods: We identified transcriptomic alterations associated with KRAS in locally advanced rectal tumors from 79 patients and validated those alterations in the TCGA CRC data set. Expression of integrin β4 (ITGB4) was measured in 39 tumor specimens by counting ITGB4-positive cells in an E-cadherin-positive epithelial cell population. We also examined the effect of introducing $KRAS^{mut}$ and the effect of knocking out ITGB4 in the CRC cell line HCT116 and in organoids from genetically engineered mice. Results: ITGB4 expression was higher in $KRAS^{mut}$ tumors than in tumors with wild-type KRAS both in the specimens from patients (P = 0.0029) and in the TCGA data set. Introduction of $KRAS^{mut}$ in HCT116 cells and mouse organoids increased ITGB4 expression 2- to 3-fold (P = 0.0101 and 0.0116, respectively). Knockout of ITGB4 reduced migration (0.45-fold, P = 0.0012) and invasiveness (0.36-fold, P = 0.0023) of HCT116 cells but did not alter proliferation (P = 0.6672). Conclusions: $KRAS^{mut}$ increases ITGB4 expression, which is associated with CRC invasiveness and cell migration. Further study is needed to identify the correlation with clinical outcome.

P137

Outcomes of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in Patients Using Oxaliplatin: A Systematic Review and Meta-analysis M.T. Alhumaid,* E. Fallatah, S. Sait, N. Alsayegh, N. Farsi, M. Nassif, N. Trabulsi. *General Surgery, King Abdulaziz University Hospital, Jeddah, Saudi Arabia.*

Introduction: Up to 25% of patients with metastatic colorectal cancer (CRC) present with only peritoneal carcinomatosis (PC). Until recently, PC was considered fatal. Cytoreductive surgery (CRS) plus hyper-thermic intraperitoneal chemotherapy (HIPEC) has become a standard treatment for limited PC. It was suggested that oxaliplatin for HIPEC may improve median and overall survival after complete macroscopic cytoreduction of peritoneal carcinomatosis of colonic origin. We aim to systematically review all the studies and obtain disease free survival (DFS) and overall survival (OS) in the patients with CRC with PC who underwent CRS and HIPEC using Oxaliplatin. Methodology: We conducted a comprehensive literature search of medical electronic databases (PubMed and Google Scholar) in February 2018. We included studies that reported survival outcomes of CRC patients with PC

that underwent CRS and HIPEC using Oxaliplatin. Outcomes of interest were DFS and OS. Quality of published trials was assessed using the MINORS index (Methodological Index for Non-Randomized Studies). Results: Out of 2,803 studies identified on initial search, only 10 matched our inclusion criteria. Included studies with patients and treatment details are presented in Table1. None of the studies were randomized control trials. Three were retrospective studies. Of the 1,467 patients across included studies, 612 received Oxaliplatin-only based HIPEC and 121 received Oxaliplatin- Irinotecan based HIPEC. The rest of the patients received other therapeutic regimens. Survival results of included studies are demonstrated in Table 1. The quality of included studies range of total score out of 16 for non-comparative studies was (10-12) and for comparative studies, the range was (13-20). Conclusion: Based on our preliminary results, there is lack of RCTs comparing Oxaliplatin with other therapeutic regimens in CRS and HIPEC in patients with CRC and PC. The overall quality of published studies is adequate, however, not all studies were prospective. Further survival analysis is underway. Future RCTs comparing Oxaliplatin with Mitomycin are needed.

Table 1: Studies Included & Their General Features

Author/ Year	Setting	Number of overall patients	Number of patients received Oxaliplatin	Male proportion (Oxaliplatin group)	mean/(Median) age in years (Oxaliplatin group)	Chemotherapeutic agent used for HIPEC	Comparison group	Previous Chemotherapy	Adjuvant used	Disease free survival (Oxaliplatin group)	Overall survival (Oxaliplatin group)	Median follow up (Months)
Cavaliere, 2010	Multi-centric, Italy	146	11	Φ	Φ	Oxaliplatin	Intraperitoneal Cisplatin OR Mitomycin C	Φ	Yes	Φ	Median = 28	19
Elias, 2009	France	96	30	64	(46 years)	Oxaliplatin	Systemic chemotherapy	Yes	Φ	Φ	Φ	63
Faron, 2015	France	173	Φ	N/A	N/A	Oxaliplatin + Irinotecan	None	Yes	Yes	N/A	N/A	48.5
Gervais, 2013	Canada	40	25	Φ	Φ	Oxaliplatin	Systemic chemotherapy	Yes	Φ	3-years: 22%	3-years: 61% 5-years: 36%	22.8
Glockzin, 2014	Germany	32	20	45	(53 years)	Oxaliplatin	Intraperitoneal Irinotecan	Yes	Φ	Φ	2-years: 70% 3-years: 65%	39.4
Hompes, 2012	Multi-centric, Belgium	48	48	35.4	60 years	Oxaliplatin	None	Φ	Yes	1- year: 65.8% 2- years: 45.5%	1-year: 97.9% 2-years: 88.7%	22.7
Leung, 2017	Australia	202	96	54.2	(55.5 years)	Oxaliplatin	Intraperitoneal Mitomycin C	Φ	Yes	Median: 19 months	Median: 56 months	Φ
Prada-Villaverde, 2014	Multi-centric, North-America & Europe	584	166	55.4	(56.9 years)	Oxaliplatin	Intraperitoneal Mitomycin C	Φ	Φ	Φ	Median: 29.8 months	Φ
Quenet, 2011	Multi-centric, France	146	43	27.9	Φ	Oxaliplatin	Intraperitoneal Oxaliplatin + Irinotecan	Yes	Yes	Median: 16.8 months 5-years: 13.8%	5-years: 41.8% Median: 40.83 months	48.5
Turrini, 2012	France	60	26	Φ	Φ	Oxaliplatin	None	Yes	Yes	Median: 11 months 1-year: 42% 3-years: 25% 5-years: 20%	1-year: 100% 3-years: 51% 5-years: 37% Median: 39 months	41

P138

Higher-average Flow Rates During HIPEC Optimize Peritoneal Hyperthermia R.J. Hendrix,[1]* J. Kassira,[1] L.A. Lambert.[2] *1. University of Massachusetts Medical School, Worcester, MA; 2. Hunstman Cancer Institute, Salt Lake City, UT.*

Background: Optimization of hyperthermic intraperitoneal chemoperfusion (HIPEC) depends on rapid heating of the peritoneum to 40-43 °C and maintenance of that target temperature for the duration of chemoperfusion. Given the potential toxicity of increasing inflow temperatures, it has been postulated that increasing flow rates may improve heating. The aim of this study was to evaluate the efficacy of higher flow rates on hyperthermia during cytoreductive surgery (CRS) and HIPEC. Methods: A retrospective review of patients undergoing CRS-HIPEC for disseminated peritoneal cancer at a tertiary academic medical center between January 2011 and July 2017 was performed. Demographics, intraoperative factors, perfusion parameters, 30-day postoperative complications, and 90-day mortality were recorded. Outcomes were stratified according to average flow rate during the 90-minute HIPEC. Results: 137 CRS-HIPEC cases were reviewed. 67 (49%) cases had a documented average flow rate >2.35 L/min. Aside from age at operation (54 vs 57.8, p=0.02), there were no significant differences in patient demographics or intraoperative characteristics. Average flow rates >2.35 L/min were associated with reduced average core body temperatures (38.0 °C vs 38.3 °C, p=0.05), increased average peritoneal outflow temperatures (41.7 °C vs 41.3 °C, p=0.01), and increased maximum peritoneal outflow temperatures (42.3 °C vs 41.9 °C, p=0.04). Furthermore, there was a reduced temperature gradient between inflow and outflow tubes when higher average flow rates were achieved (0.6 °C vs 1.1 °C, p=0.04). There was a trend toward decreased 30-day complications, however, this was not statistically significant. Conclusion: Maintaining an average flow rate >2.35 L/min during HIPEC is associated with reduced core body temperature and enhanced exposure of the peritoneum to hyperthermic chemotherapy. Flow rates >2.35 L/min were not associated with increased morbidity.

P139

Elevated Maximum Core Body Temperature During HIPEC Increases Postoperative Complications R.J. Hendrix,[1]* J. Kassira,[1] L.A. Lambert.[2] *1. University of Massachusetts Medical School, Worcester, MA; 2. Huntsman Cancer Institute, Salt Lake City, UT.*

Background: Hyperthermia is known to enhance the cytotoxicity of chemotherapeutic agents used during cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemoperfusion (HIPEC). However, this may result in an elevated core body temperature (CBT) with effects on hemodynamics, organ function and subsequently, surgical morbidity. This study evaluates the relationship of maximum CBT during CRS-HIPEC on postoperative outcomes. Methods: A retrospective review of patients undergoing CRS-HIPEC for disseminated peritoneal cancer at a tertiary academic medical center between January 2011 and July 2017 was performed. Demographics, intraoperative factors, perfusion parameters, 30-day postoperative complications, and 90-day mortality were recorded. Outcomes were stratified according to maximum CBT reached during the 90-minute HIPEC as measured by an esophageal temperature probe. Logistic regression modeling was used to adjust for potential confounders. Results: 135 consecutive CRS-HIPEC cases were reviewed. 36 (27%) cases had a documented maximum CBT > 39.5 °C. Preoperative Peritoneal Cancer Index (PCI) score was higher in this group (21.1 vs 16.6, p=0.02), however, the length of surgery and extent of cytoreduction as measured by the number of organs resected, anastomoses, and peritonectomies were similar. When CBT reached 39.5 °C during HIPEC, there was an increase in any 30-day postoperative complication (56% vs 34%, p=0.03) and severe Clavien-Dindo grade > 3 complication (22% vs 11%, p=0.03). Despite this, there was no significant impact on hospital length of stay (10.6 days vs 11.5 days, p=0.69) or 90-day mortality (0% vs 1%, p=0.32). Adjusting for age, gender, intraoperative chemotherapy agent, length of surgery, and preoperative PCI score, the odds ratio of having a Clavien-Dindo grade > 3 complication was 0.39 (95% CI 0.16 – 0.92) when maximum CBT was maintained below 39.5 °C. Conclusion: Maximum CBT > 39.5 °C is associated with an increased risk of postoperative morbidity. Adjunct cooling measures should be considered during HIPEC to prevent such severe systemic hyperthermia.

P140

Association of Time-to-Surgery with Postoperative Complication and Overall and Disease-Free Survival After Surgery for Sigmoid and Rectal Cancer H. Quereshy,[1]* T.R. Chesney,[2] A. Draginov,[3] S.A. Chadi,[3] F.A. Quereshy.[3] *1. Case Western Reserve University School of Medicine, Cleveland, OH; 2. University of Toronto, Toronto, ON, Canada; 3. University Health Network, Toronto, ON, Canada.*

Background: National and regional guidelines for cancer care recommend maximum time targets for primary cancer treatment. The evidence base is limited and inconsistent to inform these time targets, with most based on expert opinion. We aimed to assess the association of time-to-surgery with postoperative complications, overall survival (OS), and disease-free survival (DFS) for patients undergoing primary sigmoid and rectal cancer resection. Methods: We identified all patients with primary sigmoid and rectal cancer treated with non-emergent resection between 2002 and 2018 from an institutional database. A data-derived threshold in the association of time-to-surgery and survival was selected using a multivariable Cox model with restricted cubic spline and adjusted by age, tumor site, and comorbidities. This threshold was used to divide the cohort into early and late time-to-surgery subgroups, which were used to assess the association of time-to-surgery with postoperative complications, and overall and disease-free survival. Results: A total of 714 patients were included with a median age of 66 (IQR 56-74) years. Median time-to-surgery was 49 (IQR 29-70) days. Median follow-up was 60 (IQR 25-111) months. A threshold time-to-surgery of 60 days was identified. Time-to-surgery was not associated with 30-day postoperative complications. Time-to-surgery was not associated with OS or DFS when assessed as a continuous non-linear variable. Likewise, when dichotomized into early and late groups, there was no difference in OS (HR 1.17, 95%CI 0.86–1.58) or DFS (HR 1.16, 95%CI 0.86–1.58) between groups. Conclusion: While current maximum time targets for surgical treatment of colorectal cancers are based on expert opinion, we have identified a data-driven threshold for time-to-surgery of 60 days. There is no association of time-to-surgery with 30-day postoperative

complications, OS or DFS when evaluated as a continuous variable or using a 60 day threshold. While longer time-to-surgery is unlikely to affect complications, recurrence or survival, additional studies must identify optimal wait time targets for colorectal cancer.

P141

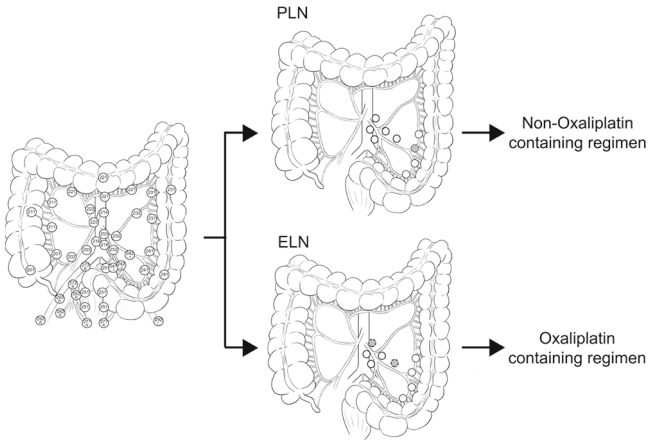
Experience of Side-to-Side Anastomosis, Circular Side-Stapling Technique During Laparoscopic Anterior Resection in Our Institute: Experience of Over One Hundred Cases K. Ando,* Q. Hu, Y. Tsuda, Y. Nakashima, H. Saeki, E. Oki, M. Mori. *Department of Surgery and Science, Kyushu University, Fukuoka, Japan.*

Background: Anastomotic leakage is a major problem in rectal surgery. The incidence of leakage is estimated to be 5-10%. Cases with anastomotic leakage after rectal cancer operation have more recurrence compared to cases without leakage. We developed a side-to-side anastomosis using a circular stapler in a circular side stapling technique (CST) to reduce leakage. Herein, we report the method and outcome of CST. Method: After removing the specimen, an anvil rod is inserted through the side of the colon wall. The entry hole is closed with autosuture device. Intraperitoneally, the shaft of the anastomosis device is pierced through the side of the rectal wall. Then, the colorectal anastomosis is performed. During this procedure, the staple line of the rectum should not be rolled into the anastomsis. Result: From January 2013 to December 2016, 138 cases (67 males and 71 females) underwent anastomosis by CST. Average age was 64.9. The locations of the lesion were sigmoid colon: 36, recto-sigmoid colon: 55, upper rectum: 41 and lower rectum: 6. Average operation time was 225.7 minutes and average amount of bleeding was 47.1 grams. A covering stoma was created in 13 cases where patients had severe diabetes or long-term use of steroids. Average hospital stay after the operation was 11.2 days. 16 cases (11.6%) had postoperative complication. Of those, five cases (3.6%) had anastomotic leakage. Among the 5 cases, 2 cases were relieved with conservative care while three cases needed an additional operation. With long term outcome, 3-years progression free survival was 82.9% and 5 year overall survival was 86.4% in all 138 cases. Cases with complication had worse progression free survival compared to cases without comlication (P=0.013 HR 3.7 95%CI [1.05-10.3]). Summary: CST was a safe and useful procedure in laparoscopic anterior resection. However, complications including leakage are still a major problem. Using various procedures we are working to prevent complications.

P142

Oncologic Impact of Anatomic Extent of Metastatic Lymph Nodes Metastasis in Stage III Colon Cancer: Implications for Choice of Adjuvant Chemotherapy I. Woo,[1]* J. Park,[2] b. gang,[2] S. Park,[2] H. Kim,[2] G. Choi,[2] J. Kim.[2] *1. Colorectal surgery, Daegu Veterans Hospital, Daegu, Korea (the Republic of); 2. Kyungpook National University Hospital, Daegu, Korea (the Republic of).*

Aim: Oxaliplatin based chemo regimen improves the survival outcomes for Stage III colon cancer patients. But, its serious toxicity is well known. The purpose of this study was to determine the difference in survival outcomes among patients who underwent curative resection for stage III colon cancer with PLN metastasis with or without oxaliplatin. Methods: Between January 2010 and December 2014, a total of 254 patients who underwent curative resection in stage III colon cancer were analyzed. Two groups were divided according to their LN distribution (PLN, n=175 vs. ELN, n=79). Clinicopathological features, three-year disease-free survival rate (DFS), and overall survival rate (OS) were analyzed with and without oxaliplatin in PLN group. Results: With a median follow-up of 48.5 months, the PLN group showed significantly improved DFS and OS compared to the ELN group (3yr DFS: 88.7% vs 69.6%, $p < 0.001$; 3yrOS: 95.8% vs 77.8%, $p < 0.001$). Whereas, there was no significantly different DFS and OS between the oxaliplatin group and non-oxaliplatin group in the PLN group (3yr DFS: 89.1% vs 88.2%, $p = 0.460$; 3yrOS: 99.0% vs 92.0%, $p = 0.137$). In the multivariate analysis, the addition of oxaliplatin showed no prognostic significance on DFS ($p = 0.073$) and OS ($p = 0.594$). The subgroup analysis in the PLN group with less than two positive LNs also revealed no association in terms of DFS ($p = 0.963$) and OS ($p = 0.683$). Conclusion: Oxaliplatin has no benefit in adjuvant chemotherapy for only PLN metastasis in colon cancer patients. Further study is necessary to determine more adequate subsequent chemotherapy after curative resection.



P143

Preoperative Chemoradiotherapy for Lower-Advanced Rectal Cancer Patients Using SOX+Bev Regimen J. Higashijima,* M. Shimada, K. Yoshikawa, T. Miyatani, T. Tokunaga, M. Nishi, H. Kashihara, C. Takasu. *Surgery, Tokushima University, Tokushima, Japan.*

[Background] Preoperative chemoradiotherapy (CRT) in rectal cancer reduces the local recurrence rate after operation and preserves the anus. We had already reported the usefulness of CRT with a single drug for lower advanced rectal cancer patients (J Cancer Ther 2012). Now we finished the phase 2 trial of CRT using multidrugs (S-1+Oxaliplatin+Bevacizumab : SOX+Bev) to improve patient's prognosis (UMIN 00013267). The aim of this study is to clarify the result of this trial and the predictive factor of CRT (miR-223). [Methods] Lower advanced rectal cancer patients (n=104) who underwent preoperative CRT using S-1 or UFT (n=59), SOX+Bev regimen (n=45) were included in this study (40Gy radiotherapy). The effects of CRT which were determined by RECIST and histopathologic examination. Additionally, miRNA 223 was measured using the biopsy specimens before preoperative CRT. [Results] Clinical response were as follows : S-1/UFT : CR/PR/SD/PD=1/32/26/0,SOX+Bev : CR/PR/SD/PD=3/38/4/0. Clinical response rate was higher in SOX+Bev group (91.1%) than S-1/UFT group (55.9%). Pathological response were as follows : S-1/UFT :1a/1b/2/3=13/16/27/3,SOX+Bev :1a/1b/2/3=7/7/21/8 (Two patients were watch and wait cases). Histological response rate (Grade2,3) was 50.8% in S-1/UFT group and 67.4% in SOX+Bev group. The pCR rate was higher in SOX+Bev group (18.6%) than S-1/UFT group (5.1%). The miR-223 in SOX+Bev group was tended to be higher in grade 3 group than in other groups (7.6±9.0 vs 2.5±3.7, p=0.06). [Conclusions] Preoperative CRT using SOX+Bev regimen may improve the clinical and histological response rate. And miR-223 may be a useful predictive marker to perform order made therapy.

P144

Novel Prognostic Scoring System for Prediction of Survival Outcomes in Patients undergoing CRS-HIPEC for Colorectal Peritoneal Metastasis K. Chin,[2]* G. Tan,[1] C. Chia,[2] J.C. Ong,[2] M. Teo.[2] *1. Department of Surgical Oncology, Singapore, Singapore; 2. Department of Surgical Oncology, National Cancer Centre, Singapore, Singapore.*

Aim: To develop a prognostic scoring system for prediction of survival outcomes in patients with colorectal peritoneal metastases (CPM) undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS-HIPEC). Methods: A single-institution review of prospectively collected data from all CPM patients who underwent CRS-HIPEC between Oct 2005-Oct 2017 was conducted. Univariate and multivariate models were used to determine pre- and intra-operative parameters independently predictive of 3- and 5-year overall survival (OS). Predictive models were developed for risk stratification of 3- and 5-year OS, using coefficients of independently significant variables, and dividing them by the smallest coefficient. Patients were classified into high, moderate and low risk groups on the basis of the 25th and 75th percentiles of the models' prognostic risk score distribution.

Performance of the model was determined by AUC. Results: 72 patients underwent CRS-HIPEC for PC from recurrent colorectal cancer (CRC). Pre-operative disease-free interval (DFI) and peritoneal cancer index (PCI) were significant independent predictors of both 3- and 5-year OS. Left upper quadrant (LUQ) disease and intra-operative blood loss were significant independent predictors of 3- and 5-year OS respectively. The 3- and 5-year OS predictive models' AUC were 0.81 and 0.79 respectively (Figure 1). Kaplan-Meier curves demonstrated good discrimination between risk stratified groups and their association with 3- and 5-year OS. Risk stratification on the 3-year and 5-year models predicted significantly for median OS and 3-and 5- year OS (Figure 1). Conclusion: The PCI, DFI, LUQ disease and intra-operative blood loss have significant predictive value for post-CRS-HIPEC outcomes in CPM patients. Risk stratification models could allow for more prudent patient selection to optimize post-operative outcomes.

Table 1: Predictive models for 3- and 5-year OS

Predictive model for 3-year OS				
Factor	**Score calculation**			
DFI (months)				
≤11 (coded as 2)	2 (2*1)			
>11 (coded as 1)	1(1*1)			
PCI				
<11 (coded as 1)	2 (1*2)			
≥11 (coded as 2)	4 (2*4)			
RUQ Disease				
Yes (coded as 1)	2 (1*2)			
No (coded as 0)	0 (0*2)			
Risk Group	**Prognostic Score**	**Percentage of patients (%)**	**Median OS (months) p<0.001**	**3-year OS rate (%) p<0.001**
Low	3 to 4	52.4 (n=37)	28	85.7
Moderate	5 to 6	35.7 (n=27)	23	10.7
High	7 to 8	11.1 (n=8)	14	2.1
Predictive model for 5-year OS				
Factor	**Score calculation**			
DFI (months)				
≤14(coded as 1)	3 (1*3)			
>14 (coded as 0)	0(0*3)			
PCI				
≤7(coded as 0)	0 (0*3)			
>7 (coded as 1)	3 (1*3)			
Blood loss (milliliters)				
>600 (coded as 1)	1(1*1)			
<=600 (coded as 0)	0 (0* 1)			
Risk Group	**Prognostic Score**	**Percentage of patients (%)**	**Median OS (months) p<0.001**	**5-year OS rate (%) p<0.001**
Low	0 to 1	36.7 (n=26)	66	72.2
Moderate	2 to 4	43.3 (n=31)	43	40.2
High	5 to 7	20.0 (n=15)	14	10.1

Predictive scoring system for 3- and 5-year OS

P145

Wait-Times for Colorectal Cancer Patients in a Universal Healthcare System Over a Decade: Is it Sustainable? M. Delisle,* R. Helewa, J. Park, D. Hochman, A. McKay. *Surgery, University of Manitoba, Boston, MA.*

Background: Delays in treatment for colorectal cancer (CRC) may worsen prognosis and increase patient anxiety. This study aims to understand population-based trends and variations in wait times (WTs) for CRC in a universal healthcare system over a decade. Methods: Patients diagnosed with stage I-IV CRC in Manitoba, Canada between 2004 and 2014 were included. Data were obtained through province-wide administrative claims and cancer registry. WTs were defined as time from index contact for a CRC symptom to pathological diagnosis (diagnosis WT), pathological diagnosis to first treatment (treatment WT) and total (diagnosis + treatment WT). Index contact was the consult preceding the first gastrointestinal investigation in the year preceding diagnosis. First treatment was radiation, chemotherapy or surgery. The association between WTs and year of diagnosis was estimated using Negative Binomial Regression and reported as incidence rate ratio (IRR). Disparities in WTs by year of diagnosis were estimated by calculating the average annual percent change (AAPC) in the Coefficient of Variation (CV). Results: A total of 5359 patients were diagnosed with CRC (1802 rectal versus 3557 colon). WTs increased overall. Total WTs for rectal cancer increased 6% (IRR 1.06, 95% CI 1.04-1.07, p<0.01) per year from a median of 90 days in 2004 to 147 days in 2014. This was due to increases in time to diagnosis (IRR 1.07, 95% CI 1.06-1.09, p<0.01) and treatment (IRR 1.04, 95% CI 1.03-1.06, p<0.01). Total colon cancer WTs increased 5% (IRR 1.05, 95% CI 1.04-1.06, p<0.01) per year from a median of 89 days in 2004 to 110 days in 2014. This was due to increases in time to diagnosis (IRR 1.05, 95% CI 1.04-1.07, p<0.01) and treatment (IRR 1.03, 95% CI 1.02-1.04, p<0.01). Disparities in WTs increased for rectal cancer (AAPC +3.85%) and colon cancer (AAPC +5.04%). Conclusion: Total WTs and disparities for CRC in Manitoba have increased from 2004 and 2014. This may reflect the growing challenges in providing increasingly complex cancer care to geographically dispersed populations in a universal healthcare system.

P146

Preoperative Radiographic Assessment Predicts Incomplete Cytoreduction in Patients with Low-grade Mucinous Adenocarcinoma (LGMA) of the Appendix A. Sabesan,* S. Felder, S. Feuerlein, C. Lam, M. McGettigan, S. Dessureault, S. Dineen. *Moffitt Cancer Center, Tampa, FL.*

Intro: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) for patients with LGMA is most effective when complete cytoreduction is possible. We externally validated the simple radiologic score (SRS) and simplified preoperative assessment of appendiceal tumor (SPAAT) scoring systems which have previously been described as semi-quantitative measures to determine preoperative resectability. Additionally we investigated if there was a radiographic change in patients given preoperative systemic therapy. Methods: We identified patients with LGMA who underwent preoperative systemic chemotherapy followed by CRS/HIPEC from 2013 to 2016. CT scans prior to surgery were graded by six physicians using the SRS and SPAAT. Positive and negative predictive values (PPV, NPV) were calculated by comparing to completeness of cytoreduction (CC score). Inter-rater agreement was assessed using the intraclass coefficient (ICC). Results: 24 patients were identified who had preoperative chemotherapy followed by surgery. Thirteen patients underwent an incomplete (CC2/3) CRS and 12 patients had complete CRS (CC0/1). Scoring of the preoperative CT demonstrated a PPV of complete cytoreduction of 75% and 66.7% for SRS and SPAAT, respectively. The NPV was 83.4% and 88.9% for SRS and SPAAT, respectively. The ICC for the preoperative SRS and SPAAT score was 0.77 [95% CI: 0.61 -0.88] and 0.76 [0.62 -0.87] respectively. Comparison of CT scans before and after systemic therapy demonstrated an increase in raw scores in 45.8% (SRS) and 50% (SPAAT) of patients. However, only 4 and 2 patients demonstrated a change in predicted resectability. Conclusion: We externally validated two preoperative radiographic scoring systems for predicting complete cytoreduction in patients with LGMA. Inter-rater agreement for both scoring systems was fair to moderate. Preoperative systemic chemotherapy did not significantly alter the resectability scores using either system. Both scoring systems strongly predicted incomplete cytoreduction. Applying these systems is recommended to minimize incomplete CRS and help set preoperative patient expectations.

Characteristics of SRS and SPAAT Score

SRS Score			
	Incomplete CRS (CC2/3)	Complete CRS (CC0/1)	
Predict Incomplete (>28mm)	10	2	NPV: 10/12 = 83%
Predict Complete (≤28mm)	3	9	PPV: 9/12 = 75%
	13	11	
SPAAT Score			
	Incomplete CRS (CC2/3	Complete CRS (CC0/1)	
Predict Incomplete (≥3)	8	1	NPV: 8/9 = 89%
Predict Complete (<3)	5	10	PPV: 10/15 = 66.7%
	13	11	

P147

Molecular Comparison of Peritoneal Metastases from Appendiceal and Colorectal Adenocarcinoma B. Deschner,[3]* F.W. Williard,[2] M.K. Stein,[1] M.G. Martin,[1] E. Glazer,[3] P.V. Dickson,[3] J.L. Deneve.[3] *1. West Cancer Center, University of Tennessee Health Science Center, Memphis, TN; 2. University of Tennessee Health Science Center College of Medicine, Memphis, TN; 3. Department of Surgery, University of Tennessee Health Science Center, Memphis, TN.*

I: Peritoneal metastases from appendiceal (pAC) and colorectal adenocarcinoma (pCRC) are associated with poor outcomes; however, molecular aberrations are poorly defined. M: We compared pAC and pCRC patient samples submitted to Caris Life Sciences. Tumor profiling included 592-gene next-generation sequencing (NGS), immunohistochemistry (IHC), copy number variant (CNV), microsatellite instability (MSI) and tumor mutational burden (TMB). Mutations were defined as pathogenic (PATH) or variants of unknown significance (VUS). TMB was compared in mutations/Mb (MMb). R: 136 pAC and 348 pCRC cases had similar age (median 59) and gender (55% male). 29 pCRC were left-sided (LS), 45 right-sided (RS), 22 rectum and 252 not otherwise specified. IHC expression in pAC was increased in ERCC1 (42% v 27%), PTEN (77% v 64%), TOPO1 (73% v 62%), and MLH1 (100% v 96%) and decreased in TOP2A (49% v 76%) and SPARC (2% v 13%) compared to pCRC (all p<0.05). By pCRC sidedness, pAC were

more commonly IHC positive for PMS2 (99% v 88%, p<0.05) versus RS and less commonly positive for PD-L1 for both RS and LS pCRC (1% v 13% and 9%, respectively; p<0.05). No PATH differences were seen in SMAD2, SMAD4, PTEN, BRCA1/2, or ATM. pAC had more PATHs in GNAS (31% v 8%, p<0.01), while pCRC had increased PATHs in APC (48% v 3%), TP53 (53% v 23%), PIK3CA (53% v 23%), KRAS (52% v 41%), BRAF (12% v 2%), ARID1A (12% v 2%), and FBXW7 (7% v 2%) [all p<0.05]. Compared to RS pCRC, pAC had reduced PATHs in KMT2D, PTCH1 and FLCN. VUS in pAC were increased in 2/592 genes compared to pCRC: MCL1 (6% v 1%, p<0.05) and STK11 (6% v 0.3%, p<0.05). Contrarily, pCRC had more VUS in 12 genes: KNL1, NOTCH2, CNTRL, ARID1A, PTPRC, TCF7L2, COL1A1, AFF3, TPR, TCF3, RAD50, and SMAD4. No difference was seen in CNV, fusion rate, or MSI. TMB was increased in pCRC (median 7) compared to pAC (median 6) for 5-11 MMb. 23% pCRC were ≥10 MMb compared to 4% pAC (p=0.02). C: pAC were more frequently mutated in GNAS, MCL1 and STK11 compared to pCRC and with increased IHC expression in ERCC1, PTEN and TOPO1. Despite harboring fewer non-synonymous mutations as evidenced by a reduced TMB, these differences may serve as biomarkers for future study in pAC.

P148

Making Sense of Cost-effectiveness of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in Patients with Colorectal Peritoneal Carcinomatosis Z. Lee,* C. Chia, G. Tan, K. Soo, M. Teo. *National Cancer Center Singapore, Singapore, Singapore.*

Introduction Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) provide survival benefit in selected patients with peritoneal carcinomatosis. This study examines the factors that affect the cost- effectiveness of CRS and HIPEC in patients with colorectal peritoneal carcinomatosis to aid patient selection. Methodology We performed a retrospective review of patients who underwent CRS-HIPEC for CPC at the National Cancer Centre Singapore. Patients were stratified into 4 groups, according to the median cost and median overall survival with groups 1, 2, 3, and 4 having low cost/ long OS, high cost/ long OS, low cost/ short OS and high cost/ short OS respectively. Results The average cost of CRS and HIPEC per patient was S$83,680.26 with a median overall survival of 47 months with a calculated cost per life year attained of S$21,365.19 per life year. Group 1 patients derived the greatest benefit from CRS-HIPEC, with low cost incurred and long OS. When compared to the other 3 groups, they were older with a median age of 62 years old (44 to 78, p=0.092), had a lower pre- operative CEA of 2.0 (0.5 – 66.6, p=0.134), CA 19-9 of 8.2 (2-48.9, p=0.679) and CA 125 of 14.7(5.8-20.9, p=0.182). Of significance was their median PCI score that was the lowest at 3 (0-9, p=0.001). and their low requirement of intra- and post- operative blood transfusion of 1.5 (0-5, p=0.001) and 0 pints (p=0.031) pints of packed cells respectively. The duration of SICU stay of 0 days (0-2, p=0.167) and overall hospitalization days of 12.5 days. (9-18, p=0.250) were also comparatively shorter. When comparing group 1 and 4 specifically, group 4 had a higher preoperative CEA of 8.9 vs 2.0 (p=0.044), and CA 125 of 36.6 vs 14.7. (p=0.042). Group 4 patients had higher PCI score of 15 vs 2 (p=0.011). Conclusion Patients with greatest benefit from CRS-HIPEC in terms of cost-effectiveness had low pre-operative tumour marker levels, low PCI scores and less need for peri- operative transfusions. We eventually aim to develop a scoring system to predict for this select group of patients to optimize management.

P149

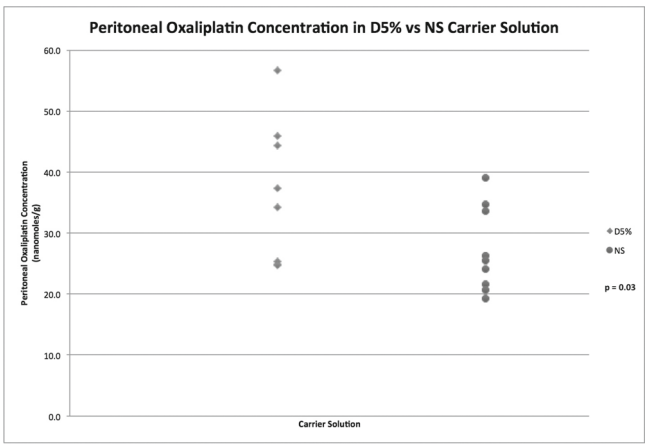
Involvement of Negative Regulator of RNA Polymerase III, MAF1 in Progression of Colorectal Cancer with MSI K. Hokonohara,* N. Nishida, N. Miyoshi, H. Takahashi, N. Haraguchi, T. Hata, C. Matsuda, T. Mizushima, Y. Doki, M. Mori. *Osaka University, Suita, Japan.*

Introduction: Colorectal cancer (CRC) with microsatellite-instability (MSI) shows distinct characteristics such as relatively better prognosis than non-MSI cases, low sensitivity of fluorouracil-based chemotherapy and benefit from immune checkpoint blockade. The aim of this study is to identify the gene involved in poor prognosis of CRC with MSI and clarify its functional significance. Materials and methods: First, we analyzed the TCGA colorectal cancer dataset (n=615) to examine the significant difference in prognosis between MSI (n=87) and non-MSI (n=528) CRCs and identified the gene which is associated with poor prognosis of CRC with MSI. In vitro loss-of-function assays of this gene including scratch wound healing assay and chemosensitivity assay were performed. Immunohistochemical analysis of 146 CRC surgical specimens was performed. Results: Analysis of TCGA dataset revealed that MAF1 Homolog, Negative Regulator of RNA Polymerase III (MAF1) is closely associated with poor prognosis in all cases (p=0.0146) and MSI cases (p=0.00845), but not in MSS cases (p=0.157). Multivariate analysis indicated that MAF1 was independent prognostic factor for overall survival in 87 CRC cases with MSI (odds ratio [OR], 0.22; 95% confidence interval [CI], 0.06–0.64; p=0.0046). In vitro loss-of-function assays revealed that MAF1 confers chemoresistance and migratory ability in CRC cancer cells. Immunohistochemical analysis in independent dataset of 146 CRC cases also revealed that high expression levels of MAF1 were associated with poor prognosis both in OS (p=0.0123) and RFS (p=0.0132). Conclusions: Our results indicate that high expression levels of MAF1 was related to poor prognosis in CRC. MAF1 gene could be a useful biomarker in CRC, especially in MSI cases.

P150

Peritoneal Absorption of Oxaliplatin Using D5% Versus NS Carrier Solution in HIPEC: An In Vivo Study Using a Murine Model M. Deban,* P. Dubé, J. Tessier, F.A. Leblond, J. Tremblay, A. Cloutier, M. Soucisse, L. Sidéris. *University of Montreal, Montreal, QC, Canada.*

Introduction: Oxaliplatin is a cytotoxic agent used in the context of hyperthermic intraperitoneal chemotherapy (HIPEC) to treat peritoneal metastases. At perfusate preparation, oxaliplatin is diluted in dextrose solutions, leading to important glycemic and electrolyte imbalances during HIPEC in patients. Recently, Mehta et al. reported stability of oxaliplatin in a chloride-containing carrier solution in vitro. Objective: Assess peritoneal tissue absorption of oxaliplatin in a physiologic chloride-containing carrier solution using a murine model. Methods: Under general anesthesia, 17 Sprague-Dawley rats were submitted to HIPEC with oxaliplatin (460 mg/m^2) using either normal saline (NS) or dextrose (D5%) carrier solution. Perfusion was carried out for 25 minutes. At the end of the experiment, peritoneal tissue was harvested and analyzed for concentration of oxaliplatin using high performance liquid chromatography. Results: 9 rats had HIPEC performed with NS as a carrier solution and 8 rats with D5%. Their mean weight was 289 g (270-300 g). One rat had respiratory arrest at t = 24 minutes. Precipitation in the form of crystals was observed in three perfusates (two in NS, one in D5%) once they were withdrawn after HIPEC. The mean concentration of oxaliplatin (nanomoles per gram of peritoneum) was 36.7 +/- 11.7 in D5% vs 27.2 +/- 7.0 in NS (p = 0.03). Conclusion: Despite resulting in important electrolyte and glycemic imbalances in patients, D5% carrier solution proves superior to NS in terms of peritoneal concentration of oxaliplatin in vivo as demonstrated in our murine models.



Peritoneal Oxaliplatin Concentration in D5% vs NS Carrier Solution

P151

Validation of a Rectal Cancer Magnetic Resonance Imaging Staging System and Development of a Local Recurrence Risk Stratification Model Q. Teo,[1]* B. Lim,[2] W. Ng,[3] M. Teo.[3]
1. Singapore General Hospital, Singapore, Singapore; 2. National University of Singapore, Singapore, Singapore; 3. National Cancer Centre Singapore, Singapore, Singapore.

Locally advanced rectal cancers (LARC) have been treated with neoadjuvant chemoradiotherapy (CRT) to reduce rates of local recurrence. It is essential that the preoperative staging system used is able to differentiate between good and poor prognosis tumours, thus affecting therapy and prognosis. The MERCURY (Magnetic Resonance Imaging and Rectal Cancer European Equivalence) Study Group has prospectively evaluated MRI in use of preoperative assessment in patients with rectal cancer, with histopathological results as the reference standard. We aim to evaluate if similar prognostication by imaging could be demonstrated in our patient population. MRI scans of 148 LARC patients from 2011-2016 were retrospectively reviewed for MRI tumour regression grade (MR-TRG) and compared to AJCC histopathological tumour regression grade (P-TRG). ROC analysis was done by collapsing the MR-TRG and P-TRG into good and poor responders where MR-TRG 1-2 and P-TRG 0-1 were good responders, MR-TRG 3-5 and P-TRG 2-3 were poor responders. Overall survival (OS), disease-free survival (DFS), local recurrence-free survival (LRFS) and distant metastasis-free survival (DMFS) were estimated using Kaplan-Meier method. Median follow-up duration of 3 years was achieved. ROC analysis of MR-TRG in predicting P-TRG showed area under curve of 0.726 (p=0.000), sensitivity 90.5%, specificity 54.7%, PPV 78.2%, NPV 76.3%, showing that MR-TRG is a good predictor of P-TRG. MR-TRG was a good predictor of survival outcomes as illustrated in Figure 1. 3-year OS (log rank p=0.001) was 100% for MR-TRG1, 96.6% for MR-TRG2, 90.1% for MR-TRG3, 81.0% for MR-TRG4 and 50.0% for MR-TRG5. 3-year DFS (log rank p=0.022) was 88.9% for MR-TRG1, 86.2% for MR-TRG2, 72.1% for MR-TRG3, 62.5% for MR-TRG4 and 33.3% for MR-TRG5. Patients with poor MR-TRG tended to develop locoregional recurrences and distant metastases. MR-TRG4 and 5 patients have 3-year LRFS of 74.9% and 50%; 3-year DMFS of 68.8% and 33.3% respectively. This group of patients should have closer follow-up intervals and considered use of systemic chemotherapy after CRT in view of their poor tumour biology and prognosis.

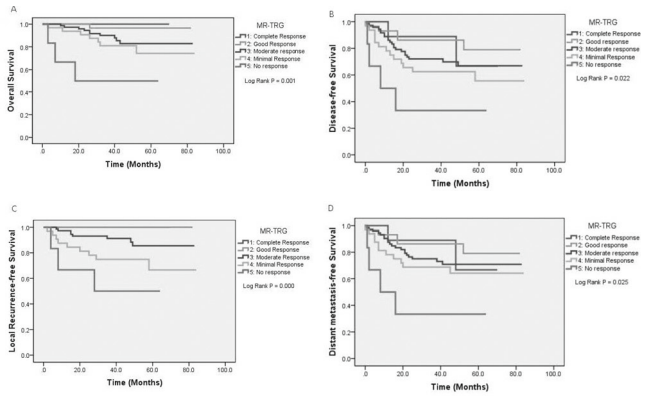


Figure 1: Overall survival (A), Disease-free survival (B), Local recurrence-free survival (C), Distant metastasis-free survival (D) of patients with MR-TRG 1-5. MR-TRG = MRI tumour regression grade

P152

Unique Plasma Exosomal Protein and miRNA Profiles in Colorectal Cancer Peritoneal Carcinomatosis Compared to Visceral Metastases M.M. Kwong,* A. Gonda, M.J. Selleck, T. Liu, J. Kabagwira, J. McMullen, C. Wang, N. Wall, M. Senthil. *General Complex Surgical Oncology, Loma Linda University Health, Loma Linda, CA.*

Background: Colorectal peritoneal carcinomatosis (PC) presents significant diagnostic and therapeutic challenges. Developing new diagnostic tools for earlier detection of PC will improve patient outcomes. Liquid biopsies offer a rapid and minimally invasive technique to detect and evaluate disease progression through analysis of circulating tumor-derived exosomes. Objective: To identify unique molecular profiles involved in the development and progression of PC compared to visceral metastases in plasma exosomes. Methods: Proteomic and miRNA analysis were performed using mass spectrometry and next generation sequencing on pooled plasma exosomes from patients with primary colorectal cancer (n = 10), liver or lung metastases (n = 10), and PC (n = 9). Results: On proteomic analysis, a total of 274 proteins were identified, of which 74 proteins were differentially expressed among the three groups. Proteins unique to or differentially expressed in the PC group compared to the visceral metastases group were involved in cancer progression (visceral metastases = 67%, PC = 93%), metastases and/or migration (visceral metastases = 6%, PC = 28%), and chemoresistance (visceral metastases = 9%, PC = 17%). There were 870 unique microRNAs identified, 495 were expressed at quantifiable differences. Compared to the visceral metastases group, there was an upregulation of miRNAs involved in chemoresistance in PC. Conclusion: We describe for the first time identification of plasma exosomal proteins and miRNA that are differentially and uniquely expressed in colorectal PC compared to visceral metastases. These proteins and miRNA have been implicated in cancer progression and chemoresistance. We propose that through identification of key plasma exosomal proteins and miRNA, an earlier and more accurate diagnosis in colorectal PC is feasible.

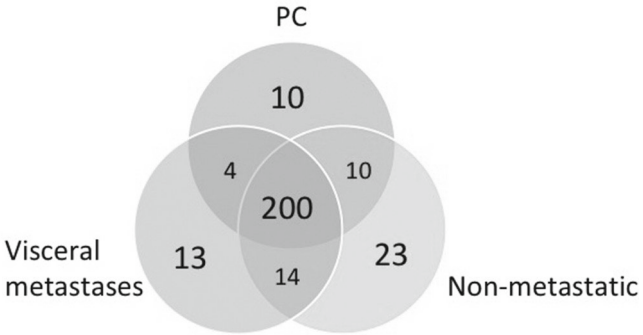
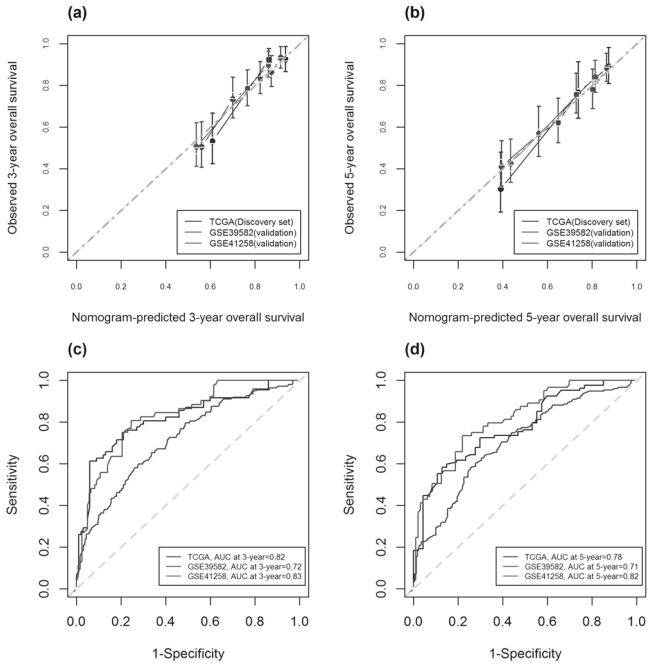


Figure 1. Venn diagram of proteomic analysis of pooled plasma exosomes from patients with primary colorectal cancer (non-metastatic), liver or lung metastases (visceral metastases), or peritoneal carcinomatosis (PC).

P153

Prognostic Nomogram of Hypoxia-Related Genes Predicting Overall Survival of Colorectal Cancer–Analysis of the Cancer Genome Atlas Database J. Lee,[2]* Y. Chai,[1] R. Song.[3] *1. Seoul National University Boramae Medical Center, Seoul, Korea (the Republic of); 2. Gachon University Gil Medical Center, Incheon, Korea (the Republic of); 3. Chung-Ang University Hospital, Seoul, Korea (the Republic of).*

Hypoxia-related gene (HRG) expression is associated with survival outcomes of colorectal cancer (CRC). Our aim was to develop a nomogram predicting overall survival (OS) of CRC with HRGs and clinicopathological factors. The Cancer Genome Atlas (TCGA) database was used as the discovery cohort and two Gene Expression Omnibus database (GSE39582 and GSE41258) served as validation cohorts. A genetic risk score model prognosticating OS was developed with candidate genes selected by qualitative literature review. Nomograms predicting OS were developed using the genetic risk score model and clinicopathological variables. The genetic risk score model included four HRGs and successfully prognosticated OS of the discovery and two validation cohorts ($p < 0.001$ for TCGA discovery set, $p < 0.003$ for the GSE39582 and $p = 0.042$ for the GSE41258 dataset). Genetic risk score = 0.520*HSPA1L -1.156*PUM1 -1.239*UBE2D2+0.309*HSP27 Genetic risk score, age, and TNM stage were included in the nomograms. C-index of the nomogram was higher than that of TNM stage alone (0.77 vs. 0.69, $p < 0.001$). For the 3-year OS nomogram, AUC was 0.82 in the TCGA, 0.72 in the GSE39582 and 0.83 in the GSE41258 dataset. For the 5-year OS nomogram, AUC was 0.78 in the TCGA, 0.71 in the GSE39582 and 0.82 in the GSE41258 dataset. Nomograms of age, TNM stage, and genetic score calculated by HRGs predicted OS of CRC patients better than TNM stage alone. The mRNA expression of the HRGs may be useful for prognosticating CRC outcome.



Calibration curve for nomogram-predicting (a) 3-year and (b) 5-year overall survival. X-axis is nomogram-predicted survival probability and Y-axis is observed survival probability respectively. Red and blue solid lines represent the performance of the nomogram relative to the 45-degree line, indicating perfect prediction. Receiver operating characteristic curves assessing discriminating ability of the nomogram in predicting (c) 3-year and (d) 5-year survival.

P154

Investigating Dec2 as a Biomarker of Dormant Disseminated Tumor Cells in Metastatic Colorectal Cancer S.H. Greco,* C. Dudgeon, A. Roberts, D.R. Carpizo. *Rutgers Cancer Institute of New Jersey, Department of Surgical Oncology, New Brunswick, NJ.*

Recurrence after curative-intent hepatic resection for patients with colorectal liver metastases is extremely high (>80%). Activation of dormant disseminated tumor cells (DTCs) is thought to be a driver of recurrence, but there is little data characterizing human metastatic DTCs. Dec2, a transcriptional repressor and mediator of circadian rhythm, is upregulated in mouse models of cancer cell dormancy. We aimed to develop methods of isolating dormant DTCs using Dec2 as a biomarker in patients undergoing liver resection for metastatic colorectal cancer and to identify DTC signatures which may predict clinical outcomes. We isolated DTCs in the tumor and normal adjacent liver tissue (NAT) of nine patients who underwent liver resection for metastatic colorectal cancer. Flow cytometry and single-cell sort was performed using extracellular staining for CEA and intracellular staining for Dec2 and Ki67. We collected demographic and clinical parameters. 56% of patients had colon cancer, 78% had synchronous disease, and 88% received preoperative chemotherapy (mean/median number of cycles 20.2/5.5) including FOLFOX (67%), Avastin (22%), and immunotherapy (22%). We found fewer CEA^+ cells in NAT (2.3% median, range 0.2-30%) versus tumor (52.8% median, range 10-70%) (Table 1). The frequency of $Dec2^{hi}$ cells in the CEA^+population ranged from 0.5-28% in the NAT versus 0.09-2.7% in tumor. Within the CEA^+Dec2^{hi} population, the range of cells that were $Ki67^-$ was 3.9-25% in the NAT versus 0-3.5% in tumor (n=3). The dormant DTC phenotype ($CEA^+Dec2^{hi}Ki67^-$) was higher in NAT (range 0.002-0.011%) vs. 0-0.009% in tumor, n=3. Single cell RNA sequencing of 120 CEA^+ cells in NAT, revealed that 14 expressed Dec2 and 9 expressed Ki67 (n=1). Of the 7 cells that expressed both, levels of Dec2 and Ki67 were inversely correlated. Interestingly, one patient with a high percentage of CEA^+ DTC in NAT (30%) and fewer dormant DTCs in NAT (5%) developed lung and liver metastases 4 months after surgery. Our results show that colorectal cancer DTCs can be isolated from the liver by flow cytometry and that Dec2 may be a reliable biomarker of tumor cell dormancy in resected metastatic colorectal cancer.

Table 1 Selected Tumor and NAT DTC Populations (n=5)

	1	2	3	4	5
CEA % (Tumor)	48.8	52.8	9.78	70.1	57.4
CEA % (NAT)	1.8	2.25	2.64	0.16	30.5
CEA^+Dec2^{hi} % (Tumor)	0.09	0.14	2.67	1.51	0.46
CEA^+Dec2^{hi} % (NAT)	5.11	3.04	1.97	27.8	0.51
$CEA^+Dec2^{hi}Ki67^-$ % (Tumor)	ND	ND	3.49	0.095	0
$CEA^+Dec2^{hi}Ki67^-$ % (NAT)	ND	ND	3.85	25	5.16
Recurrence (Y/N)	N	Y	N	N	Y
Post-resection follow-up time (months)	9	7	1	4	4

NAT normal adjacent liver tissue, *DTC* disseminated tumor cells, *n* sample size, *CEA* carcinoembryonic antigen, *ND* not detected

P155

Incidental Appendicular Neoplasms in Emergency Appendectomy G. Herrera,* C. Restrepo, S. Rey, E. Pinto, D. Camargo, F. Arias, M. Cadena, F. Diaz, R. Fajardo, E. Londoño, R. Nassar, F. Perdomo, J.D. Hernandez. *Surgery, Fundacion Santa Fe de Bogotá, Bogota, Colombia.*

Introduction Non-operative management has been proposed as a treatment alternative for uncomplicated appendicitis. An important consideration for this approach is understanding the risk of missed tumors of the appendix. The incidence of appendiceal tumors in Colombia is unknown. The purpose of this study was to evaluate the incidence and type of tumor identified in patients taken to the operating room with a diagnosis of acute appendicitis. Methods A review of a prospectively maintained database was performed between January the 1stof 2012 to September the 15th of 2018. Inclusion criteria were patients older than 18 years who were operated with a diagnosis of acute appendicitis. Patients with a preoperative diagnosis of appendiceal tumor were excluded. Patients who underwent right hemicolectomy or appendectomy for an indication other than acute appendicitis were also excluded. Results A total of 2993 patients were identified and included for analysis. Sixty seven percent of patients were female. Mean age was 45 years for females and 48 years for males. A total of 64 appendiceal tumors were identified (2.14%). Fifty cases corresponded to simple appendectomy and 14 cases required additional procedures (cecum resection, management of peritonitis). There were 23 mucinous neoplasms of the appendix (35.9%), 27 neuroendocrine tumors (42.2%), 2 adenocarcinomas of the appendix (3.1%), 1 high grade dysplasia adenoma (1.6%) and 11 serrated adenomas (17.2%). Conclusion The incidence and histologic subtype of appendiceal tumors in Colombia has not been previously described. The incidence of incidental appendiceal neoplasms is higher than previously reported series. This information needs to be incorporated into decision making when contemplating treatment options for acute appendicitis.

P156

Preoperative Neutrophil-Lymphocyte Ratio (NLR) and CEA is Associated with Poor Prognosis in Patients with Synchronous Colorectal Cancer Liver Metastasis (sCRLM) M. Baek,* H. Jung, D. Kang, T. Ahn, D. Cho, S. Kwon. *Surgery, Soonchunhyang University Hospital, Cheonan, Korea (the Republic of).*

Backgrounds: Recently, the neutrophil-to-lymphocyte ratio (NLR), an inflammatory response marker, has been reported to be associated with the prognosis in patients with various type of cancer. However, there have been no studies until now that have explored the prognostic role of combined detection of NLR and CEA in patients with synchronous liver-limited colorectal metastases (sCRLM). Materials and Methods: Eighty-three patients who histologically diagnosed as sCRLM were selected. Their laboratory and clinical data were collected retrospectively. Using ROC curve analysis, the cutoff value of NLR was calculated based on which patients were assigned to a high NLR (more than 1.94) group and low NLR (less than 1.94) group. A cutoff value of 100 ng/mL for serum CEA level was used in light of the previous literature. Results: CEA level and Poorly differentiated histology of colon cancer was significantly correlated with high NLR ($p = 0.005$ and $p = 0.048$, respectively). The multivariate analysis identified the high NLR as independent prognostic factors for OS and DFS in all patients ($p = 0.010$, $p = 0.006$, respectively). Patients with both low levels of NLR and CEA had a significantly longer OS and DFS ($p = 0.026$ and 0.009, respectively). Conclusions: In conclusion, elevated preoperative NLR is strongly correlated with both survival and recurrence in patients who have been diagnosed with resectable sCRLM. The combination of NLR and CEA level could be a more powerful prognostic marker than NLR alone.

P157

Cytoreductive Surgery and HIPEC: Patient Selection and Outcomes for Metastatic Colon Cancer J. TSeng,* R.F. Alban, A. Gangi, F. Amersi. *Cedars-Sinai Medical Center, Los Angeles, CA.*

Background: Patients with peritoneal metastases (PM) from colon cancer have median survival of 6-9 months, and most are treated with palliative chemotherapy. Cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC) has been shown to prolong survival in patients with PM. We identified factors associated with selection for CRS-HIPEC and evaluated postoperative and long-term outcomes. Methods: National Cancer Database was queried for stage 4 colon cancer with PM. Patient demographics, tumor characteristics, treatment modalities, and outcomes were reviewed. Patients were compared by treatment, including chemotherapy, chemotherapy/surgery, and CRS-HIPEC. Multivariate logistic regression was used to identify factors associated with CRS-HIPEC selection. Kaplan-Meier estimate was used to assess survival. Results: 52,893 patients were identified; 16,788 (31.7%) had chemotherapy, 35,572 (67.3%) had chemotherapy/surgery, and 533 (1.0%) patients had CRS-HIPEC. CRS-HIPEC patients were more likely to be younger (OR 0.96, 95% CI 0.94-0.97), male (OR 1.40, 95% CI 1.11-1.76), Caucasian (OR 2.35, 95% CI 1.50-3.70), insured with private insurance, Medicare, and VA insurance (OR 6.05, 95% CI 1.91-19.20, OR 5.36, 95% CI 1.63-17.68, and OR 8.96, 95% CI 2.01-39.92, respectively), treated in an academic center (OR 9.31, 95% CI 4.74-18.28), have a Charlson/Deyo Score of 0 (OR 1.67, 95% CI 1.17-2.38), have low grade tumors (OR 3.67, 95% OR 1.91-7.03) and mucinous adenocarcinoma (OR 10.70, 95% CI 8.43-13.58). CRS-HIPEC and chemotherapy/surgery patients had similar 30 and 90-day postoperative mortality (0.4% vs 0.7%, p=.78 and 4.6% vs 4.1%, p=.59). CRS-HIPEC had longer overall median survival compared to chemotherapy/surgery and chemotherapy (54.5 vs 24.0 vs 11.9 months, p<.01). Conclusion: Patients selected for CRS-HIPEC are more likely to be young, male, insured, treated at an academic center, and have low grade mucinous tumors. CRS-HIPEC and chemotherapy/surgery had similar postoperative mortality, but CRS-HIPEC had longer median survival times compared to all other treatment. CRS-HIPEC should be considered in highly selected patients in colon cancer patients with PM.

P158

Undertreatment of the Elderly with Rectal Cancer: Outcomes from the National Cancer Data Base C. Tsai,[1]* J. Fiechter,[1] R. Warschkow,[2] D. Nussbaum,[3] B. Schmied,[2] D. Blazer,[3] B. Gloor,[1] M. Worni.[3] *1. Visceral and Transplantation Surgery, Inselspital, Bern University, San Jose, CA; 2. Kantonsspital St. Gallen, St. Gallen, Switzerland; 3. Duke Medical Center, Durham, NC.*

Introduction: The incidence of colorectal cancer increases with age, and 60% of cases are diagnosed in patients over 70. While survival rates for rectal cancer have been increasing, this survival improvement is not as pronounced in the elderly. We aimed to asses treatment patterns and outcomes with increasing age as a continuous measure using the National Cancer Database (NCDB). Methods: The NCDB 2002-2014 was queried for invasive rectal adenocarcinoma patients stage I-IV over age 50 with defined treatment. Advanced statistical models were applied to assess treatment trends, adequate lymphadenectomy (LNE) (12 or more lymph nodes per NCCN guidelines), short-term outcome trends, and overall/relative survival (OS/RS) using age as a continuous measure. Results: A total of 25,798 patients were identified with mean age 65.6 (SD 10.2). Of them, 15,650 (60.7%) were males. With increasing age, patients were less likely to receive an oncologic resection, LNE, radiation, and chemotherapy while it was least pronounced for surgical resection (Ptrend<0.001). Adequate LNE was achieved in 11,885 (46.1%) patients. For Stage I-III patients, increasing age was associated with increased 30- and 90-day mortality, hospital stays >10 days, but lower 30-day readmission rates (Ptrend<0.001). Restricted mean RS for patients treated with oncologic resection decreased with age for stage I-II disease (90% to 70% and 80% to 65%, respectively) while it was stable across age in stage III disease (60%). In comparison, OS decreased steadily with increasing age, almost in parallel with the population life expectancy. For patients treated according to NCCN guidelines with Charlson-Deyo score 0, RS was better for patients treated at high-volume compared to low-volume centers. Conclusion: Patients with rectal cancer and increasing age receive less surgical and medical treatment which is associated with worse short-term outcomes. However, RS of patients undergoing oncologic resection in stage III disease is stable with increasing age. While age is a risk factor for "poor" outcomes, more emphasis should be placed in identifying patients who benefit from adequate treatment which might be best assessed by RS.

P159

Nodal Retrieval and Oncologic Outcomes of Robotic and Laparoscopic Colectomies for Colon Cancer T. Nguyen,* S. Stern, A. Dehal, B. Vuong, A. Bilchik. *Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA.*

Background: It is debatable whether robotic colectomies are advantageous over laparoscopic colectomies for colon cancer (CC). We aim to evaluate oncologic and perioperative outcomes between robotic and laparoscopic colectomies in a national database. Methods: The National Cancer Database was queried from 2010-2014 for patients with resectable (stage I-III) CC. Lymph node (LN) retrieval, length of stay (LOS), perioperative outcomes and OS were analyzed based on type of surgery: right colectomy vs. left colectomy and robotic (ROBO) vs. laparoscopic (LAP) colectomy. Results: 61,903 patients met inclusion criteria. There was no difference in inadequate LN retrieval (< 12 LN), or short-term mortality between ROBO and LAP groups. There was a significant decrease in conversion to an open operation and LOS for ROBO vs. LAP groups as well as increased 5 year OS (Table 1). The number of ROBO colectomies performed increased four-fold over 5 years. About half were done at community hospitals (56%) and at low ROBO volume hospitals (47.2%). Inadequate LN retrieval in the ROBO group was greater at low volume centers (9.2%) compared to high volume centers (12.3%) ($p < 0.0001$) as well as at community hospitals (12.2%) compared to academic hospitals (8.5%) ($p = 0.0003$). Conclusions: This population analysis showed that robotic colectomies were associated with equivalent short-term outcomes and LN retrieval as laparoscopic colectomies. However, half of robotic colectomies were done at community hospitals or low volume hospitals, where the rate of inadequate LN retrieval was higher than at academic hospitals or high volume centers. As the number of robotic colectomies performed increases, it is important that technology is implemented judiciously so that oncologic outcomes are not compromised.

Table 1: Outcome by surgical approach

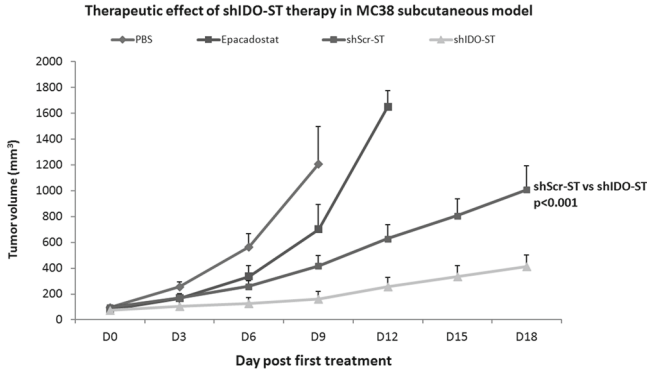
	Left Colectomy n=22146, 35.8%			Right Colectomy n=39757, 64.2%		
	LAP	ROBO	P value	LAP	ROBO	P value
N, %	20356, 91.9%	1790, 8.1%		37230, 93.6%	2527, 6.4%	
LN retrieval (<12 LN)	15.3%	15.1%	ns	7.5%	7.5%	ns
Conversion to open	**14.0%**	**8.5%**	**<0.001**	**12.3%**	**8.3%**	**<0.001**
LOS (median, days)	**4.0**	**4.0**	**<0.001**	**5.0**	**4.0**	**<0.001**
Prolonged LOS (>75th %tile)	**22.6%**	**15.4%**	**<0.001**	**24.3%**	**20.1%**	**<0.001**
90 day mortality	2%	2%	ns	3%	3%	ns
Estimated 5 year OS rate ±SE, %	**76.6 ± 0.6**	**77.0 ± 3.6**	**<0.001**	**70.0 ± 0.5**	**71.5 ± 2.7**	**<0.001**

P160

Salmonella-Mediated Therapy Targeting Indoleamine 2, 3-Dioxygenase (IDO) Activates Innate Immunity and Mitigates Colorectal Cancer Growth T. Phan,* M.S. D'Alincourt, V.H. Nguyen, E. Manuel, T. Kaltcheva, W. Tsai, D.J. Diamond, L.G. Melstrom. *Surgery, City of Hope, Duarte, CA.*

IIntroduction: Bacteria-mediated therapy has emerged as a promising cancer treatment strategy. IDO is an important enzyme in tumor-mediated immunosuppression. This study aims to assess the efficacy and contribution of immune cell subsets to tumor control by the attenuated Salmonella(VNP20009) that delivers an shRNA plasmid against the immunosuppressive molecule indoleamine 2,3-dioxygenase (shIDO-ST) in a mouse model of colorectal cancer. Methods: Western blot (WB) and High-performance liquid chromatography (HPLC) were used to assess IDO expression and function by shIDO in CT26/MC38 colon cancer cells in vitro. RT-PCR was performed to confirm expression of IDO in CT26/MC38 tumors. An in vivo flank model was treated with:PBS (control), epacadostat (oral IDO inhibitor in trials), scrambled control-ST (shScr-ST) or shIDO-ST. Tumor volume was assessed every 3rd day. In a parallel experiment, tumors were excised on days 7 and 14 post treatment and immune cell markers were analyzed. Results: IFN-γ (10ng/ml) and TNF-a (100ng/ml) optimally stimulate IDO expression in CT26 and MC38

cells in vitro. IDO protein expression and function were significantly reduced after treatment with shIDO-ST in both cell lines (CT26:1.10M v 2.13M; MC38:2.11M v 3.94M; p<0.01). In vivo, shIDO-ST treatment significantly mitigated CT26/MC38 tumor growth and prolonged survival compared to shScr-ST or epacadostat (CT26-Day 21: 178 vs 518 or 1148 mm3, p<0.01; MC38 –Day 9: 161 vs 418 or 700 mm3, p<0.05). At 7 days there was a significant increase of intratumor neutrophils (Ly6G+CD11b+) in the shIDO-treated group compared to shScr-ST controls (CT26: 76 vs 52%; p<0.005). Conclusion: IDO has a well-established immunosuppressive role in solid tumors. In this in vivo immunocompetent model of colorectal cancer, we demonstrate that treatment with shIDO-ST markedly delays tumor growth and is associated with an early influx of neutrophils and activation of the innate immune system. Further characterization of tumor infiltrating neutrophils is necessary to understand this mechanism of tumor growth inhibition. Figure 1: shIDO-ST mitigates growth of MC38 cells in vivo



Female, 6 week-old C57BL6 mice (n = 5/group) were subcutaneously injected (into the right thigh) with MC38 cells (2.5×10^5). When the tumor volume reached 80-100 mm^3, mice received three single daily doses of an retro-orbital injection of PBS, shScr-ST (5×10^6 CFU), or shIDO-ST (5×10^6 CFU) (Day 0). For IDO inhibitor, mice received seven single daily doses of an oral administration of Epacadostat (4mg/mouse). Tumor volume was measured every 3 days until the end of experiment. Mice were then euthanized when the tumor volume reached 1000mm^3.

P161

Preoperative Bevacizumab Does Not Increase Complications Following Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy B.H. King,* J. Baumgartner, K.J. Kelly, R.A. Marmor, A.M. Lowy, J. Veerapong. *Surgical Oncology, University of California San Diego, La Jolla, CA.*

Introduction: Preoperative bevacizumab has been reported to increase the risk of postoperative complications following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC). We aimed to elucidate if bevacizumab increases postoperative morbidity or mortality in patients undergoing CRS/HIPEC for peritoneal surface malignancy. Methods: A retrospective review of patients who received neoadjuvant systemic therapy with or without bevacizumab within 3 months prior to CRS/HIPEC from 2008-2018 was performed using data from a high-volume academic center. Results: A total of 123 patients received neoadjuvant systemic chemotherapy alone (n = 67) or in combination with bevacizumab (n = 56) prior to CRS/HIPEC. Histopathology was distributed as follows: colorectal cancer (n = 65), appendiceal cancer (n = 32), and diffuse malignant peritoneal mesothelioma (n = 26). Baseline demographic data between the two groups were similar in terms of patient factors (age, gender, BMI) and surgical factors (peritoneal cancer index score, completeness of cytoreduction, duration of surgery, estimated blood loss). The median time from bevacizumab discontinuation until CRS/HIPEC was 9.1 [$Q_1$7.6, Q_3 10.4] weeks. There were no differences in 60-day overall complication rate (67.2 vs. 62.5%, p = 0.59), 60-day major morbidity (Clavien-Dindo III/IV complications) (14.9 vs. 17.9%, p = 0.40), or 60-day mortality (0 vs. 0%) between patients receiving systemic therapy alone or in combination with bevacizumab, respectively (Table 1). The odds of having received neoadjuvant bevacizumab compared to systemic chemotherapy alone was not significantly different for overall complications (OR 0.81, 95 % CI 0.39-1.71, p = 0.54) or major morbidity (OR 1.05, 95% CI 0.36 - 3.03, p = 0.59). Conclusions: Preoperative bevacizumab is not associated with increased morbidity or mortality following CRS/HIPEC for colorectal and appendiceal cancer. Neoadjuvant therapy employing this biologic agent prior to surgery is safe and should not be a deterrent for aggressive cytoreduction with curative intent.

	Systemic chemotherapy (n = 67)	Bevacizumab (n = 56)	Odds ratio	p
Overall morbidity	45 (67.2%)	35 (62.5%)	OR = 0.81 95% CI: 0.39 - 1.71	0.54
Grade I/II	35 (52.2%)	25 (44.6%)	OR = 0.75 95% CI: 0.34 - 1.65	0.47
Grade III/IV	10 (14.9%)	10 (17.9%)	OR = 1.05 95% CI: 0.36 - 3.03	0.59
60-day mortality	0 (0%)	0 (0%)	--	--

Table 1. Morbidity and mortality in patients receiving systemic chemotherapy alone or in combination with bevacizumab. The worst 60-day Clavien-Dindo morbidity was used to stratify each patient. Odds ratios were calculated by comparing patients who experienced complications to those without any morbidity in the bevacizumab vs. systemic chemotherapy groups.

P162

Discordant Diagnostic Terminology and Pathologic Grading of Mucinous Appendix Neoplasms Reviewed at a High-Volume Center H.A. Choudry,* A. Parimi, L. Totin, J.F. Pingpank, M.P. Holtzman, R.K. Pai, D.L. Bartlett. *Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Diagnostic terminology and pathologic grading of mucinous appendix neoplasms (MAN) lacks uniformity. We sought to identify discordance in pathologic reporting of primary MAN by re-reviewing cases referred to our high-volume institution for surgery. Methods: Using updated guidelines proposed by Peritoneal Surface Oncology Group International (PSOGI) and American Joint Committee on Cancer 8th edition (AJCC8), we retrospectively compared diagnostic terminology and pathologic grading of primary MAN cases (n=115) between pathology reports from referring institutions and re-review of pathology slides by expert pathologists at our high-volume institution. Results: All 7 patients diagnosed with mucinous adenoma (MA) at the referring institution had low grade appendiceal mucinous neoplasm (LAMN) on our review. Of the 72 patients diagnosed with mucinous adenocarcinoma (MACA) at the referring institution, 8 patients had LAMN (11.1%) and one patient had a MA on our review. A higher grade MACA was found in 53% of patients originally diagnosed with well-differentiated MACA (G1) and 17.6% of patients originally diagnosed with moderately-differentiated MACA (G2). Of the 32 patients with diagnosis of LAMN at the referring institution, 3 patients (9.4%) were treated with chemotherapy prior to referral. Chemotherapy was administered to 7 of 27 patients (25.9%) diagnosed with primary well-differentiated MACA (AJCC8 grade G1) at the referring institution. Conversely, 6 of 31 patients (19.4%) diagnosed with moderately-poorly differentiated or signet ring primary MACA (AJCC8 grades G2/G3) at the referring institution were not treated with chemotherapy. Conclusions: We found significant variability in diagnostic terminology and pathologic grading of MAN following re-review of cases referred to our institution for surgery, likely related to variable published classification schemes and lack of expertise with these rare tumors. Inaccurate pathologic assessment was associated with over- or under-treatment with chemotherapy. These data highlight the need for pathologic review of such rare cases at high-volume centers.

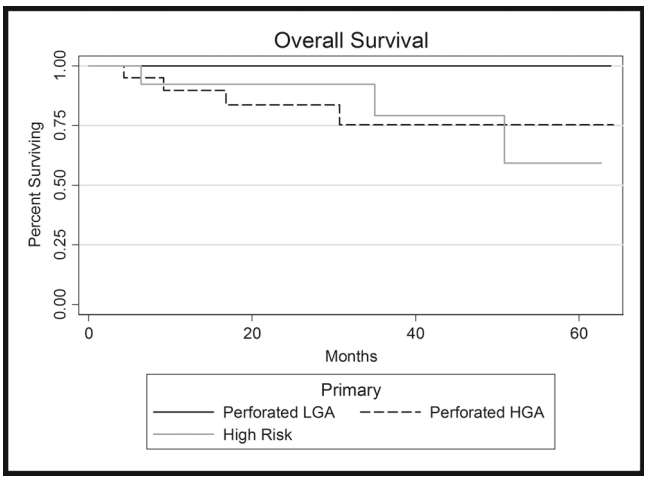
		Pathology re-review at our institution				
		Adenoma	MACA	LAMN	GCC	NMACA
Referring institution pathology report	Adenoma (n=7)	-	-	7	-	-
	LAMN (n=32)	-	2	30	-	-
	HAMN (n=1)	-	-	1	-	-
	MACA (n=72)	1	56	8	6	1
	Mucinous Neoplasm (n=3)	-	1	2	-	-

GCC: goblet cell carcinoid, NMACA: nonmucinous adenocarcinoma

P163

Outcomes After Adjuvant Hyperthermic Intraperitoneal Chemotherapy for High-risk Primary Appendiceal Neoplasms After Complete Resection L.M. Enomoto,[1]* H.A. Choudry,[2] D.L. Bartlett,[2] L. Totin,[2] G.N. Mann,[3] J.J. Skitzki,[3] K. Perry,[1] K.I. Votanopoulos,[1] E. Levine,[1] P. Shen.[1] *1. Surgery, Wake Forest Baptist Medical Center, Winston Salem, NC; 2. University of Pittsburgh, Pittsburgh, PA; 3. Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

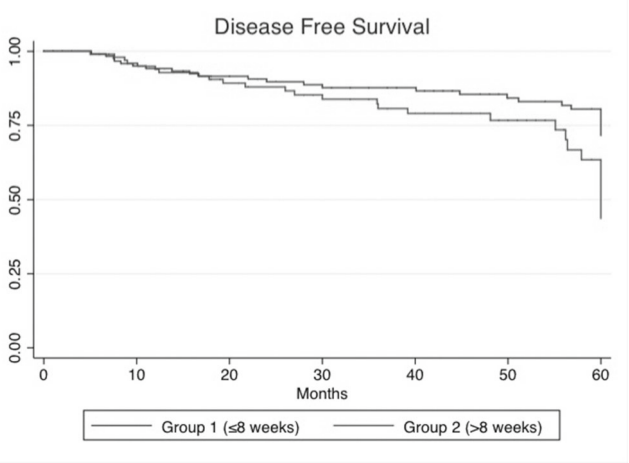
Introduction. Appendiceal neoplasms are uncommon tumors. Optimal treatment for patients with perforation or high grade pathology after initial resection is unknown. This study evaluated the outcomes of patients who presented with increased risk for peritoneal dissemination after primary resection but no current evidence of disease who underwent adjuvant hyperthermic intraperitoneal chemotherapy (HIPEC). Methods. This was a retrospective, multi-institutional cohort study evaluating patients with high risk (HR) appendiceal neoplasms with a peritoneal carcinomatosis index of 0 who underwent HIPEC. Overall survival (OS) and disease-free survival (DFS) were estimated by Kaplan-Meier analysis. Results. 56 patients at 3 high volume tertiary cancer centers were included. The most common indication for HIPEC was perforated high grade appendiceal (HGA) carcinoma (39.3%), followed by perforated low grade appendiceal (LGA) carcinoma (37.5%). 23% of patients had HR features including positive margins after initial resection, goblet cell carcinoma or adenocarcinoma with signet ring cell features. 5 patients with minimal macroscopic peritoneal disease that was previously resected or completely responded to systemic chemotherapy prior to HIPEC were included in the HR group. 5-year OS was 82.5% for the entire cohort while for patients with perforated LGA, perforated HGA, and HR features, it was 100%, 75.4%, and 59.3%, respectively (p=0.06) (Figure 1). 5-year DFS was 77.1% for the entire cohort while for patients with perforated LGA, perforated HGA, and HR features, it was 91.7%, 65.5%, and 55.4%, respectively (p=0.04). 9 patients recurred after HIPEC; 1 had perforated LGA, 5 had perforated HGA, and 3 had HR lesions. All recurrences were peritoneal with 1 concurrent mediastinal recurrence. OS was significantly worse in patients who recurred (p=0.001). Conclusion. Patients with perforated LGA neoplasms have excellent outcomes with primary resection and adjuvant HIPEC. Patients with perforated HGA neoplasms and HR lesions have increased recurrence rates leading to worse survival. The role of adjuvant HIPEC in these patients requires further study.



P164

Does Delayed Surgery Influence Long-Term Survival Outcomes in Patients with Locally Advanced Rectal Cancer Who Do Not Respond to Neoadjuvant Treatment? S. Deidda,* A. Melis, M. Cerci, A.S. Carboni, L. Zorcolo, A. Restivo. *University of Cagliari, Selargius, Italy.*

Introduction The treatment of locally advanced rectal cancer consists of a neoadjuvant chemoradiotherapy (nCRT), followed by a Total Mesorectal Excision (TME), plus or minus adjuvant chemotherapies. The interval between the end of nCRT and surgery tumor response and long-term outcome. However, no studies analyzed the influence on survival outcomes of a delayed surgery in patients who did not respond to the nCRT. The aim of the present study was to investigate if an interval time between nCRT and surgery >8 weeks impacts the long-term oncologic outcome in a large series of non-responders patients. Methods Data of 413 patients, underwent nCRT and TME, for locally advanced rectal cancer, at the Colorectal Surgery Center of the University of Cagliari (Italy), between January 1995 and November 2013, were identified from a prospectively maintained database. A total of 231 patients, who did not achieve a good or complete pathological response (non-responders), were included in our study. The study population was divided into two groups according to the preoperative chemoradiotherapy-surgery interval: ≤ 8 weeks (Group 1) and > 8 weeks (Group 2). Results A total of 231 patients, non-responders to the nCRT and underwent TME were enrolled in the study. There were 126 patients (56.5%) in Group 1 and 105 (45.4%) in Group 2. The two groups were homogeneous for demographics and clinical characteristics. The 5-years overall survival and 5-years disease-free survival were lower in Group 2 than in Group 1 (55.1% vs 69.9%; p=0.05), and 33.3% vs 64.4%; p=0.02, respectively). Multivariate Cox regression revealed that a prolonged interval between the end of nCRT and surgery was independently associated with reduced disease-free survival (HR=1.9; 95% CI=1.1-3.2; p=0.03). Conclusion Prolonged interval between the end of preoperative chemoradiotherapy and surgery, in patients who did not respond to the therapies, is associated with worse survival outcome. This finding could be clinically relevant and should be further investigated with randomized trials.



P165

Venous Thromboembolism Following Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion for Colorectal Peritoneal Metastases A.C. Kim,* L. Totin, Y. Shuai, J.F. Pingpank, M.P. Holtzman, D.L. Bartlett, H.A. Choudry. *Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Patients with colorectal cancer (CRC) are at an increased risk of venous thromboembolism (VTE), especially following complex operations. We sought to examine the incidence and risk factors associated with VTE in patients with peritoneal metastases from CRC undergoing cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion (CRS-HIPEC). Methods: Using a prospectively maintained database of patients with peritoneal metastases from colorectal and appendiceal cancer undergoing CRS-HIPEC between 2010 and 2018 (n=735), we identified associations between in-hospital VTE incidence and perioperative patient variables. Chi-Square, Fisher exact, or Wilcoxon two-sample tests were utilized. Results: The incidence of in-hospital VTE following CRS-HIPEC was 7.3% (55 patients). Higher mean preoperative CEA level (6.6 vs 4.7), peritoneal cancers index (PCI) (20.1 ± 8.2 vs 15.6 ± 9.3), peritoneal surface disease severity (PSDSS) (10.1 ± 5.8 vs 7.9 ± 4.7), operative time (735 vs 620 min), estimated blood loss (EBL) (1200 vs 800 ml), in-hospital comprehensive complication index (53.2 vs 36.2), and hospital length of stay (35 vs 17 days) were significantly associated with VTE ($p<0.05$). Categorical data significantly associated with the incidence of VTE included CRC histologic differentiation, blood transfusion requirement, overall in-hospital complications (Clavien Dindo grades), and ICU admissions ($p<0.05$). Conclusions: The incidence of in-hospital VTE was associated with

higher burden of peritoneal disease (represented by higher preoperative CEA level, PCI and PSDSS) and more extensive/complex operations (represented by increased operative time, EBL, postoperative complications, ICU admissions, and longer hospital length of stay). A better understanding of baseline incidence and modifiable risk factors will allow us to formalize VTE-related preventative and therapeutic guidelines following CRS-HIPEC for colorectal peritoneal metastases. This is important given the growing number of centers performing CRS-HIPEC procedures.

P166

Is Metastasectomy a Worthy Option? The Role of Surgery in Metastatic Colon Cancer to Liver and Lungs R. Lemini,[1] K. Attwood,[2] S.P. Bagaria,[1] K.N. Partain,[1] J. Gunn,[1] T. Almerey,[1] T. Yeager,[1] A.W. Elias,[1] D.T. Colibaseanu,[1] E.M. Gabriel.[1]* *1. Surgery, Mayo Clinic, Jacksonville, FL; 2. Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Introduction The role of surgery and especially metastasectomy is still controversial in the treatment of stage IV colon cancer (CC), and discrepancies exist between guidelines and surgical practice. The aim of this study was to investigate the relationship between surgery and survival in patients diagnosed with stage IV CC. We hypothesized that resection in select patients with liver and/or lung metastases leads to better outcomes. Methods The National Cancer Data Base was retrospectively queried for patients diagnosed with colon adenocarcinoma between 2004 and 2013. Selection criteria included pathological stage IV, presence of liver and/or lung metastases, absence of brain and/or bone metastases, and known surgery status. Patient demographic and clinical characteristics, and short-term outcomes were collected. Associations with surgical group were evaluated using Kruskal-Wallis and Pearson Chi-square tests. Overall survival (OS) was summarized by surgical group using standard Kaplan-Meier methods. The association between surgical group and OS was evaluated using the log-rank test. Results A total of 31,172 patients were included. Of these, 13,214 (42.4%) had surgery while 17,958 (57.6 %) did not. 81.3 % of patients had liver metastases only, while 18.7 % of patients had both liver and lung metastases. Chemotherapy was administered to 66.5 % of patients, with no significant difference between those who did and did not receive surgery. The median OS was 15.1 months (95% CI 14.8 to 15.5) for the entire cohort. However, the median OS was significantly better for those who had surgery compared to those who did not (21.8 vs 7.5 months, $p < 0.01$). Conclusions Metastasectomy plays a controversial role for stage IV CC treatment. However, early data shows it may be beneficial. Despite this striking difference in OS, a main limitation of this study is lack of granularity, especially for the number of metastases and the type of performed procedure. More research is needed to better define the role of surgery in the setting of metastatic colon cancer.

P167

Lymph Node Positivity and Long-Term Survival in Patients with Appendiceal Cancer C. Webb,* J. Chang, R. Gray, B. Pockaj, C. Stucky, N. Wasif. *Surgery, Mayo Clinic Arizona, Phoenix, AZ.*

Background: Appendiceal cancers represent a diverse group of malignancies with varying biological behavior. The significance of lymph node metastases in relation to long term survival is unclear for many of the subtypes. Methods: The National Cancer Database was queried to find patients diagnosed with appendiceal cancer from 1998-2012. Kaplan-Meier curves and multivariable Cox regression analyses were used to study the association between lymph node status and survival outcomes. Results: Of the 13,654 patients identified, 4575 (33.5%) had nodal metastases. The histological subtypes included were mucinous adenocarcinoma 34.0%, nonmucinous adenocarcinoma 29.7%, goblet cell 22.7%, signet cell 8.1%, and carcinoid 5.6%. The rates of lymph node involvement for each type of cancer are as follows: signet ring 15.8%, goblet cell 19.2%, mucinous adenocarcinoma 24.7%, nonmucinous adenocarcinoma 33.1%, and carcinoid 7.2%. Nodal involvement showed an adverse association with long term survival for all subtypes with the exception of carcinoid tumors; Figure 1. On multivariable regression analysis a similar association was seen with the hazard rate for death: signet cell HR 3.71 (95% CI 2.62-5.26), goblet cell HR 3.31 (95% CI 2.44-4.48), mucinous adenocarcinoma HR 2.41 (95% CI 2.06-2.81) and nonmucinous adenocarcinoma HR 2.12 (95% CI 1.86-2.41). Carcinoid tumors with positive nodes had a HR for death of 1.22 (95% CI 0.71-2.09). Conclusions: Lymph node positivity in all subtypes of appendiceal cancers, with the exception of carcinoid tumors, is associated with significantly decreased survival. Performance of additional surgery for regional nodal staging is unlikely to provide prognostic information for patients with appendiceal carcinoids.

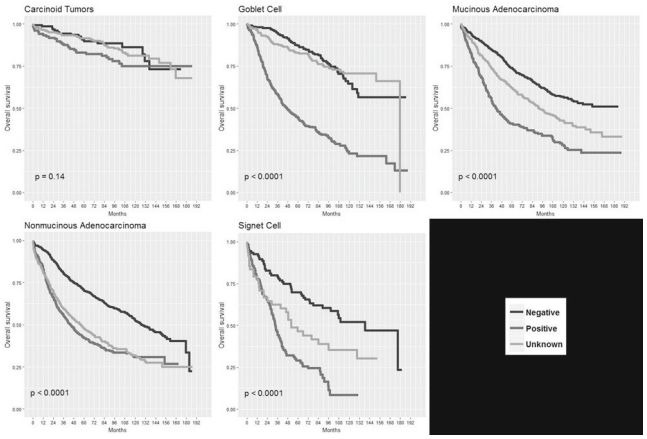


Figure 1: Association between long term survival and nodal involvement stratified by histologic subtype

P168

Enhanced Recovery After Surgery: Improving Outcomes After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: A Feasibility Study P. Lu,[1]* A.C. Fields,[1] G. Shabat,[1] K. Lee,[2] J. Irani,[1] J. Goldberg,[1] R. Bleday,[1] N. Melnitchouk.[1] *1. Brigham and Women's Hospital, Department of Surgery, Boston, MA; 2. Brigham and Women's Hospital, Center for Surgery and Public Health, Boston, MA.*

Introduction: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) utilized for patients with peritoneal carcinomatosis has historically been associated with high morbidity given the significant physiologic insult of an extensive operation. Enhanced Recovery after Surgery (ERAS) pathways, which utilize a multimodal approach to temper the physiologic response to surgery, have been successful in improving post operative outcomes for many different procedures, however their use has not been well examined in CRS/HIPEC cases. The goal of this study is to examine the effect of ERAS pathway implementation for patients undergoing CRS/HIPEC at a single institution. Methods: Patients with peritoneal carcinomatosis who underwent planned CRS/HIPEC with mitomycin C between October 2015 to September 2018 were identified. Data including patient characteristics, disease pathology and perioperative outcomes were obtained. Primary outcomes were hospital length of stay (LOS), renal dysfunction, and readmission. Results: 29 patients met inclusion criteria. 11 (37.9%) patients underwent CRS/HIPEC prior to implementation of ERAS pathway, and 18 (62.1%) patients underwent CRS/HIPEC according to ERAS pathway guidelines. The patient cohorts had no significant difference in age and gender ($p>0.05$). There was a significant decrease in LOS after implementation of ERAS pathway management from 9.8 days to 6.4 days ($p=0.003$). No patients from either cohort experienced acute kidney injury postoperatively. There was a significant difference in postoperative readmission rates with 3 (27.3%) in pre-ERAS and 0 after ERAS was implemented ($p=-0.045$). Conclusions: In this feasibility study, ERAS pathway utilization for patients undergoing CRS/HIPEC significantly decreased postoperative LOS and readmission, without evidence of increased postoperative complications. ERAS may be an effective method to improve outcomes for patients who undergo CRS/HIPEC. Further studies are needed to investigate the effects of ERAS utilization on recovery outcomes after CRS/HIPEC.

P169

Disparities in Rectal Cancer Outcomes: Does Treatment Location or Facility Matter? A.W. Elias,[1]* T. Almerey,[1] R. Lemini,[1] K.N. Partain,[1] T. Yeager,[1] S.P. Bagaria,[1] K. Attwood,[2] D.T. Colibaseanu,[1] E.M. Gabriel.[1] *1. General Surgery, Mayo Clinic Florida, Jacksonville Beach, FL; 2. Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Background: Superior outcomes for patients with rectal cancer treated in urban centers as compared to rural centers have been identified. However, it is unknown whether these disparities are eliminated based on treatment facility type, i.e. academic vs community centers. The objective of this study was to analyze disparities in rectal cancer post-surgical outcomes based on geographic setting and treatment facility type. Methods: We retrospectively identified patients from the NCDB with stage 1-3 rectal cancer undergoing resection between 2004-2013. Overall survival was compared among geographic settings (metropolitan, urban, or rural), as well as by facility type (academic center, comprehensive community cancer program, or community center) within each geographic setting. Results: For each geographic setting, 43,495 (79.4%) metro, 9,897 (18.1%) urban, and 1,419 (2.6%) rural patients were identified. Median age was 61 years for metro and 63 years for urban and rural. More patients in rural (72%) and urban (66.1%) areas received care at community and comprehensive community centers than did patients in metro areas (56.1%) ($p < 0.001$). There was no significant difference in 5-year overall survival between settings metro (45%), urban (43%), and rural (45%) areas ($p = 0.32$). In metro areas, overall survival was highest in comprehensive (47%), then community (46%), and academic centers (43%) ($p < .001$). In urban areas, overall survival was highest in community (48%), then academic (46%), and comprehensive centers (44%) ($p<.001$). In rural areas, there were no significant differences in overall survival among the facility types. Conclusion: Unlike prior studies, differences in survival were not noted between geographic settings, and academic institutions did not demonstrate a survival advantage. While there are limitations in the granularity of patients treated at these different sites and facilities, contributing to selection bias within the study, these early results suggest that similar surgical and peri-operative care can be obtained regardless of geographic location or treatment facility type.

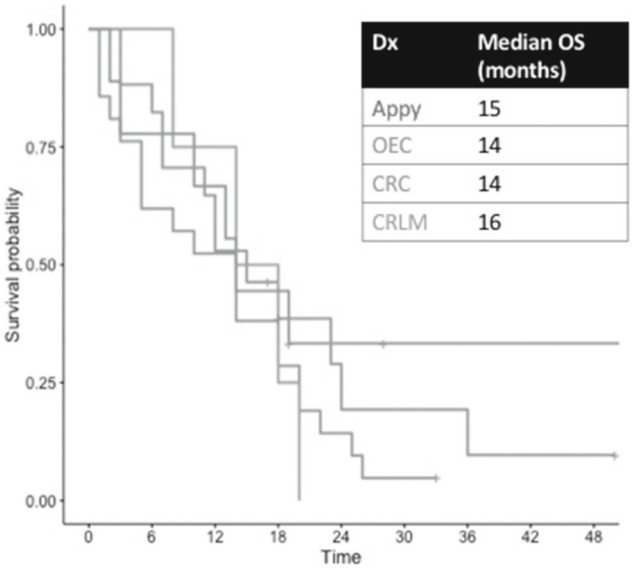
Rectal Cancer Survival by Location and Facility Type

	Rural				Urban				Metropolitan				p-value
	Academic	Comprehensive	Community	Total	Academic	Comprehensive	Community	Total	Academic	Comprehensive	Community	Total	
No. of patients, N (%)	358 (26)	778 (57)	214 (16)	1419 (3)	2921 (30)	4647 (48)	1695 (18)	9897 (18)	15135 (36)	19604 (47)	3753 (9)	43495 (79)	<.001
5-year overall survival, OS (%)	40	44	47	45	46	44	48	43	43	47	46	45	-
Median survival estimate (mo.)	54.2	54.0	55.6	54.3	55.9	54.8	58.1	55.2	54.1	57.2	55.6	55.6	Total: 0.322 Rural: 0.822 Urban: <.001 Metro: <.001

P170

Is CRS & HIPEC a Safe and Effective Palliative Treatment Strategy in Patients with Chemo-refractory Symptomatic Peritoneal Metastasis? A.D. Patel,* J.M. Foster, M. Betha, K. Brown, G. Malhotra. *Surgery, University of Nebraska Medical Center, Omaha, NE.*

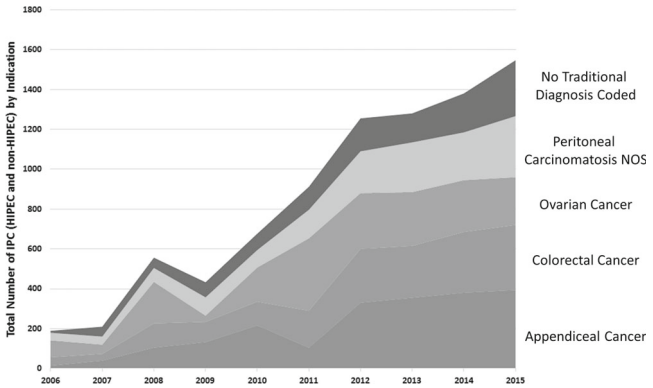
INTRODUCTION Although early surgical referral for peritoneal metastasis patients is advocated, many patients are referred after multiple rounds of chemotherapy while experiencing disease progression often with symptomatic disease. Further systemic therapy for this group of patients is not option due to symptomatic disease and/or chemotherapy intolerance/fatigue. This study investigate the safety of palliative surgery and oncologic outcomes. METHODS Palliative surgery for this study was defined as failing at least two lines of chemotherapy, progression on current chemotherapy, and/or symptomatic disease progression including ascites, obstruction, and pain. A 2010-2017 retrospective analysis identified 56 patients who met the criteria. Data collected included demographics, histology, LOS, perioperative complications, perioperative mortality, peritoneal recurrence, overall recurrence, and overall survival. RESULTS The median number of chemotherapy cycles receive by patients was 3.5 lines of therapy. There were no postoperative deaths and complication rate was 22%. Ostomy rates and abdominal wall reconstruction was performed in 24% and 21% respectively. The median LOS was 11 days and palliation achieved in 97% of patients. Overall survival was 13.5 months and survival rates were similar for each histology (Figure 1). Incomplete CRS (>R2a) was associated with poor survival at 2.8 months while R1/R2a associated 18 months. ($p<0.05$) Synchronous liver metastasis in CRC-PM survival was 16 months not negatively impacting survival benefit. CONCLUSION CRS/HIPEC was performed safely in the palliative setting in symptomatic, heavily chemotherapy treated patients. Observed median survival was a year and R1/R2a CRS was associated with prolong survival. CRC liver metastasis did not preclude survival benefit if optimal CRS was achieved. Patients with symptomatic disease should be referred to peritoneal center for evaluation.



P171

Appropriateness of Intraperitoneal Chemotherapy in the United States: Time for a Dedicated Registry? R.J. Ellis,* A.D. Yang, K.Y. Bilimoria, R.P. Merkow. *Surgical Outcomes and Quality Improvement Center, Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL.*

INTRODUCTION: Cytoreductive surgery (CRS) and intraperitoneal chemotherapy (IPC) is an aggressive treatment option for patients with peritoneal carcinomatosis (PC). Although CRS/IPC is now part national treatment guidelines for colorectal, appendiceal and ovarian cancers, appropriate national utilization of this complex procedure for these and other malignancies is poorly understood. The objectives of this study were to (1) describe population based trends in national utilization of CRS/IPC, (2) define the most common indications for the procedure, and (3) characterize the types of hospitals performing the procedure. METHODS: The National Inpatient Sample (NIS) database was used to identify patients from 2006-2015 who underwent IPC (hyperthermic [HIPEC] and non-hyperthermic) and CRS. Oncologic indication and associated abdominal procedures were assessed. Hospitals performing IPC were classified based on size and teaching status using NIS definitions. RESULTS: Between 2006 and 2015, the estimated annual number of CRS/IPC cases increased significantly from 189 to 1547 ($P=0.002$; Figure). Overall, appendiceal cancer was the most common indication (24.5%) and increased over the study period (14 cases to 393 cases), followed by ovarian cancer (23.2%; 85 cases to 240 cases) colorectal cancer (20.9%; 42 cases to 327 cases) and unspecified PC (17.5%; 38 cases to 307 cases; all $P<0.05$). The remaining cases (13.8%) were performed for non-guideline recommended indications, including sarcomas and small bowel malignancies. Most cases were performed in large teaching hospitals (65.9%), compared to smaller teaching hospitals (25.6%), large non-teaching hospitals (5.3%), or small non-teaching hospitals (3.2%). CONCLUSION: Utilization of IPC is increasing steadily in the US and is performed at many types of facilities, and often performed for non-guideline recommended indications. This is concerning given the morbidity of the procedure and unproven clinical utility outside of a few indications previously studied. A national registry dedicated to cases of intraperitoneal chemotherapy is necessary in to further evaluate use of this complex procedure.



National increase in utilization of CRS/IPC from 2006-2015 stratified by surgical indication. Nearly a 10-fold increase in cases was observed, with nearly 15% of cases being performed for non-guideline indications.

P173

Treatment Variances in Elderly Patients in Stage III Colon Cancer
W. Wang,* C. Seo, J.C. Ong, G. Tan, C. Chia, K. Soo, M. Teo.
National Cancer Centre Singapore, Singapore, Singapore.

Introduction: Adjuvant chemotherapy is important in Stage III colon cancers as these patients are at higher risk of systemic failure. However, chemotherapy comes with toxicities and side-effects which may be poorly tolerated in the elderly population and many patients may not receive standard of care treatment. In this study, we aim to investigate if advanced age affected treatment received. Methods: Patients with treatment-naive Stage III colon cancers diagnosed and resected upfront between 2002 and 2015 at our institution were included. Demographic and clinicopathological data were retrospectively collected. Results: 117 patients were included. Median age was 60 (range: 31 - 76), with 86 patients <70 years(73.5%) and 31(26.5%) ≥70 years. In the younger group, 5(5.8%) had T2, 46(53.5%) had T3, 35(40.7%) had T4 disease, whilst 23(74.2%) had T3 and 8(25.8%) had T4 disease in the older group(p=0.103). 52 had N1 and 34 had N2 disease in the younger group vs 20 with N1 and 11 with N2 disease in the older group(p=0.652). 9(10.5%) patients had perforated tumours, 29(33.8%) had perineural invasion, 34(39.5%) had vascular invasion, 8(10.3%) had lymphatic invasion in the younger group as compared to 2(6.5%), 11(35.5%), 13 (43%) and 3(9.7%) in the older group respectively (p=0.512, 0.818, 0.971, 0.993). In the younger group, 67(77.9%) patients received adjuvant chemotherapy as compared to 18 patients in the older group (58.1%)(p=0.018). Of the younger patients who received adjuvant chemotherapy, 53(79.1%) completed the course as compared to only 10(55.6%) in the older group and this difference was statistically significant (p=0.046). The median overall survivals were 90 and 71 months in the younger and older patients respectively (p=0.817). Discussion: Whilst there were no histopathological differences in the tumours seen in the older patients, they were less likely to undergo and/or complete a full course of planned adjuvant chemotherapy. Despite that, there was no significant difference between the overall survivals of the two populations. Further investigation into the tumour biology is warranted to determine if if there were indeed distinct differences.

P174

Chemoradiation Versus Local Excision in Treatment of Stage I Anal Squamous Cell Carcinoma: The Importance of Appropriate Patient Selection X. Gao,* P. Goffredo, A. Kahl, M. Charlton, R.J. Weigel, I. Hassan. *Surgery, University of Iowa, Iowa City, IA.*

Introduction: Chemoradiation therapy (CRT) represents the standard treatment for anal squamous cell carcinoma (ASCC) but can have significant treatment related toxicities. Recent studies have demonstrated the feasibility of local excision (LE) for stage I ASCC with comparable oncologic outcomes to CRT. We aimed to validate this finding in a large population-based database and hypothesized that for smaller stage I tumors (≤1 cm), LE would be associated with better overall survival (OS). Methods: Adult patients diagnosed with T1N0M0 ASCC from 2004-2015 were identified from the Surveillance, Epidemiology, and End Results database. Treatment type was categorized as CRT or LE alone. Analyses were performed for the entire cohort and then stratified by tumor size (≤1 cm and 1-2 cm). Results: The study cohort included 883 patients, of which 56% had ASCCs 1-2 cm in size and 77% received CRT. Mean age, insurance status, and residence were similar between CRT and LE groups, but the distribution of gender (female 68% vs. 52%), tumor grade (moderately/poorly differentiated 62% vs. 38%) and race (White 91% vs. 84%) were significantly different (p<0.05). There was no difference in 5-year OS between CRT (83%) and LE (87%, p=0.89, Figure 1). When stratified by tumor size, the 5-year OS after CRT and LE for tumors ≤1 cm were 81% vs. 90% (p=0.22), and for tumors 1-2 cm were 83% vs. 78% (p=0.22), respectively. Factors independently associated with receiving CRT were being female, higher tumor grade, and tumor size 1-2 cm. On multivariate regression, younger age, female gender, being White, and insured were associated with increased 5-year OS (p<0.03). Conclusion: In appropriately selected patients with well differentiated ASCCs ≤1 cm, LE could be an acceptable option. However, since larger ASCCs with moderately/poorly differentiated histology were more likely to receive CRT, the equivalence of OS between treatment groups should be interpreted with caution. The similar OS may be due to biological differences rather than non-inferiority of treatments. Further investigation to determine the ideal treatment strategy for early ASCC is necessary.

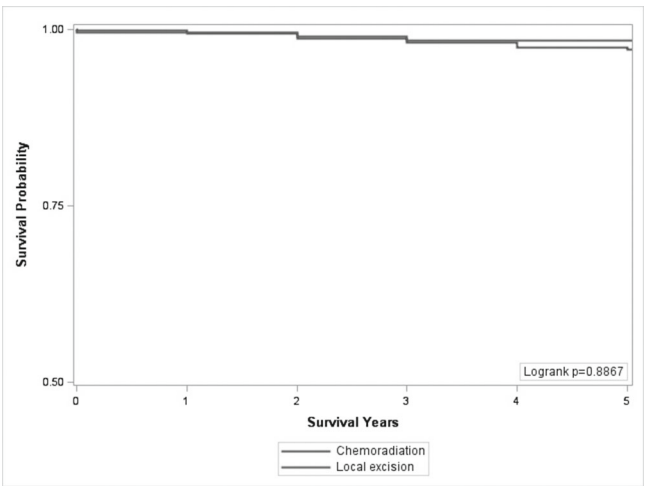


Figure 1. Kaplan Meier overall survival curve for stage I anal squamous cell carcinoma by treatment

P175

Outcome of Upfront Cytoreductive Surgery of Colorectal Peritoneal Carcinomatosis After Initial Misdiagnosis of Metastatic Ovarian Cancer H. Phillips,* C.H. Chan, B.S. Jensen, M. Belding-Schmitt.
Surgery, Univeristy of Iowa, Iowa City, IA.

Background: Ovarian masses are often presumed to be primary ovarian neoplasms and are commonly treated with upfront surgery. However, some cases are found post-operatively to be ovarian metastases of colorectal origin. Here we aim to examine the impact of this erroneous initial presumptive diagnosis on the oncological outcome of patients with metastatic colorectal cancer. Methods: Retrospective review of patients treated for stage IV colorectal cancer with ovarian metastasis in the institutional Oncology Registry between 2006 and 2016 was conducted. Survival probabilities were estimated using the Kaplan-Meier method. Time was calculated from diagnosis to death for overall survival (OS). Cox regression models were used to assess the effects of demographic, clinicopathologic, and treatment variables including initial diagnosis, degree of cytoreduction and chemotherapy approach on OS. Results: Of 30 patients identified, 11 (37%) had an incorrect initial diagnosis of ovarian cancer. These patients were less likely to have complete cytoreduction (9.1% vs. 26.3%, P=0.23) and neoadjuvant chemotherapy (9.1% vs. 47.4%, P=0.08). Although not statistically significant, patients with incorrect diagnosis had a longer median OS in comparing to those with correct diagnosis (60 vs. 30 months, P=0.53). While there was no significant difference between complete and incomplete cytoreduction in the multivariate analysis, patients received adjuvant chemotherapy had a significantly better OS than those who received neoadjuvant chemotherapy (median OS: 108 vs. 26 months, HR: 0.26, 95% CI: 0.08-0.81, P=0.02). Conclusions: Incorrect initial diagnosis does not have

a negative impact on the outcome of stage IV colorectal cancer with ovarian metastases. While this retrospective study is clearly limited by selection bias, upfront cytoreductive surgery followed by adjuvant chemotherapy in selected patients may confer survival benefit. Further studies are warranted to compare the neoadjuvant vs. adjuvant chemotherapy approach for patients with colorectal peritoneal carcinomatosis.

Table 1: Univariate and Multivariate Analysis for Overall Survival

			Univariate			Multivariate		
Covariate	**Value**	**N**	**HR**	**95% CI**	**P-Value**	**HR**	**95% CI**	**P-Value**
Age		30	1.03	0.99-1.08	0.11			
Obesity	No	20	Ref	--	--			
	Yes	10	1.20	0.74-1.93	0.47			
Diabetes	No	26	Ref	--	--			
	Yes	4	1.25	0.60-2.61	0.56			
Smoking History	No	24	Ref	--	--			
	Yes	6	1.31	0.70-2.44	0.40			
Primary site	Colon	20	Ref	--	--	Ref	--	--
	Rectum	7	0.48	0.25-0.95	**0.03**	4.13	0.97-17.6	0.06
	Missing	3	--	--	--			
Tumor grade	G1/2	4	Ref	--	--			
	G3	19	0.71	0.26-1.93	0.51			
	Missing	7	--	--	--			
Nodal status	Negative	5	Ref	--	--			
	Positive	19	0.53	0.23-1.26	0.15			
	Missing	6	--	--	--			
Cytoreduction	Complete	6	Ref	--	--	Ref	--	--
	Incomplete	22	1.66	0.47-5.84	0.43	0.90	0.20-3.93	0.88
	None	2	9.36	1.36-64.6	**0.02**	47.6	1.58-1438	**0.03**
Chemotherapy	Neoadjuvant	10	Ref	--	--	Ref	--	--
	Adjuvant	17	0.30	0.11-0.82	**0.02**	0.17	0.04-0.71	**0.02**
	None	3	7.83	1.04-58.9	**0.05**	14.9	0.78-286	0.07
Initial Diagnosis	Correct	19	Ref	--	--	Ref	--	--
	Incorrect	11	1.34	0.54-3.32	0.53	0.47	0.10-2.14	0.33

P176

Methylation-Specific Inactivation of PAX6, ATP10A, and ASCL1 in HPV-Associated Cancers L. Hendrick,[1]* A. Elahi,[1] J.L. Lomax,[1] A. Ajidahun,[1] A. Berglund,[2] E.M. Siegel,[2] S.M. Husain,[1] I. Getun,[1] E. Glazer,[1] D. Shibata.[1] *1. Surgery, University of Tennessee Health Science Center, Memphis, TN; 2. Moffitt Cancer Center, Tampa, FL.*

Introduction: Human papillomavirus (HPV) infection results in extensive alterations in host DNA methylation which may contribute to carcinogenesis. Using a genome-wide methylation array platform, we have previously characterized specific DNA methylation changes in genes that develop across the spectrum of anal and cervical neoplastic progression. After filtering for biologic relevance, methylation of the PAX6, ASCL1 and ATP10A genes were of particular interest. We sought to confirm the epigenetic regulation of the PAX6, ASCL1 and ATP10A genes in a comprehensive panel of anal, cervical and oropharyngeal (OP) cancer cell lines. Methods: Expression of PAX6, ASCL1 and ATP10A was evaluated by reverse transcriptase PCR and Western Blot analysis in anal (HPV+: ACC), cervical (HPV+: SiHa, HeLa; HPV-: C33), and OP (HPV+: CRL3212, HPV-: HTB43) cancer cell lines. The methylation status of genes was examined by methylation specific PCR (MSP). Cells were treated with the demethylating agent, 5-Aza-2′-Deoxycytidine (5AzaDC) at 2, 4, and 6 days and the corresponding impact on gene re-expression was evaluated. Results: PAX6 and ASCL1 were significantly downregulated in ACC and HPV+ cervical cell lines. ATP10A expression was absent in all anal and cervical cell lines regardless of HPV status. Expression of all genes was maintained in OP lines. PAX6 and ASCL1 (but not ATP10A) demonstrated methylation in cell lines with reduced expression. 5AzaDC treatment induced re-expression of PAX6 and ASCL1 while ATP10A expression was not affected. Of note, C33 (HPV-) had only slight reduction in PAX6 expression with moderate methylation with no significant re-expression with 5AzaDC. Conclusions: The transcriptional regulation of PAX6 and ASCL1 (but not ATP10A) HPV+ anal and cervical cancer is mediated by DNA methylation. PAX6 and ASCL1 are candidate epigenetic drivers of HPV-associated neoplastic progression in anal and cervical cancers. Further functional analyses of these genes are warranted.

P177

Do "Critical Lesions" Have an Impact on Outcome Following Cytoreductive Surgery and Hyperthemic Intraperitoneal Chemotherapy. A. Ben-Yaacov,[1]* M. Goldenshluger,[1] y. dux,[2] y. nevo,[1] g. Schtrechman-Levi,[1] D. Aderka,[1] E. Shacham-Shumeli,[1] N. Halpern,[1] M. Adileh,[2] D. Zippel,[1] D. Hazzan,[1] A. Nissan.[1] *1. surgical oncology, Chaim Sheba Medical Center, Givataym, Israel; 2. Memorial Sloan Kettering Cancer Center, NY, NY.*

Background: Peritoneal Cancer Index (PCI) is the best available outcome measure of cytoreductive surgery (CRS) and HIPEC. However, a lesion located in a critical area, regardless of PCI, may complicate surgery and as a result contribute to post-operative complications and may have an impact on cancer-related outcomes. Methods: Since 2015 we have defined "critical lesions" (CL) as lesions penetrating the hepatic hilum, major vessels, pancreas, ureters or urinary bladder. All cross-sectional imaging were reviewed in a multidisciplinary conference before surgery and CL were defined and recorded. A total number of 215 patients with PSM were treated between 2015-2018. Patients were excluded due to incomplete CRS (n=53) and incomplete data (n=14). We compared patients with (n=53) and without CL (n=95) by the following parameters: OR time, estimated blood loss (EBL), blood transfusions, hospital stay, post-operative complications and mortality (Clavien-Dindo classification). Our primary end point was overall survival (OS) and disease free survival (DFS). Results: A total number of 148 patients were included. There was no difference in mean age, gender or co-morbid conditions. Mean operating time was longer, (6.0h vs 4.5h, p<0.01) and the EBL was higher (711ml Vs 341ml, p<0.01) in patients with and without CL, respectively. Operative PCI was higher in patients with CL (14.9 Vs 9.2, p<0.01 respectively). Median hospital stay was 11 days for patients without CL Vs 14 days for patients with CL. Major complications were recorded in 9.4% Vs 6.3% (grade 3, p=0.075) and 15.1% Vs 5.3% (grade 4, p=0.073) for patients with and without CL. Reoperation rate for patients with CL was 16% compared to 9.1% for patients without CL (p=0.272). There was no difference in 90-days mortality between the study groups (2% Vs 2.7%). There was no difference in 3-year overall survival (84.9% Vs 94.7%, median survival was not reached) in patients with and without CL, and no major difference in DFS between the two study groups Conclusions: Critical lesions complicate surgery and as a result are associated with worse short-term outcomes but have no impact on cancer-related outcomes.

P178

Clinical Significance of Extended Lateral Lymph Node Dissection for Patients with Lower Rectal Cancer: A Propensity Score Analysis in a Multicenter Retrospective Study S. Yamauchi,* Y. Aoyagi, Y. Yamamoto, A. Takaoka, H. Baba, A. Kikuchi, S. Okazaki, T. Matsuyama, T. Ishikawa, Y. Nakajima, K. Kojima, H. Uetake, Y. Kinugasa, K. Sugihara. *Tokyo Medical and Dental University, Tokyo, Japan.*

Background Total mesorectal excision (TME) with lateral lymph node dissection (LLND) for lower rectal cancers (RCs) is the standard surgical procedure in Japan, while preoperative chemo-radiotherapy followed by TME is applied in Western countries. In the Guidelines for treatment of colorectal cancer by Japanese Society for Cancer of the Colon and Rectum, it is expected that the risk of intra-pelvic recurrence decreases by 50 %, and 5-year survival improves by 8 to 9 % after performing LLND for lower RCs. The aim of this study is to estimate the prognostic impact of LLND in patients with lower RCs in a Japanese large cohort. Methods A total of 4268 patients with pathological stage I-III lower RC who underwent curative surgical resection with or without LLND (LLND group or non-LLND group) on during the period from 1997 to 2008 at 23 institutions in Japan were retrospectively collected. The association between LLND and clinico-pathological factors was analyzed statistically. Patients' backgrounds were matched using propensity scores. Results The median age of this cohort was 63 years (range, 19-96), and the median follow-up time was 73 months (range, 1-179). After using propensity scores, 1008 matched pairs were extracted. Kaplan-Meier curves showed there is a tendency that all patients of LLND group (n=1008) had better overall survival (OS) (p=0.14). In LLND group, stage III patients and patients with higher preoperative CEA, more often low grade histological status, and more often T3/T4 tumor received survival benefit in OS (P=0.015, 0.034, 0.007, 0.04, respectively). Multi-variate analysis in this matched cohort shows that TME without LLND is an independent better prognostic factor for OS (HR 0.80,

P=0.18). Conclusion Although there are limitations that this is a retrospective study and the indication for LLND differs from each institutions and surgeons, this study suggests that there are patients with lower RC who receive prognostic benefit from TME with LLND.

P179

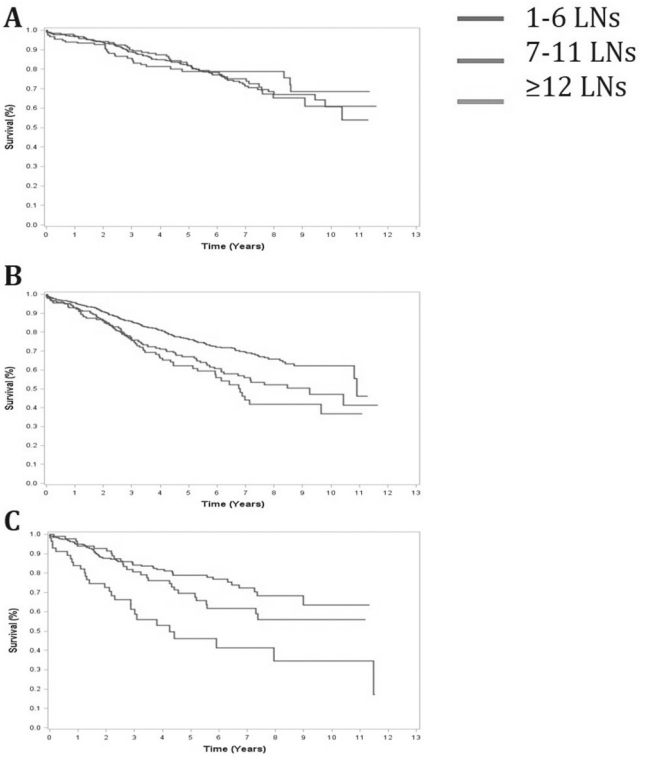
Treatment of Stage II and III Rectal Cancer in the Elderly Patient
W. Wang, C. Seo,* J.C. Ong, C. Chia, G. Tan, K. Soo, M. Teo.
National Cancer Centre Singapore, Singapore, Singapore.

Introduction:Treatment of rectal cancer requires multidisciplinary care, carries significant morbidity and may be especially challenging for elderly patients. However, there is paucity of data in the treatment of elderly patients as they are often under-represented in clinical trials. In this study, we compare the treatment practices for Stage II and III rectal cancers of patients <70 years and those ≥70 years. Methods:Patients with primary Stage II and III rectal cancers diagnosed between January and December 2015 in our institution were included. Demographic and clinicopathological data were retrospectively collected. Results:74 patients were included. Median age of the patient cohort was 61 (range: 36 - 92), with 59 patients <70 years(79.7%) and 15(20.3%) ≥70 years. In the younger group, 43(72.9%) patients had cT3 and 16(27.1%) patients had cT4 disease; 13(22%) had cN0, 27(45.7%) had cN1 and 18(30.5%) had cN2 disease. In the older age group, 9(60%) had cT3 and 4(26.6%) had cT4 and 2(13.3%) had unknown cT stage; 11(73.3%) had cN0, 2(13.3%) had cN1 and 2(13.3%)had unknown cN stage. There were no significant differences in histopathological charcteristics between both groups. 51(86.4%) and 11(73.3%) in the younger and older groups received neoadjuvant chemoRT respectively (p=0.07). 50(98%) and 10(90.9%) in the younger and older groups received long-course radiation (p= 0.458). However, more younger patients underwent curative surgery: 49(83.1%) vs 8(53.3%) (p=0.033). Of younger patients who did not receive surgery, 3 declined surgery and 3 had disease progression. In the older group, 2 became unfit, 2 had progressive disease, 2 declined surgery. 39(66.1%) in the younger group received adjuvant therapy as compared to 5(33.3%) in the older group, although this was not statistically significant(p=0.07). Conclusion:In our study, the initial planned line of treatment in both young and elderly patients appeared similar with no significant difference observed in the rates and type of neoadjuvant chemoRT but less elderly patients underwent curative surgery eventually. Better pre-treatment evaluation of the elderly patients may have enabled more appropriate treatment strategies to be devised upfront.

P180

Impact of Tumor Grade and Extent of Lymphadenectomy on Survival for Appendix Cancer A. Lee,* Y. Chiang, K. Raghav, M. Overman, C. Eng, M. Taggart, B. Feig, K. Fournier. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

INTRODUCTION Appendix adenocarcinoma (AA) is a rare cancer with inferred management guidelines based on colon cancer. Lymphadenectomy with removal of ≥12 lymph nodes (LNs) is required for optimal surgical management of colon cancer. However, the extent of lymphadenectomy for AA remains poorly defined. The aim of this study is to determine the impact of adequate lymphadenectomy and tumor grade on survival outcome for AA. METHODS Utilizing the National Cancer Data Base (NCDB), we identified all patients with AA who had undergone surgical resection between 2004 and 2014. Only patients with complete pathologic and survival variables were included. Kaplan-Meier survival analysis was performed to determine the impact of tumor grade and lymphadenectomy on overall survival (OS). RESULTS Of 5,858 patients with AA, most of the patients had advanced T-stage (T3/4: 81.6%), were LN negative (N0: 63.8%) and had non-metastatic (M0: 67.9%) disease. 28.8% had well differentiated (WD), 42.5% had moderately differentiated (MD), and 28.7% had poorly differentiated (PD) tumors. The median number of resected LNs was15 in WD and PD groups and 16 in the MD group. The number of LN's resected did not have any impact on OS (p=0.982) in patients with WD/N0/M0. However, patients with ≥12 LNs resected had significantly improved OS for MD/N0/M0 (p<0.001) or PD/N0/M0 disease (p<0.001), compared to patients who had less than 12 LN resected. CONCLUSIONS Both tumor grade and the extent of LN resection have significant impact on survival in AA. While extent of LN resection did not have any impact on survival in patients with WD tumors, patients with higher grade tumors had improved survival when ≥12 LNs were resected, suggesting that removal of <12 LNs in this setting results in under-staging. Therefore, while simple appendectomy may be sufficient for patients with WD AA, patients with higher grade AA should undergo surgical resection which includes adequate locoregional lymphadenectomy (ie. right hemicolectomy).



Survival of appendix adenocarcinoma patients staged as pN0M0, stratified by extent of lymphadenectomy and tumor grade A) well differentiated (p=0.982), B) moderately differentiated (p<0.001), and C) poorly differentiated (p<0.001).

P181

Lymph Node Positivity and the Role of Right Hemicolectomy in Patients with Mucinous Neoplasms of the Appendix C. Wai,[1]* C. Sutanto,[2] R. Zhu,[2] C. Nagapetyan,[1] B. Bagdasarian,[3] M. Shirinian,[3] Y. Nasseri,[2] A. Artinyan.[1] *1. Surgery, Verity Medical Foundation, Los Angeles, CA; 2. The Surgery Group of LA, Los Angeles, CA; 3. Glendale Adventist Medical Center, Glendale, CA.*

Intro: Mucinous neoplasms of the appendix (MNAs) are rare and relatively little is known about their behavior. We sought to determine the risk factors for lymph node positivity and identify patients that may benefit from right hemicolectomy (RHC). Methods: The NCDB (2004-2015) was queried for all patients >18 y/o with non-metastatic mucinous neoplasms of the appendix. Demographic, clinical and pathologic criteria were recorded. Standardized classification schemes were utilized. Univariate and multivariate predictors of lymph node positivity were determined in patients undergoing RHC. Univariate and multivariate survival analyses were performed to determine the impact of RHC on overall survival. Results: 3,796 pts were identified. 56 (1.8%) were classified as low grade mucinous neoplasms, 3 (0.1%) with high grade mucinous neoplasm, 2,694 (86.4%) with low grade mucinous adenocarcinoma, and 364 (11.7%) with high grade mucinous adenocarcinoma. 2,016 (53.1%) underwent RHC. 385 (19.1%) pts had positive nodes. Margin positivity, LVI, high grade histology, and increasing T-stage were univariate predictors of lymph node positivity (all p <0.01). Tumor size was marginally significant (p=0.51). On multivariate analysis, margin status, grade and LVI remained independent predictors of lymph node positivity. In those with invasive disease, the combination of low-grade, margin negative, no LVI, and T-stage <=2 identified a subset of patients with low risk of lymph node positivity 6.6% vs. the remainder of the patients 21.3%. RHC did not improve survival in the overall population of MNA pts or in any subset of grade, classification, LVI, lymph node status, margin status, or T-stage. On multivariate analysis, RHC was not an independent predictor of survival. Conclusion: Margin status, LVI

and high grade histology are independent predictors of lymph node status in MNA patients. With invasive disease, a subset was identified with low risk for lymph node positivity in whom hemicolectomy can be avoided. Formal hemicolectomy did not improve survival even in high risk subsets, likely because peritoneal disease is a more important determinant of outcome than hematogenous spread.

P182

A Meta-Analysis of Surgical Outcomes Comparing Robot-Assisted and Laparoscopic-Assisted Surgery for Colorectal Cancer C. Lau,[1]* N. Ghalyaie,[2] R. Chamberlain.[2] *1. Oncology, Abrazo Central Campus, Phoenix, AZ; 2. Abrazo Central Campus, Valley Surgical Clinics, Phoenix, AZ.*

Introduction: Colorectal cancer (CRC) is the third leading cause of cancer-related deaths in the United States, accounting for >50,000 deaths/year. Robotic-assisted surgery (RAS) has greatly improved surgeon dexterity; however, its impact on surgical outcomes among CRC patients remains controversial. This meta-analysis compares the use of RAS and laparoscopic-assisted surgery (LAS) for CRC. Methods: A comprehensive literature search of all published randomized control trials (RCT) comparing RAS and LAS in patients with CRC was conducted using PubMed, Cochrane Central Registries of Controlled Trials, and Google Scholar. Primary outcomes analyzed included duration of surgery, length of stay (LOS), and rates of conversion to open surgery. Secondary outcomes included estimated blood loss (EBL), complication rates, time to first flatus, time to regular diet, 30-day readmission, reoperation, and mortality. Results: Seven RCTs including 954 patients were analyzed. RAS was associated with significantly longer operations (MD 41.988mins; p=0.010) compared to LAS. There was a trend towards a reduction in the rate of conversion to open surgery (RR 0.616; p=0.056) with RAS. No significant difference in EBL (MD -13.731mL; p=0.609), total complications (RR 1.089; p=0.421), major complications (RR 1.463; p=0.470), SSI (RR 1.016; p=0.953), anastomotic leak (RR 1.285; p=0.302), intraabdominal abscess (RR 0.679; p=0.712), bleeding (RR 0.819; p=0.795), ileus (RR 0.837; p=0.637), LOS (MD -0.262days; p=0.626), time to first flatus (MD -0.027days; p=0.839 days), time to regular diet (MD -0.237days; p=0.327), reoperation (RR 0.355; p=0.363), or mortality (RR 0.865; p=0.842) was observed between surgical techniques. A single study reported on 30-day readmission, and reported no significant difference between RAS and LAS. Conclusion: RAS for CRC is associated with significantly longer operations than LAS. There is a trend towards fewer conversions to open surgery with RAS, but no difference in rates of surgical complications, LOS, or return of bowel function. RAS and LAS are safe and effective minimally invasive approaches for the treatment of CRC.

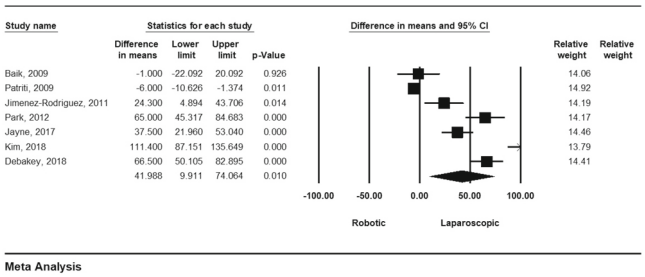
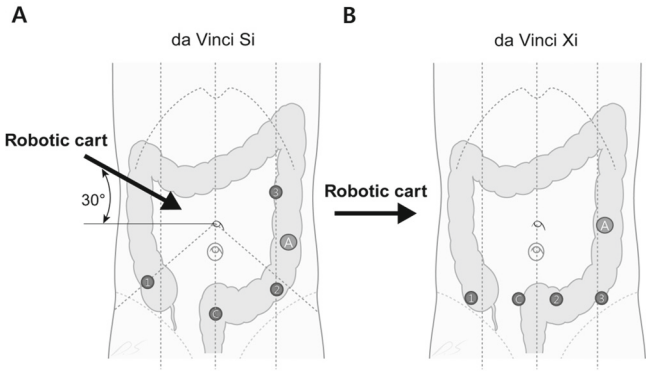


Figure 1: Forest plot comparing duration of surgery with robotic-assisted and laparoscopic-assisted surgery in colorectal cancer patients

P183

Totally Robotic Modified Complete Mesocolic Excision and Central Vascular Ligation for Right-Sided Colon Cancer: Technical Feasibility and Initial Outcomes S. Bae,[1]* B. Min.[2] *1. Keimyung University Dongsan Medical Center, Daegu, Korea (the Republic of); 2. Yonsei University College of Medicine, Seoul, Korea (the Republic of).*

Background: Recently, an operative strategy involving complete mesocolic excision (CME) and central vascular ligation (CVL) for colonic cancer has been introduced. We aimed to describe our initial experience and assess the long-term outcomes of robotic modified CME (mCME) and CVL (mCME+CVL) for right-sided colon cancer. Methods: Of the 677 patients with histologically confirmed, right-sided colon adenocarcinoma that underwent curative mCME+CVL between February 2008 and October 2016, we included 43 patients treated entirely using the robotic approach. Results: The total operation and docking times were 293 (180–644) min and 5 (3–19) min, respectively, with an estimated blood loss of 50 (10–400) mL. The time to soft diet was 4 (1–16) days and the length of hospitalization was 8 (4–48) days. Based on the Clavien-Dindo classification, grade I, II, IIIa, IIIb, and IV complications were noted in 3 (7.0%), 5 (11.7%), 2 (4.7%), 1 (2.3%), and 0 (0%) patients, respectively. The proximal and distal resection margins were 14 (4–54) and 19 (4–48) cm, respectively, and 29 (6–157) lymph nodes were harvested per patient. The patients were followed-up for a median of 55 (2–109) months, during which the overall survival rate, median disease-free period, disease-free survival rate, and tumor recurrence rate were 93.6%, 38 (2–109) months, 81.1%, and 16.3% (7 patients), respectively. Conclusions: Robotic mCME and CVL for right-sided colon cancer was feasible and safe. It can be added to the surgeon's toolbox as an optional strategy for the management of colon cancer patients.



P184

On the Road Again: Travel Patterns and Outcomes in Rectal Cancer M. Garland-Kledzik,* S. Chang, A.J. Scholer, J. Santamaria-Barria, A.M. Khader, T.D. Fischer, M. Goldfarb. *General Surgery, John Wayne Cancer Institute, Santa Monica, CA.*

Background: Associations between high volume centers and improved outcomes have many advocating for centralization of cancer care, which can lead to increased travel, patient burden, and cost. There is, however, conflicting data regarding outcomes for patients with more advanced disease. Therefore, this study aims to explore factors associated with travel and the impact on survival for patients receiving surgery for rectal adenocarcinoma. Methods: All patients >18 years of age with rectal adenocarcinoma that had a surgical resection were identified using the National Cancer Database from 2004-2014. In 83,933 patients, univariate and multivariate (MV) regression determined factors associated with increased travel distance (<50 miles, 50-100 miles, >100 miles) stratified by stage, and cox regression explored the impact of distance on overall survival (OS). Results: Of 83,933 patients, those that traveled for rectal cancer care were younger, white non-Hispanic, insured, and had less comorbidities (all p<0.05 on MV analysis). Travel distance was not associated with cancer stage, surgical approach, or type of surgery (all p=NS), but stage III/IV patients traveling >100 (OR 0.8, p<0.001) and >50 miles (OR 0.72, p=0.01), respectively were less likely to receive adjuvant therapy at any facility. Moreover, stage II/III patients that traveled >50 (OR 1.13, p=0.01) and >100 miles (OR 1.21, p<0.001), respectively were more likely to have >12 lymph nodes harvested and stage III patients were less likely to have a positive surgical margin (OR p=0.03). Patients with Stage IV disease were most affected by travel distance. Those that traveled >50 miles were more likely to have a metastectomy (OR 1.25, p=0.02), particularly if the received surgery at an academic or higher volume center, and their 5-year OS improved by 10% (p=0.002), even when controlling for other factors. Conclusions: Despite travel burden, non-early stage rectal cancer patients may benefit from traveling for surgical care, presumably to higher volume and academic centers, which demonstrate improved oncologic surgical outcomes and survival.

P185

The Association of PD-L1 Expression with Infiltrating Lymphocyte Densities in the Colon Adenocarcinoma Tumor Microenvironment on Endoscopic Biopsy and Final Pathology A.T. Hickerson,[1]* J.L. Campf,[1] J.L. Lombardo,[1] L.M. Messersmith,[1] G.M. Williams,[1] D.F. Hale,[1] T.J. Vreeland,[2] J.W. Myers, III,[1] T.A. Brown II,[1] R.A. Collins,[1] R.O. Brady,[1] G.E. Peoples,[3] G.T. Clifton.[1] *1. San Antonio Military Medical Center, San Antonio, TX; 2. MD Anderson Cancer Center, Houston, TX; 3. Cancer Vaccine Development Program, San Antonio, TX.*

Introduction: Evaluation of the tumor microenvironment (TME) is critical to improving applications of immunotherapy. In colorectal cancer (CRC), regulatory T cell (Treg) density and PD-L1 expression have been associated with improved disease-free survival. There is little data, however, exploring correlation between PD-L1 expression and T cell infiltration of tumors. Additionally, little is known about differences in the TME between endoscopic biopsy (EB) and surgical resection (SR) specimens. Here, we explore this relationship of PD-L1 expression with infiltrating lymphocytes, including, CD3, CD4, CD8 and Tregs in both EB and SR of colon adenocarcinoma. Methods: EB cases diagnosed with colon adenocarcinoma with subsequent curative SR were collected from 2007-2017 at a single institution. Formalin-fixed, paraffin embedded tissue blocks were selected from the EB and SR that contained the invasive margin (IM) and center of tumor (CT). 10 unstained slides were cut of each. FoxP3, CD3, CD4, CD8 and PD-L1 immunohistochemical stains were performed. Immunostained slides were counted with a digital imager software program and reported as cells per square mm. PD-L1 was interpreted per manufacturer, Biocare Medical. T cell populations were compared to PD-L1 status of EB and SR specimens using a Mann-Whitney-U test. Disease free survival (DFS) compared with a log rank test. MSI status was recorded as available. Results: 93 matched specimens were analyzed. Median densities of FoxP3, CD3, CD8, and CD4 cells at the IM and CT were higher in tumors with PD-L1 expression in the EB, SR, or both(Table 1). There as a trend towards more PD-L1 expression in MSI High tumors (4/6) compared to MSI low tumors(n=12/42) in the SR (p = 0.064). PD-L1 expression was associated with improved DFS (97.98% vs 65.85%; p = 0.05). Conclusion: PD-L1 expression in CRC TME is associated with increased immune infiltrate of CD3, CD8, CD4, and FoxP3+ lymphocytes in both EB and in the SR specimens. PD-L1 status may serve as a useful marker for immunogenic tumors, and the EB used to guide neoadjuvant therapy and selection for clinical trials.

			PD-L1 negative (n=69)		PD-L1 positive (n=23)		
			Median	Interquartile range	Median	Interquartile range	P value
Biopsy	FoxP3	IM*	231.0	143.0-283.0	394.0	206.0-524.0	0.026
		CT	283.0	159.0-454.0	335.0	224.0-577.0	0.111
	CD3	IM*	1035.0	768.0-1582.0	1620.0	918.0-2125.0	0.017
		CT	904.0	572.0-1404.0	1288.0	706.0-1757.0	0.057
	CD4	IM*	1111.0	866.0-1429.0	1451.0	795.0-1844.0	0.417
		CT*	1145.0	857.0-1532.0	1614.0	1267.0-2424.0	0.001
	CD8	IM*	242.0	135.0-435.0	445.0	225.0-932.0	0.005
		CT	157.0	80.0-326.0	236.0	100.0-525	0.071
			PDL-1 negative (n=56)		PDL-1 positive (n=37)		
			Median	Interquartile range	Median	Interquartile range	P value
Resection	FoxP3	IM*	140.5	96.0-244.5	308.0	192.0-453.0	0.001
		CT*	207.0	138.5-378.5	386.0	244.0-577.0	0.002
	CD3	IM*	728.5	521.0-963.5	1032.0	605.0-1551.0	0.002
		CT*	392.0	189.0-625.0	545.0	283.0-1190.0	0.022
	CD4	IM*	1096.5	593.5-1408.5	1335.0	926.0-1698.0	0.043
		CT	860.5	580.0-1378.5	1162.0	575.0-1680.0	0.218
	CD8	IM*	320.0	135.5-560.5	482.0	260.0-697.0	0.028
		CT*	120.5	14.5-256.6	254.0	144.0-513.0	0.002

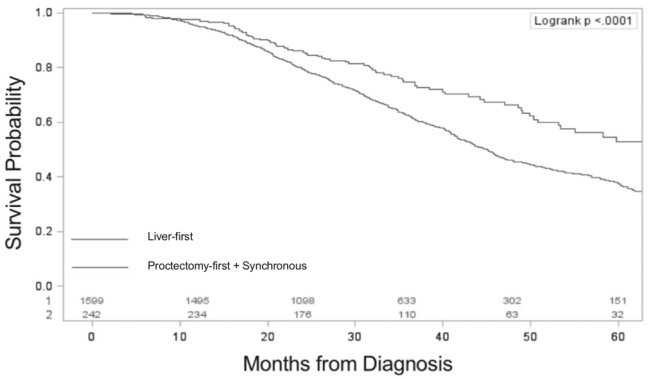
Table 1. Comparison of median values of FoxP3, CD3, CD4, CD8 expression at invasive margin (IM) and tumor center (CT) in tumors with and without expression of PD-L1 at endoscopic biopsy and final resection. *Indicates statistical difference between groups

P186

Liver-First Approach to Stage IV Rectal Cancer with Synchronous Isolated Liver Metastases V. Kurbatov,[1]* B. Resio,[1] D.R. Heller,[1] R.S. Salem,[2] C. Cha,[2] J. Lu,[3] J. Blasberg,[1] Y. Zhang,[1] S. Khan.[2] *1. Yale Department of Surgery, New Haven, CT; 2. Division of Surgical Oncology, Department of Surgery, New Haven, CT; 3. Yale Department of Genetics, New Haven, CT.*

Background: The only possibility for cure in patients with rectal adenocarcinoma (RAC) and isolated liver metastases (ILM) is resection of both the primary and metastatic tumors. Despite efforts to optimize surgical approach, the clinical impact of sequence of resection is not clear. This study analyzes whether the sequence in which a proctectomy and hepatectomy are performed impacts clinical outcomes. Study Design: The National Cancer Database was queried for cases of RAC with hepatic metastases from 2010-2015 with exclusion of extrahepatic metastases. We compared clinicopathologic differences between patients treated with a liver-first approach to those treated with a proctectomy-first or simultaneous approach. Survival was compared with Kaplan Meier and multivariable Cox Proportional Hazards analysis adjusted for patient, tumor, treatment and facility characteristics. Results: A total of 3,344 rectal cancer patients with synchronous ILM who underwent resection were identified. The liver-first approach was uncommon (N=404, 12%), but was associated with higher rates of completion resection of the remaining tumor (47% vs. 31%, P<0.001) compared to other cohorts. Patients managed by a liver-first approach were younger, more commonly treated in an academic facility, had higher CEA levels, and were more likely to receive chemotherapy and radiation (P<0.05). The liver-first cohort was associated with increased median survival (55 months 95%CI: [50.0-66.0] vs. 41 months 95%CI[39.5-42.8], logrank P<0.001). Cox Proportional Hazards analysis adjusted for clinical, demographic, pathologic, treatment, and facility characteristics also identified a decreased risk of mortality for the liver-first cohort (HR 0.75 95%CI:[0.62-0.92], P=0.005). Conclusion: The liver-first approach to RAC with synchronous ILM is not commonly employed, yet is associated with a higher likelihood of resecting all disease burden, administration of chemotherapy and radiation therapy, and prolonged survival. This data supports the utilization of a liver-first approach in appropriately select patients.

Figure 1. Intention to treat Kaplan Meier analysis comparing overall survival between liver-first (red) and rectum-first + simultaneous resection (blue) groups. Survival analysis was restricted to cases with follow up data.



P187

Integrative Analysis of Transcriptomic and Proteomic Profiles of Ascites Identified a Targetable Non-Canonical STAT3-Epithelial-Mesenchymal-Transition Pathway in Colorectal Carcinomatosis

J.C. Ong,* J. Hendrikson, W. Ng, X. Qiu, J.W. Tan, N.B. Shannon, C. Chia, G. Tan, K. Soo, O. Kon, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

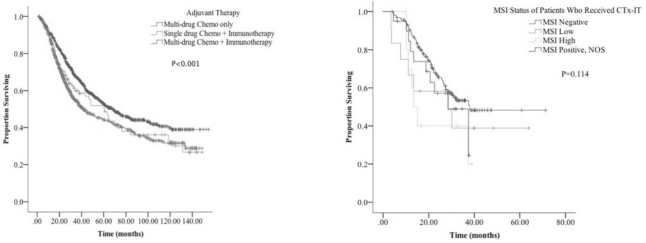
Introduction Presence of ascites in colorectal peritoneal carcinomatosis (CPC) portends a poor prognosis. We hypothesize that ascites is biologically relevant that can be exploited for novel therapy. Methods Gene expression profiling of cell lines treated with ascites coupled with mass spectrometry and cytokine array was performed to identify key signalling pathways and upstream ligands in ascites (n=6). The Cancer Genome Database (TCGA, n=345) was interrogated to identify the link between STAT3 signalling and Epithelial-Mesenchymal-Transition (EMT), and its prognostic significance. In-vitro and in-vivo mouse models were used to demonstrate proof of concept of a novel therapeutic strategy. Results Gene expression profiling of 2 CPC cell lines treated with ascites revealed activation of STAT3 signalling. Validation experiments on ascites (n=13) demonstrated STAT3 to be most relevant in CPC. Clinically, colorectal cancer patients in the TCGA database (n=345) with STAT3-EMT activation had poorer prognosis. Interestingly, receptor tyrosine kinase arrays showed no phosphorylation of JAK kinase, suggesting non-canonical activation of STAT3 signalling. Cytokine array and mass spectrometry identified potential STAT3 activating ligands independent of JAK kinase including POSTN, CD24, and CD44. In-vitro treatment of cell lines exposed to ascites demonstrated exquisite sensitivity to STAT3 inhibitors, suggesting a phenomenon of paracrine derived oncogenic addiction. Consistent with this data, intraperitoneal instillation of STAT3 inhibitors in a unique mouse model of paracrine driven PC demonstrated gross decrease in the modified peritoneal carcinomatosis index ($p<0.05$). Conclusion We have demonstrated that ascites present in CPC drives paracrine signalling via the STAT3-EMT pathway. Integrative analysis suggests non-canonical activation of STAT3 via soluble ligands, creating a phenomenon of oncogenic addiction to STAT3 signalling independent of signalling cross-talks. Intra-peritoneal instillation of STAT3 inhibitors provides a novel therapeutic strategy in the clinical setting.

P188

The Impact of Adjuvant Immunotherapy Following Resection of Stage III Colon Cancer

T. Tran,[1]* A. Maker.[2] *1. University of Illinois at Chicago-MGH, Chicago, IL; 2. University of Illinois at Chicago, Chicago, IL.*

Background:Surgery remains the mainstay of treatment for colon cancer(CRC) of all stages. Adjuvant chemotherapy (CTx) has been recommended to improve survival compared to observation alone in Stage III CRC. However, the potential oncologic impact of IT in patients with stage III CRC remains unknown. Method:Patients undergoing resection for Stage III CRC from 2004 -2015 were identified using the National Cancer Database. Cox proportional hazard models were utilized to determine predictors of overall survival(OS). Patients were stratified into type of therapy and microsatellite status(MSI). Propensity score weighted analysis was performed through one-to-one matching based on the nearest neighbor method. Results:Of 207,591 patients who underwent resection for Stage III CRC,133,038 (64%) received adjuvant CTx. Multidrug CTx was received by 25,459(19%) patients and 1478(1%) were treated with CTx+IT. Receipt of CTx, with or without IT, was associated with improved OS. N2 and positive margins were associatd with poor OS regardless of treatment strategy on multivariate analysis. Propensity score analysis matched patient and tumor characteristics of 1417 patients treated with IT to 1529 patients not treated with IT. The majority of patients had tumors that were >4cm and staged T3-T4. There were no differences in KRAS mutation or MSI status. The 5-yr OS was higher among those treated with multi-drug CTx alone compared to CTx+IT, single drug CTx+IT, or none (52%,44%, 46%, 33%, respectively, $P<0.001$). Subgroup analyses demonstrated no differences in 5-yr OS with or without IT based on Nstage(N1: 59vs.56%, P=0.27; N2: 37vs. 36%, P=0.12), or Tstage(T3: 47vs.47%, P=0.439;T4: 29.2%vs.29.5%, P=0.23). Among those who received IT, there were no differences in OS based on MSI status. Conclusion:Modern-era multidrug chemotherapy was associated with improved survival after resection of stage III colon cancer, however, the addition of adjuvant immunotherapy was not associated with improved outcomes regardless of tumor MSI status. Future research on immunotherapies stratified by MSI status is warranted to identify effective treatment strategies to improve outcomes of Stage III colon cancer over chemotherapy alone.



P189

Symptom Burden at the End of Life for Neuroendocrine Tumors: A Population-Based Analysis of Patient-Reported Outcomes

J. Hallet,[1]* L. Davis,[1] A. Mahar,[2] C. Law,[1] E. Isenberg-Grzeda,[1] L. Bubis,[1] S. Singh,[1] S. Myrehaug,[1] H. Zhao,[3] K. Beyfuss,[1] L. Moody,[1] N. Coburn.[1] *1. Surgery, University of Toronto, Toronto, ON, Canada; 2. University of Manitoba, Winnipeg, MB, Canada; 3. Institute of Clinical Evaluative Sciences, Toronto, ON, Canada.*

Introduction: How to best support neuroendocrine tumor (NET) patients remains unclear. While the peri-diagnostic period has been investigated, there is no data regarding symptoms at the end of life, when suboptimal symptom control may be particularly burdensome. This study examined symptom trajectories and factors associated with high symptom burden in NET at the end of life. Methods: We conducted a population-based retrospective cohort study of NET diagnosed from 2004-2015, who died between 2007-2016. Prospectively collected patient-reported Edmonton Symptom Assessment System scores were linked to provincial administrative datasets. Moderate-to-severe symptom scores in the 6 months prior to death were presented by 2-week intervals. Multivariable Poisson regression identified factors associated with moderate-to-severe symptoms scores. Results: Among 677 decedents, 2,579 symptom assessments prior to death were analyzed. Overall, moderate-to-severe scores were most commonly reported for tiredness (86%), wellbeing (81%), lack of appetite (75%), and drowsiness (68%) at any time. This proportion changed over time, progressively increasing closer to death: 56.8% to 83.9% tiredness, 50.5% to 73.1% wellbeing, 40.9% to 80.6% lack of appetite, and 41.5% to 68.8% drowsiness. The increase was steeper in the 8 weeks before death for lack of appetite, drowsiness, and shortness of breath. On multivariate analyses, the risk of moderate-to-severe symptoms was significantly higher in the last 2 months prior to death and with shorter survival from diagnosis (<6 months). Women reported a higher burden of anxiety, nausea, and pain, compared to men. There was no association between symptom burden and age or primary tumor site. Conclusion: NET patients suffer a high symptom burden at the end of life, not previously described. The proportion of moderate-to-severe symptoms increases steeply as death nears, highlighting an opportunity for improved management. Combined with identified factors associated with moderate-to-severe symptom, this information is important to improve patient-centred and personalized supportive care for NET at the end of life.

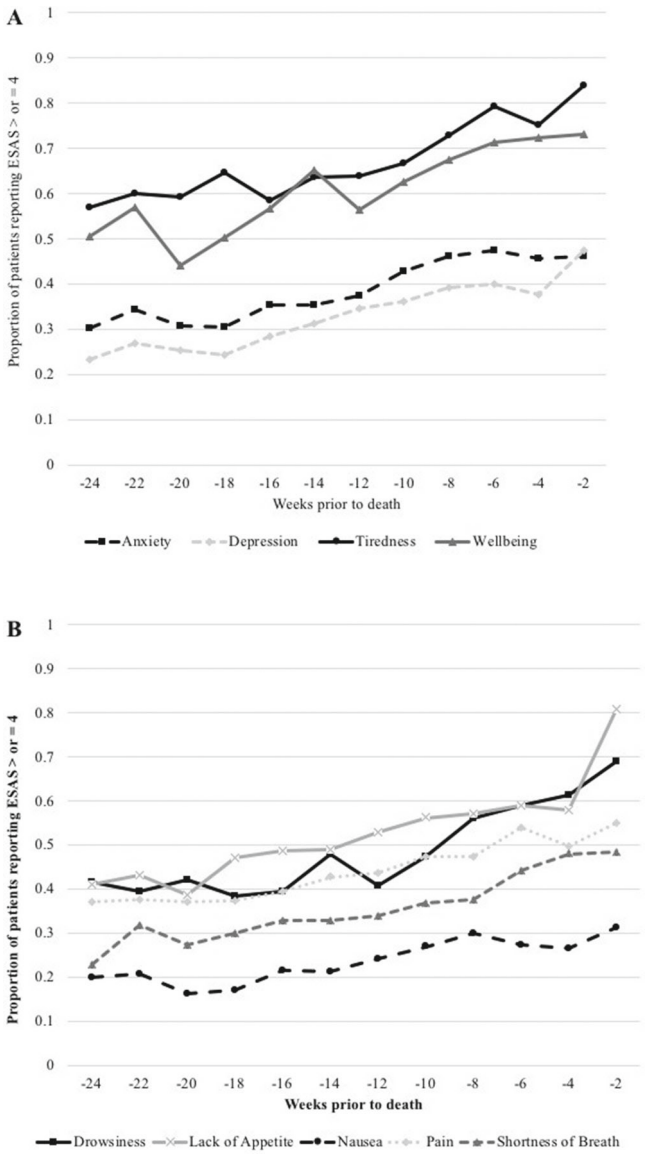


Figure 3. Proportion of patients with NETs reporting at least one moderate-to-severe (>=4) ESAS score in the last 6 months of life, for each symptom (anxiety, depression, tiredness, and overall wellbeing – A, and drowsiness, lack of appetite, nausea, pain, and shortness of breath – B).

P190

The Prognostic Significance of the Lymph Node Ratio in Gastric Neuroendocrine Tumors T. Yeager,[1]* K.N. Partain,[1] J. Gunn,[1] T. Almerey,[1] R. Lemini,[1] W. Ji,[2] K. Attwood,[2] S.P. Bagaria,[1] E.M. Gabriel.[1] *1. General Surgery, Mayo Clinic, Jacksonville, FL; 2. Roswell Park, Buffalo, NY.*

INTRODUCTION: The significance of lymph node ratio in gastric neuroendocrine tumors (GNETs) has yet to be evaluated. Prior studies have found that a lymph node ratio possesses a strong prognostic value in pancreatic and small bowel neuroendocrine tumors. Currently, nodal staging for GNETs is either absence or presence of nodal disease, N0 or N1, respectively. We hypothesized that the lymph node ratio (LNR) can provide further information regarding a patient's prognosis. METHODS: Patients with gastric neuroendocrine tumors who underwent formal resection were queried from the National Cancer Data Base (2004-2013). Associations with the short-term outcomes were evaluated using the Mann-Whitney U test. The association between LNR and survival was evaluated using a Cox regression model, from which the hazard ratio and corresponding 95% confidence interval was obtained. RESULTS: From 2004-2013, a total of 200 patients underwent radical resection with nodal dissection for a gastric neuroendocrine tumor. Grade was variable with 76 (42.2%) well differentiated, 26 (14.4%), and 78 (42.4%) poorly or undifferentiated tumors. Median follow-up was 32 months. The average number of lymph nodes examined and lymph nodes positive was 13.85 and 3.73, respectively. The average positive LNR was 0.35. When examining lymph node ratio, there was a significant association with overall survival (p=0.032), suggesting worse outcome with increasing LNR. The LNR compared with overall survival revealed a hazard ratio of 2.44 (95% CI: 1.08-5.50). There were no significant associations between LNR and short-term outcomes (30-day and 90-day mortality). CONCLUSIONS: LNR has a significant association with overall survival for patients with GNETs. A consideration could be made to include lymph node ratio in nodal staging criteria, potentially providing additional prognostic information.

P191

In Search of Parathyroid Adenomas: The Utility of Four-Dimensional Computed Tomography in the Absence of Ultrasound Localization T. Yeager,* L. Okromelidze, E.M. Gabriel, V. Gupta, J.D. Casler. *General Surgery, Mayo Clinic, Jacksonville, FL.*

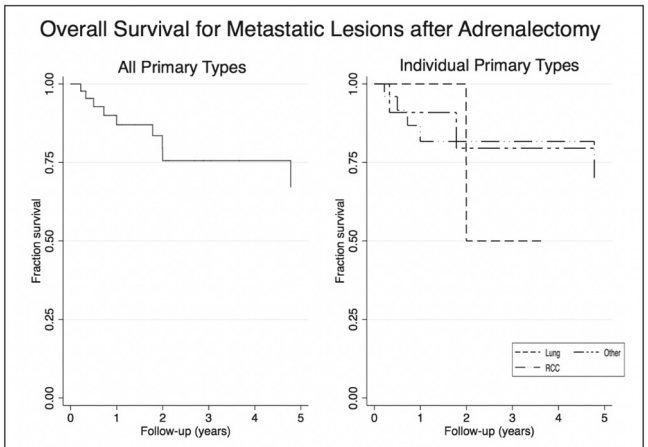
Four-dimensional computed tomography (4D CT) has been shown to be very sensitive in pre-operative localization of parathyroid adenomas. Controversy exists regarding its role as a first line modality or whether it should be utilized in the absence of anatomical findings on ultrasound. The goal of our study was to determine the sensitivity of 4D CT in the presence of a negative ultrasound and to identify patient characteristics that are prominent in this group. METHODS: Patients undergoing parathyroidectomy from 2003 to 2018 for parathyroid adenoma carried out at a tertiary care center were analyzed. All of the patients received a non-localizing sestamibi and ultrasound scan, and proceeded to 4D CT scan for localization. The pre-operative localization rate and sensitivity of the 4D CT scan were calculated. RESULTS: A total of 59 patients received non-localizing ultrasound and sestamibi scans and went on to receive a 4D CT scan. The sensitivity of the 4D CT was 79.25% (CI 95% 65.89-89.16%) in identifying the adenoma. The accuracy was 71.19% (CI 95% 57.92-82.24%). Pre-operative PTH was measured to be 133.6. The average patient BMI in this group was 31.1. In addition, 39% of the patients had received prior neck surgery, and 15.3% of the adenomas were found in the mediastinum. The average number of surgical specimens removed during the operation was 1.55, suggesting that there was still some difficulty intraoperatively in identifying the adenoma. CONCLUSIONS: 4D CT is a reliable modality even in the presence of non-localizing ultrasound and sestamibi images. In the presence of elevated BMI or prior neck surgery, 4D CT can be considered as a first line modality. Lastly, 4D CT is an excellent method of detecting mediastinal adenomas.

P192

Long-term Outcomes After Adrenalectomy for Solid Tumor Metastases: A Single-Center Perspective M. Bryant,[1]* S. Laks,[2] P. Strassle,[1] C. Gaber,[1] L. Kim.[1] *1. University of North Carolina at Chapel Hill, Raleigh, NC; 2. East Carolina University, Greenville, NC.*

Introduction: Adrenalectomy is often considered as part of the treatment strategy for malignancies that are metastatic to the adrenal glands. The benefit of adrenalectomy in this setting is uncertain. Small case series and retrospective reviews have shown conflicting all-cause mortality data. The aim of this study is to assess the risk of all-cause mortality and cancer recurrence after surgical excision of adrenal metastases. Methods: A single-center retrospective observational study of 50 patients with metastatic disease to the adrenal glands that underwent adrenalectomy. Descriptive statistics were calculated for categorical and continuous variables. Metastases were denoted as synchronous (<6 months) or metachronous (≥6 months) reflective of the interval since primary diagnosis. Non-parametric Kaplan-Meier estimators were used to calculate survival and distant-recurrence-free-survival over 5 years. These estimates were made for the whole cohort and stratified by site (lung cancer and renal cell carcinoma, and other). Results: Patients undergoing adrenalectomy for non-adrenal primary malignancies were a median age of 61 (IQR 55-71) and more likely to be white (80%) males (78%) with history of tobacco use (76%). Renal cell carcinoma (RCC) represented the primary tumor for over half (56%) of the cohort with the remaining tumors compromised of lung (18%), colorectal (6%), melanoma (4%), liver (2%), and other (14%).

Twenty-seven adrenal metastases were synchronous and twenty-three metachronous. Thirty-seven patients had isolated disease to the adrenal glands at the time of surgery. Patients were followed for a median of 21.4 months (range 9 - 2996 days). For patients followed 5 years, the overall survival was 67% (95% CI 0.42,0.83) and the distant recurrence-free survival was 0.33 (95% CI 0.16, 0.51). When stratified by site of primary, sites other than RCC and lung had higher probabilities of overall survival at 5 years [0.80 vs 0.70 (RCC) vs 0.50 (Lung)]. Conclusion: Regardless of primary site, surgical treatment for adrenal metastases should be considered on an individual basis given favorable durable overall and recurrence-free survival



Overall survival, probability (95% CI), n at year	1 year	3 years	5 years
All primary sites, n=50	0.87 (0.71, 0.94), n=33	0.76 (0.56, 0.87), n=16	0.67 (0.42, 0.83), n=11
Lung, n=9	1.00, n=5	0.50 (0.58, 0.84), n=3	0.50 (0.58, 0.84), n=2
RCC, n=28	0.82 (0.58, 0.93), n=17	0.82 (0.58, 0.93), n=8	0.70 (0.37, 0.88), n=7
Other, n=14	0.91 (0.51, 0.99), n=10	0.80 (0.39, 0.95), n=5	0.80 (0.39, 0.95) n=2

Figure 1. Kaplan Meier survival analysis showing overall survival for all primary sites and individually for lung, RCC, and other sites. Patients at risk are tabulated below the figures along with overall survival at time points 1, 3, and 5 years. Abbreviations: OS = overall survival, RCC = renal cell carcinoma.

P193

Interaction of Race and Pathology for Neuroendocrine Tumors: Epidemiology, Natural History, or Racial Disparity? D.K. DePalo,[1]* R.M. Lee,[1] A.G. Lopez-Aguiar,[1] M.Y. Zaidi,[1] F. Rocha,[2] Z. Kanji,[2] G. Poultsides,[3] E. Makris,[3] M. Dillhoff,[4] E.W. Beal,[4] R. Fields,[5] R.Z. Panni,[5] K. Idrees,[6] P. Marincola Smith,[6] H. Nathan,[7] M. Beems,[7] D. Abbott,[8] V. Rendell,[8] S. Maithel,[1] M.C. Russell.[1] *1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Virginia Mason Hospital and Medical Center, Seattle, WA; 3. Stanford University School of Medicine, Stanford, CA; 4. Ohio State University Comprehensive Cancer Center, Columbus, OH; 5. Washington University School of Medicine in St. Louis, St. Louis, MO; 6. Vanderbilt University Medical Center, Nashville, TN; 7. University of Michigan, Ann Arbor, MI; 8. University of Wisconsin Carbone Cancer Center, Madison, WI.*

BACKGROUND: The prognostic value of pathologic variables is not consistent for gastroenteropancreatic neuroendocrine tumors(GEP-NETs). We previously demonstrated a limited prognostic role of lymph node(LN) positivity in small bowel NETs(SBNET) compared to pancreatic NETs(panNET). Although minority race is often associated with worse cancer outcomes, the interaction of race with pathologic and oncologic outcomes of pts with GEP-NETs is not known. METHODS: Pts with GEP-NETs who underwent curative intent resection at 8 institutions of the US NET Study Group from 2000-16 were included. Given few pts of other races, only Black(Blk) and White(Wht) race pts were analyzed. RESULTS: Of 2182 pts, 1143 met inclusion criteria. Median age was 58yrs, median f/u was 3yrs, 48% were male, 14%(n=157) were Blk, and 86%(n=986) were Wht. Blk pts were more likely uninsured(7vs2%,p=0.005), had symptomatic bleeding(13vs7%,p=0.006), required emergency surgery(7vs3%, p=0.003), and had LN positive disease(47vs36%,p=0.016). Despite this, Blk pts had improved 5yr recurrence free survival (RFS) compared to Wht pts(90vs80%,p=0.008). The quality of care received was comparable between both groups, demonstrated by similar LN yield at surgery, neg margin resection rate, post-op complications, and need for reoperation or readmission(all p>0.05). Blk pts were more likely to have SBNET(22vs13%) and less likely to have panNET(43vs68%) compared to Wht pts(p<0.001). Consistent with prior data, pts with LN pos panNET had decreased 5yr RFS(67vs83%,p=0.001); however, for SBNET, LN involvement was not prognostic(77vs96%,p=0.08). The prognostic value of LN pos disease was similar between Blk and Wht pts in both SBNET(p=0.34) and panNET(p=0.95). CONCLUSIONS: Blk pts with GEP-NET present with more advanced disease, including higher LN positivity. Despite this, Blk pts have improved RFS compared to Wht pts. Although there may be delays in seeking or reaching care, Blk pts received similar quality of care compared to Wht pts. The improved RFS seen in Blk pts may be attributed to the epidemiologic differences in the site of presentation of GEP-NETs and variable prognostic value of LN pos disease.

P194

Surgical Considerations of Genomic Profiling of Nodular Thyroid Disease and Thyroid Cancer L. Avila,[1]* E. Benedetti,[2] A. Breslin,[2] E. Chung,[2] D. Weingrad,[1] A. Duran,[1] S. Gulec.[2] *1. Aventura Hospital and Medical Center, Miami, FL; 2. Florida International University Herbert Wertheim College of Medicine, Miami, FL.*

The current management decisions for thyroid nodules are based on ultrasound features and cytology. Genomic profiling has a known application in the work up of indeterminate thyroid nodules. Our study aims to evaluate the value of genomic profiling for all thyroid nodules, regardless of cytology. We also acknowledge the surgical implications that arise due to genomic profiling. Miami Thyroid Oncology Consortium instituted a prospective registry for patients with thyroid nodular disease. During the period between January 1, 2017 and December 31, 2017, the registry collected complete data on 202 patients with 227 thyroid nodules. There were 162 nodules (71.3%) with benign cytology, and ThyroSeq was positive in 27 (16.6%). There were 40 nodules (17.6%) with AUS or FLUS cytology, and 20 nodules in this group had positive ThyroSeq results (50%). There was 1 nodule with Bethesda 4 cytology and it had positive ThyroSeq results. There were 8 nodules with malignant cytology (3.5%), and 7 of these had positive ThyroSeq (87.5%). There were 7 nodules (3.1%) with BRAF mutations, and there were 25 nodules (11.0%) with RAS mutations. The subsequent surgical pathology results from BRAF and RAS nodules were consistent with known pathologies associated with these mutations. While already established as a clear step in the work up of indeterminate nodules, our study suggests that genomic profiling likely has a broader role in the treatment of thyroid nodular disease. For example, several cases of thyroid cancer were discovered through positive gene mutations in nodules with benign cytology. We also identified the BRAFV600E-like and RAS-like subtypes of thyroid cancer, which have an impact on surgical management.

P195

Racial Disparities in Primary Hyperparathyroidism J.H. Fieber,* R.R. Kelz, J.P. Ermer, C. Wirtalla, D. Fraker, H. Wachtel. *General Surgery, University of Pennsylvania, Philadelphia, PA.*

Background: The impact of racial disparities in surgery is being increasingly recognized. We evaluated the impact of race on the care of patients undergoing parathyroidectomy for primary hyperparathyroidism (PHPT). Methods: We performed a retrospective cohort study of patients undergoing initial parathyroidectomy for PHPT at our institution from 1997-2015. Patients were classified as White or non-White (Black, Asian, Hispanic, Other) based on self-identified race. Patients with unknown race were excluded. The primary outcome was severity of disease at surgical evaluation defined by biochemical testing and symptomatology. Our secondary outcome was completeness of diagnostic evaluation prior to surgical referral. Operative outcomes were also evaluated. Results: A total of 2,709 patients were included, with a mean age of 58.6 years (SD: 13.0); 77.5% were female. Almost 80% of patients were White, 11.2% Black, 1.1% Asian, 0.6% Hispanic, and 7.7% Mixed-race or

Other. Non-White patients were overall sicker by Elixhauser score (1.1 vs. 0.6, p<0.001) than White patients. Non-White patients had significantly higher preoperative calcium (11.0 vs 10.8 mg/dl, p<0.001) and PTH levels (110 vs. 96 pg/ml, p<0.001) than White patients although there was no significant difference in preoperative signs or symptoms (Table 1). Non-White patients had lower rates of complete preoperative evaluation with DXA scan (65.2 vs. 73.5%, p<0.001) and Sestamibi and ultrasound (61.6 vs. 72.9%, p<0.001) prior to surgical consultation (Table 1) than White patients. Operatively, non-White patients had larger glands by both size (1.6 (IQI: 1.2, 2.0) vs. 1.5 cm (IQI: 1.1, 1.9), p<0.001) and mass (518 vs. 358 mg, p<0.001) than White patients. Non-White patients had a similar operative success (98.1 vs. 96.9%, p=0.150) and long-term cure rates (96.5 vs. 96.4%, p=0.953) compared with White patients. Conclusions: At the time of surgical referral, non-White patients with PHPT have more advanced disease and higher rates of incomplete evaluation compared to White patients. Despite larger abnormal parathyroid glands, surgical cure rates are comparable between groups. Further research is needed to understand racial disparities in patients with PHPT.

Table 1: Group comparisons of preoperative characteristics, by race

	Non-White	White	p-value
n (%)	558 (20.6)	2151 (79.4)	
Demographics:			
Age, mean (sd)	57.7 (12.9)	58.8 (13.0)	0.068
Female gender, n (%)	444 (79.6)	1655 (76.9)	0.185
Elixhauser score, mean (sd)	1.1 (2.0)	0.6 (1.2)	**< 0.001**
Family history of PHPT, n (%)	7 (1.3)	38 (1.9)	0.368
Multiple endocrine neoplasia, n (%)	6 (1.1)	28 (1.3)	0.669
Primary payer, n (%)			0.103
Medicare	111 (19.9)	510 (23.7)	
Commercial	440 (78.9)	1624 (75.5)	
Other	7 (1.3)	17(0.8)	
Signs & Symptoms:			
Nephrolithiasis, n (%)	97 (17.7)	453 (21.4)	0.059
Bone mineral density loss, n (%)	260 (71.4)	1181 (74.7)	0.192
Systemic symptoms, n (%)	373 (67.6)	1464 (69.2)	0.466
Preoperative Labs:			
Serum calcium (mg/dl), mean (sd)	11.0 (0.8)	10.8 (0.7)	**<0.001**
Preoperative urinary calcium (24 hr), median (iqi)	282 (176; 403)	292 (191; 412)	0.359
Intact PTH (pmol/ml), median (iqi)	110 (82; 158)	96 (72; 130)	**<0.001**
Serum creatinine, median (iqi)	0.9 (0.7; 1.1)	0.8 (0.7; 1.0)	**<0.004**
GFR, mean (sd)*	83.1 (30.5)	76.6 (20.3)	**<0.001**
Preoperative Evaluation:			
24-hour urinary calcium, n (%)	285 (51.1)	1066 (49.6)	0.523
DXA scan, n (%)	364 (65.2)	1580 (73.5)	**<0.001**
Sestamibi only, n (%)	135 (24.2)	366 (17.0)	**<0.001**
Ultrasound only, n (%)	29 (5.2)	54 (2.5)	**0.001**
Sestamibi & ultrasound, n (%)	344 (61.6)	1569 (72.9)	**< 0.001**

SD – Standard deviation; IQI – Interquartile interval; GFR – Glomerular filtration rate calculated by MDRD equation

P196

Evaluation and Clinical Relevance of Dutch and ATA Guidelines in the Treatment of Patients with Differentiated Thyroid Cancer

J.Th.M. Plukker,* A.H. Groen, D. van Dijk, T. van Veen, T. Links.
Universitair Medisch Centrum Groningen, Groningen, Netherlands.

Introduction Guidelines for differentiated thyroid cancer (DTC) in the Netherlands were presented in 2007 (NL-07) and revised in 2015 (NL-15). There is a great discussion regarding treatment intensity and the biological aggressiveness of these tumors. It is still hard to perform prospective studies regarding different treatment approaches in DTC. Retrospactively we analyzed current treatment options and evaluated the Dutch (NL-07 and NL-15) guidelines compared with the ATA-15. Patients and methods Patients diagnosed between January 2007 and March 2017, were included from a preexisting UMCG thyroid-database. For each patient the risk classification was scored according to guidelines (ATA-15, NL-15 and NL-07) in under-treatment, over-treatment and probably adequate treatment. Patients in group A and B scored as low risk or as high risk by all three guidelines, respectively. Patients in group C had rather differences in risk classifications. McNemar test was used to compare the degree of under- and over-treatment according to both Dutch guidelines and the ATA-15. Results If NL-15 was compared with ATA-15 in the whole study population, we found significantly more under-treatment in ATA-15 and more over-treatment in NL-15, but also more adequate treatment in NL-15. When NL-07 was compared with ATA-15 results were basically the same as comparying NL-15 with ATA-15, although the degree of under- and over-treatment were slightly more apart. Most of differences in treatment were observed in patients among group C. No differences were found in group B. Group A had more over-treatment in NL-15 and NL-07 with more adequate treatment in ATA-15. Conclusion Comparing ATA-15 with current Dutch guidelines, patients with DTC were presumably treated too aggressive. Especially in the congruent low-risk group the less aggressive approach of ATA-15 seemed to be more adequate. However, DTC patients in the incongruent group C were more often undertreated when using the ATA-15 compared to treatment according to the NL-15 guidelines. These results support the ongoing current discussion about the de-escalation of treatment in patients with DTC in the Netherlands.

P197

What Factors Predict Parathyroid Autograft Use in Thyroid Cancer? A Multi-Institutional Analysis Utilizing NSQIP

J.Y. Liu,* N.D. Saunders, C. Weber, J. Sharma, S.G. Patel. *Emory University, Atlanta, GA.*

Background: The role of parathyroid autograft (PA) in thyroid surgery for malignancy remains unclear. Using multi-institutional, thyroidectomy specific data, our aim was to describe PA and determine predictors of its use. Methods: Patients undergoing partial and total thyroidectomy for malignancy between 2013-2016 in ACS NSQIP were included in this cohort study. A multivariable logistic regression model with adjustment for hospital clustering and patient characteristics was constructed to identify patient factors associated with PA. Results: There were 5,719 patients analyzed from 110 institutions, of which 3755 (74.64%) underwent total or subtotal thyroidectomy and PA occurred in 644 (11.26%). On multivariable analysis, central neck dissection (OR 1.40; 95% CI 1.07-1.84; p=0.02), total thyroidectomy (OR 4.19; 95% CI 2.51-6.97; p<0.01), higher number of lymph nodes removed (OR 1.87; 95% CI 1.42-2.47; p<0.01), and indication of differentiated malignancy (OR 1.86; 95% CI 1.18-2.94; p<0.01) were associated with increased use of PA. Compared to all patients, PA had their postoperative calcium and parathyroid hormone measured more frequently and received more oral calcium supplementation (Table 1). Conclusions: PA is used more frequently in patients undergoing central neck dissection, total thyroidectomy, higher number of lymph nodes removal, and in patients undergoing thyroidectomy for differentiated malignancy. Further research is necessary to determine the role of PA in reducing the incidence of hypocalcemia in patients undergoing thyroidectomy for malignancy.

Postoperative measurement of calcium, parathyroid hormone, and supplementation of calcium/Vitamin D of PA vs all patients.

	Parathyroid Autograft; (%)	All Patients; (%)
Postop Calcium Measured	89.12%	73.74%
Postop Parathyroid Hormone Measured	60.32%	38.67%
Postop Vitamin D and/or Calcium Supplementation	81.86%	61.46%

P198

The Incidence and Outcomes of Carcinoid Heart Disease

R. Macfie,* J. Lim, E. Dewey, S.J. Pommier, H.K. Song, R.F. Pommier.
Oregon Health & Science University, Portland, OR.

Introduction: Carcinoid heart disease (CHD) is a well described sequela of carcinoid tumor however the natural history of CHD is poorly understood. As the treatment of carcinoid tumor is primarily surgical it is essential to understand the preoperative risks, including CHD. We reviewed a large cohort of carcinoid patients to establish the incidence and risk factors associated with development of CHD. Methods: We reviewed all patients treated for carcinoid tumor at our institution from 2001-2018. CHD was defined as thickening of the tricuspid and/or pulmonic valves or isolated moderate to severe regurgitation of these valves on echocardiography. Results: We reviewed 430 patient records. Demographic and oncologic characteristics are found in Table I. An echocardiogram was documented in 55% of all patients, and in 65% of those with liver metastases (165/255). Of patients with an echocardiogram, 17% (and 10% of all patients) had CHD (n=41). Patients who developed CHD were significantly more likely to have liver metastases than those who did not (87.8% vs 65.5% p=0.01). However, there was no significant difference in whether patients had undergone liver debulking, in extent of debulking, or in dose of outpatient long-acting octreotide therapy between groups. Patients who developed CHD had significantly higher mean peak plasma Chromogranin A (CgA) (666 ng/mL vs 164 ng/mL; p=0.0001) and peak urinary 5-HIAA (76mg/d vs 9.2mg/d; p=0.0001). Patients with peak 5-HIAA >5 mg/d or peak CgA >92 ng/mL were significantly more likely to develop CHD (5-HIAA OR 4.2 p=0.03; CgA OR

4.8 p=0.01). Nine patients (2.0%) underwent valve replacement for CHD; the majority (55%) for optimization prior to carcinoid tumor operation. The five-year survival was significantly lower for patients with CHD (63.4% v 85.6% p=0.002). Conclusions: This the largest study of carcinoid heart disease to date. Previous authors suggest that 20-37% of patients with metastatic carcinoid tumor develop CHD. We demonstrate that proportion may be smaller, with even fewer patients undergoing valve replacement surgery for CHD. There is a clear correlation between elevated biomarker levels and the development of CHD which may assist in preoperative risk stratification.

Demographic and Oncologic Characteristics for Study Sample

Characteristic	All Participants (N=430)		No CHD on Echocardiogram (N=197)		With CHD on Echocardiogram (N=41)		p-value
With Documented Echocardiogram	238	(55%)	--	--	--	--	--
Mean Age (years) at Diagnosis of Primary Carcinoid (95% CI)	59.5	(58.2, 60.7)	59.7	(58, 61.3)	62.1	(58.6, 65.6)	0.22 [t]
Mean Age (years) at Diagnosis of Metastatic Disease (95% CI)	61.4	(60, 62.8)	62.1	(60.4, 63.8)	63	(59.2, 66.8)	0.64 [t]
Peak CgA (ng/mL)	195.5	(82, 809.5)	164	(77, 616.3)	666	(222, 2916.8)	0.0003 [w]
Peak 5-HIAA (mg/d)	13	(5, 67.9)	9.2	(4.2, 37.2)	76	(16.9, 219.7)	<0.0001 [w]
Gender (Female)	194	(45.1%)	83	(42.1%)	18	(43.9%)	0.97
Primary Tumor Location:							
Small Bowel	195	(45.3%)	103	(52.3%)	17	(41.5%)	--
Terminal Ileum	87	(20.2%)	36	(18.3%)	12	(29.3%)	--
Lung	51	(11.9%)	25	(12.7%)	3	(7.3%)	--
Occult	42	(9.8%)	13	(6.6%)	6	(14.6%)	--
Rectum	14	(3.3%)	6	(3.1%)	2	(4.9%)	--
Appendix	13	(3.0%)	5	(2.5%)	0	(0%)	--
Stomach	10	(2.3%)	2	(1.0%)	0	(0%)	--
Other	3	(0.7%)	2	(1.0%)	1	(2.4%)	--
Primary Tumor Resected	355	(82.6%)	173	(87.8%)	34	(82.9%)	0.22
Documented Liver Metastases	255	(59.3%)	129	(65.5%)	36	(87.8%)	0.01
Patient Has Undergone Liver Debulking	141	(32.8%)	81	(41.1%)	15	(36.6%)	0.15
Non-Surgical Treatment for Metastases:							
None	298	(69.0%)	137	(69.5%)	27	(65.9%)	0.39
Everolimus	42	(9.7%)	24	(12.2%)	6	(14.6%)	0.80 [f]
Y-90	57	(13.2%)	30	(15.2%)	8	(19.5%)	0.64 [f]
Carboplatin/Cisplatin	27	(6.3%)	7	(3.5%)	1	(2.4%)	0.55 [f]
Etoposide	19	(4.4%)	6	(3.1%)	0	(0%)	0.59 [f]
Capcitabine	11	(2.6%)	6	(3.1%)	2	(4.8%)	0.64 [f]
Chemoembolization	20	(4.6%)	7	(3.6%)	4	(9.8%)	0.11 [f]
Tenzolamide	8	(1.9%)	4	(2.0%)	1	(2.4%)	1 [f]
Radiation Therapy	11	(2.6%)	2	(1.0%)	1	(2.4%)	0.45 [f]
Five-Year Survival	348	(80.9%)	166	(85.6%)	26	(63.4%)	0.002

Data reported as median (IQR) or N (%) unless otherwise noted.
t: t-test; w: Wilcoxon Rank-sum test; f:Fisher's Exact test; Not marked: Chi-Square test
CgA: Plasma Chromogranin A Level; 5-HIAA:Urinary 5-HIAA Level

P199

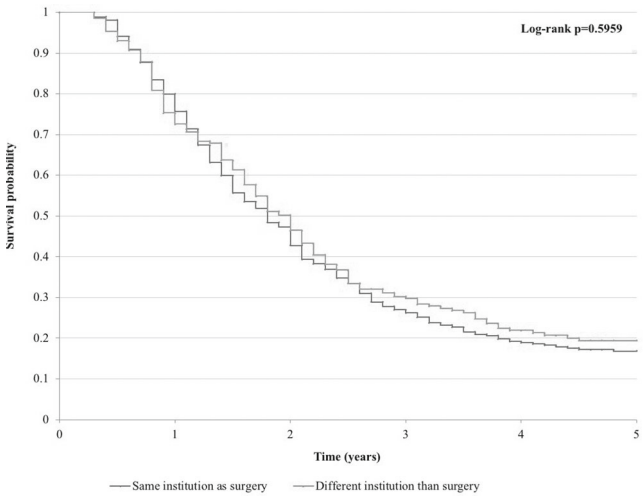
Is the Use of Intraoperative Frozen Section During Pancreaticoduodenectomy Justified? R. Zheng,[1]* C.J. Yeo,[1] H. Lavu,[1] J. Winter.[2] *1. Surgery, Thomas Jefferson University Hospital, Philadelphia, PA; 2. University Hospitals Cleveland Medical Center, Cleveland, OH.*

Introduction: Intraoperative frozen section (IFS) is routinely utilized by some surgeons during pancreaticoduodenectomy. However, benefits have not been rigorously studied. Methods: Data were extracted from an institutional surgical database at Thomas Jefferson University Hospital. All patients underwent pancreaticoduodenectomy between 2006-15. Descriptive performance metrics of frozen sections with respect to final histology and resection margin status are reported. Categorical variables were evaluated using Chi-square analysis or univariate logistic regression. Results: The cohort included 1,076 patients, where 78.8% of the specimens were malignant. Pancreatic ductal adenocarcinoma (n=518, 48.1% of total) was the most common diagnosis. Preliminary IFS and final pathologic review were discrepant for histologic diagnosis and margin status in only 5.3% and 3.3% of all cases, respectively. The sensitivity, specificity, accuracy, and negative and positive predictive value of IFS with regards to malignancy were 97.2%, 95.3%, 96.7%, 90.6%, and 98.7%, respectively. A positive neck margin was the most common indication for a change in surgical management, with 64.1% of positive neck margins (7.8% of total) resulting in further resection. Bile duct and duodenal margins were positive among 3.8% and 0.2% of all cases. A positive uncinate margin impacted the decision to forego revision of a second positive margin in 5.8% of all positive margins (1.7% of total). Factors that increased the likelihood of modifying operative strategy included positive resection margins (OR 31.4 [18.8-100.5]) and ductal adenocarcinoma (OR 2.9 [1.9-4.4]). Further resection was rare in the presence of neuroendocrine tumor (PNET) (n=2, 3.8% of all PNET) or chronic pancreatitis (n=0). Conversion from partial to total pancreatectomy was performed in 15 cases (1.4% of total). Discussion: IFS is highly accurate but major operative changes resulting from IFS results are rare. Selective omission of frozen sections may be supported in those with a very high pre-test probability of benign disease. Conversely, surgeons should be cautious to dismiss benign pathology on IFS when clinical suspicion for malignancy remains high.

P200

Does Fragmentation of Care Impact Long-term Cancer Outcomes? A 10-Year Population-based Analysis of Adjuvant Therapy Decentralization for Pancreatic Adenocarcinoma N. Latchana,[1]* L. Davis,[1] N. Coburn,[1] A. Mahar,[2] Y. Liu,[1] A. Mohammad,[1] D. Kagedan,[1] C. Earle,[1] J. Hallet.[1] *1. Surgery, University of Toronto, Toronto, ON, Canada; 2. University of Manitoba, Winnipeg, MB, Canada.*

Introduction: With regionalization of cancer surgery, treatments are often fragmented across different institutions. Patients and providers have voiced concerns regarding potential associated outcomes disparities. We examined the impact of adjuvant chemotherapy (AC) decentralization (receipt at a different institution than where surgery is performed) on survival for pancreatic adenocarcinoma (PA). Methods: We conducted a provincial population-based study of patients receiving AC after PA resection performed at ten designated hepato-pancreato-biliary centres over 2004-2014. Groups were based on whether AC was administered at the same (SI) or different institution than surgery (DI). Primary outcome was overall survival (OS) examined using Kaplan-Meier methods and log-rank test. Multivariable Cox regression assessed the association between OS and AC group while accounting for potential confounders. Results: Among 589 patients, no difference was observed in baseline characteristics between groups. Median time from surgery to AC did not differ, with 70 days (IQR 58-85) for SI and 69 days (IQR 57-84) for DI (p=0.51). Patients received the same median number of AC cycles. Median OS was 21.3 months (IQR 12.8-37.5) for SI compared to 23.5 months (IQR 11.5-40.4) for DI (p 0.66). Actuarial 5-year OS of 16.8% (95%CI 13.2-20.9%) for SI and 19.3% (95%CI 14.2-25.1) for DI did not differ (log-rank p 0.44). When adjusting for age group, sex, comorbidity burden, socio-economic status, rural living, stage, positive margin, and year of surgery, the AC institution was not associated with OS (hazard ratio - HR 1.04, 95%CI 0.86-1.26). For patients undergoing AC at DI, mean travel distance was longer to access the surgery institution (106.7 km Vs. 30.9 km, p<0.001). Conclusion: Receiving AC at a different institution than surgery did not impact OS for PA. Partnerships between specialized surgical centres and community institutions for delivery of AC are safe and effective. It contributes to patient-centred care by reducing travels to access care.



Overall survival stratified by location of receipt of adjuvant chemotherapy.

P201

DPD and hENT1 are Not Predictive in Patients with Resected Pancreatic Cancer Treated with Adjuvant S-1 or Gemcitabine Chemotherapy: Collaborative Study of the JASPAC 01 Trial

Y. Okamura,[1]* S. Yasukawa,[2] K. Mori,[1] N. Boku,[3] F. Akira,[1] M. Konishi,[5] S. Morinaga,[4] H. Toyama,[6] Y. Kaneoka,[7] Y. Shimizu,[8] S. Nakamori,[9] N. Sata,[10] O. Kainuma,[11] Y. Kitano,[12] H. Sakamoto,[13] R. Yamaguchi,[14] S. Hishinuma,[15] S. Hirano,[16] A. Yanagisawa,[2] K. Uesaka.[1] *1. Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center Hospital, Sunto-Nagaizumi, Japan; 2. Kyoto Prefectural University of Medicine, Kyoto, Japan; 3. National Cancer Center Hospital, Tokyo, Japan; 4. Kanagawa Cancer Center, Yokohama, Japan; 5. National Cancer Center Hospital East, Kashiwa, Japan; 6. Kobe University, Kobe, Japan; 7. Ogaki Municipal Hospital, Ogaki, Japan; 8. Aichi Cancer Center Hospital, Nagoya, Japan; 9. National Hospital Organization Osaka National Hospital, Osaka, Japan; 10. Jichi Medical University, Shimotsuke, Japan; 11. Chiba Cancer Center, Chiba, Japan; 12. Asahikawa Medical University, Asahikawa, Japan; 13. Saitama Cancer Center, Saitama, Japan; 14. Kasugai Municipal Hospital, Kasugai, Japan; 15. Tochigi Cancer Center, Utsunomiya, Japan; 16. Hokkaido University, Sapporo, Japan.*

BACKGROUND: The expression of dihydropyrimidine dehydrogenase (DPD) and human equilibrative nucleoside transporter-1 (hENT1) are reported to predict survival in patients treated with adjuvant 5-fluorouracil (5FU)-based (S-1) and gemcitabine (GEM) chemotherapy, respectively. We analyzed the expression of these genes in patients enrolled in the JASPAC 01 trial (Uesaka, Lancet, 2017), and investigated their possible roles as biomarkers for predicting treatment outcomes and selecting a chemotherapeutic agent. METHODS: Formalin-fixed, paraffin-embedded specimens were available for 326 of 377 (86.5%) patients. The DPD (anti-DPD mouse monoclonal antibody [Immune-Biological Laboratories Co, Ltd, Gunma, Japan]) and hENT1 (anti-hENT1 rabbit monoclonal antibody [Roche Tissue Diagnostics Co, Ltd, Basel, Switzerland]) expression was evaluated by immunohistochemistry and the patients were classified into four groups according to the intensity of staining (no, weak, moderate, or strong) by two independent pathologists who were blinded to all of the clinical information. High and low expression of DPD and hENT1 was defined as strong/moderate staining and no/weak staining. RESULTS: High expression of DPD and hENT1 was observed in 63 and 100 of 319 patients (19.7% and 31.3%), respectively. In the GEM arm, median overall survival (OS) of the low DPD expression group was 25.9 months and that of the high DPD expression group was 25.5 months (P = 0.53), and the median OS of the low hENT1 expression group was 25.9 months and that of the high hENT1 expression group was 25.5 months (P = 0.63). In the S-1 arm, the median OS of the low DPD expression group was 44.6 months and that of the high DPD expression group was 49.6 months (P = 0.87), and the median OS of the low hENT1 expression group was 57.1 months, while that of the high hENT1 expression group was 30.9 months (P < 0.01). CONCLUSION: While the median OS of the low hENT1 expression group was significantly better than that of the high hENT1 expression group in the S-1 arm, its mechanism should be investigated in further studies.

P202

Effects of Adjunctive Therapy on Survival in Pathological Stage I Pancreatic Cancer Patients B. Zhao,* M. Bouvet, A.M. Lowy, K.J. Kelly. *University of California, San Diego, La Jolla, CA.*

INTRODUCTION: It is believed that pancreatic cancer is a systemic disease at diagnosis and systemic therapy is recommended for all patients as part of curative intent treatment. However, the benefit of systemic therapy for patients with true pathological stage I disease has not been well defined. METHODS: We analyzed the National Cancer Database for all pathologic stage I pancreatic ductal adenocarcinoma patients treated with curative intent resection between 2004 and 2015. Patients were grouped into no adjunctive therapy, chemotherapy only (neoadjuvant or adjuvant), radiation only, and chemo-radiation cohorts. Patient characteristics, disease characteristics, surgery-related characteristics, and clinical outcomes were analyzed. Kaplan-Meier analysis was performed to compare survival and Cox proportional hazards modeling was used to evaluate the effects of adjunctive therapy on survival. RESULTS: A total of 4309 patients were included in our analysis. 61% underwent a pancreaticoduodenectomy, 18.1% underwent a partial pancreatectomy, and 4.4% underwent a total pancreatectomy. 37.7% of patients underwent no adjunctive therapy, 26.4% of patients underwent chemotherapy only, 1.6% underwent radiation therapy only, and 34.3% underwent chemo-radiation therapy. Patients who received any form of chemotherapy had significantly longer median survival (34.0 vs. 21.1 months, p<0.001). From 2004 to 2013, the proportion of patients receiving any form of chemotherapy increased, along with median overall survival (Figure). Chemotherapy, negative margins, and greater than 10 lymph nodes examined were independent predictors of improved overall survival after controlling for Charlson-Deyo comorbidity scores, age, tumor size, treatment facility, and surgical procedure performed. CONCLUSIONS: Adjunctive systemic therapy is associated with improved overall survival in pathological stage I pancreatic cancer and its increased utilization may be the reason for the improvement in survival outcomes in patients with stage I disease over the past 15 years. Additional independent predictors of improved overall survival included negative resection margins and resecting greater than 10 lymph nodes.

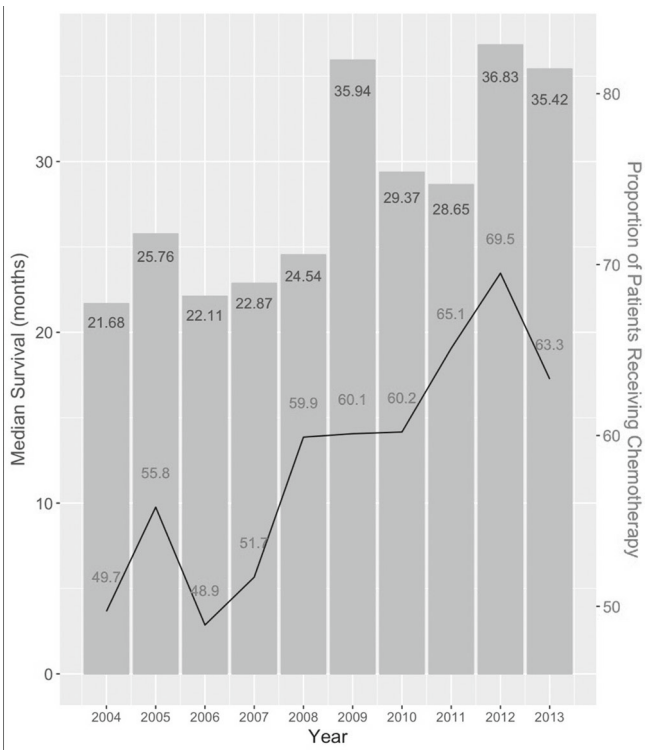


Figure. Comparison of the median survival (blue axis) and the proportion of patients receiving chemotherapy (red axis) from 2004 to 2013.

P203

The Impact of Pathologic Complete Response on Survival in Pancreatic Ductal Adenocarcinoma N.M. Sell,[1]* G.C. Lee,[1] C.R. Ferrone,[1] C. Fernandez del Castillo,[1] A.L. Warshaw,[1] L.S. Blaszkowsky,[2] K.D. Lillemoe,[1] M. Qadan.[1] *1. Surgery, Massachusetts General Hospital, Boston, MA; 2. Massachusetts General Hospital, Boston, MA.*

Objective: Multimodal treatment, including total neoadjuvant therapy, has resulted in prolonged survival in the treatment of pancreatic ductal adenocarcinoma (PDAC). Small studies have shown improved outcomes among those who have a pathologic complete response (pCR) after neoadjuvant therapy followed by surgical resection. We sought to evaluate the impact of pCR on overall survival (OS) of these patients through use of a large national database. Methods: The National Cancer Database (NCDB) was utilized to retrospectively study patients diagnosed with PDAC from 2004-2014. A pCR was defined as no tumor identified in the pancreas or associated lymph nodes by final pathology following surgical resection. A near complete response (nCR) was defined pathologically as a primary tumor less than 1cm without lymph

node metastases. The primary outcome measured was OS. Results: A total of 5,364 patients with PDAC underwent neoadjuvant chemotherapy and/or radiation followed by pancreatectomy. Forty-one patients had a pCR (0.8%), 54 (1%) had a nCR, and the remaining 5266 (98.2%) had an incomplete response (iCR; Table 1). Patients with a pCR had a median OS of 43 months compared with 24 months for nCR and 23 months for iCR (p<0.0001). A pCR was the only variable associated with an improved OS on adjusted Cox regression. While there were no significant differences in the median time from diagnosis to either chemotherapy or radiation among the groups, the pCR group had a significantly longer interval from diagnosis to surgery (195 days pCR vs. 157 days nCR vs. 139 days iCR; p=0.0001). Conclusion: For patients who are diagnosed with PDAC and undergo neoadjuvant treatment followed by surgical resection, achieving a pCR is associated with improved OS when compared to those with residual tumor within the specimen. Interestingly, an association between nCR and improved survival was not observed.

Table 1. Patient Demographics, Perioperative Variables & Overall Survival

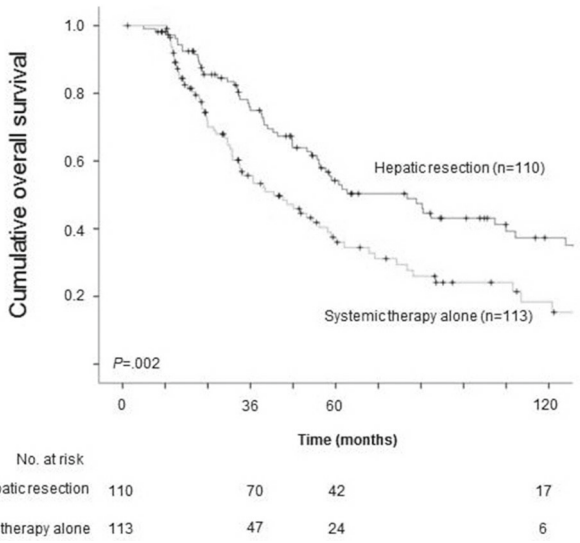
Total (n = 5364)	pCR (n = 41)	nCR (n = 57)	iCR (n = 5266)	p value
Age, yr, median (IQR)	63 (52-69)	64 (57-68)	64 (57-70)	0.29
Male, n (%)	20 (49%)	34 (60%)	2203 (51%)	0.43
Race, n (%)				
White	34 (85%)	47 (85%)	4613 (89%)	0.68
Black	4 (10%)	7 (13%)	467 (9%)	
Asian	2 (5%)	1 (2%)	120 (2%)	
Hispanic, n (%)	3 (8%)	3 (5%)	180 (4%)	0.29
Morbidity, n (%)				
Charlson-Deyo 0	31 (75%)	43 (75%)	3599 (68%)	0.38
Charlson-Deyo 1	10 (25%)	12 (21%)	1358 (26%)	
Charlson-Deyo 2+	0 (0%)	2 (4%)	309 (6%)	
Time to Chemotherapy, d, median (IQR)	28 (20-36)	29 (20-41)	27 (18-40)	0.83
Time to Radiation, d, median (IQR)	51 (36-98)	45 (26-95)	68 (31-128)	0.14
Time to Surgery, d, median (IQR)	195 (124-276)	157 (127-212)	139 (106-186)	**0.0001**
Clinical Stage, n (%)				
Stage I	6 (15%)	17 (30%)	1251 (24%)	0.06
Stage II	28 (68%)	24 (42%)	3091 (59%)	
Stage III	7 (17%)	16 (28%)	924 (17%)	
Procedure, n (%)				
Pancreaticoduodenectomy	30 (73%)	43 (75%)	3873 (75%)	0.51
Distal Pancreatectomy	7 (17%)	4 (7%)	558 (11%)	
Total Pancreatectomy	4 (10%)	10 (18%)	742 (14%)	
Resection Margin, n (%)				
Negative	41 (100%)	54 (95%)	4152 (82%)	**0.03**
Microscopic	0 (0%)	2 (3%)	528 (10%)	
Macroscopic	0 (0%)	0 (0%)	20 (1%)	
NOS	0 (0%)	1 (2%)	328 (7%)	
LOS, d, median (IQR)	8 (7-12)	7 (6-10)	8 (6-12)	0.23
Readmission, 30d	3 (8%)	6 (11%)	418 (8%)	0.80
Mortality, 90d	0 (0%)	2 (4%)	141 (3%)	0.23
Overall Survival, m, median (IQR)	43 (29-54)	24 (16-37)	23 (15-35)	**0.0001**

yr, year; IQR, interquartile range; d, day; LOS, length of stay; m, month

P204

Hepatic Resection is Associated with Improved Survival Compared to Chemotherapy Alone in Patients with Isolated Breast Cancer Liver Metastases J. Cloyd,* T. Mizuno, K. Omichi, H.A. Lillemoe, H. Kuerer, K. Hunt, I. Bedrosian, A. Caudle, R. Hwang, F. Meric-Bernstam, Y. Chun, C.D. Tzeng, T. Aloia, J. Vauthey. *University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: The role of hepatic resection in patients with isolated breast cancer liver metastases (BCLM) is controversial. Methods: From prospectively compiled databases, we identified patients with isolated BCLM who underwent chemotherapy followed by hepatic resection (n=110) or chemotherapy alone for potentially resectable metastases (n=113) during 1997-2016. The impact of hepatic resection on overall survival (OS) was assessed in unmatched and propensity-score matched analyses. Results: Among all patients, OS was better in patients who underwent resection than in those who received chemotherapy alone (5-year OS rate, 54% vs 36%; P=0.002; Figure). A partial or complete radiographic response to chemotherapy was observed in 74% of patients who underwent resection and 66% of patients who did not (p=0.237). Resection was associated with improved OS in patients who experienced a radiographic response (P=0.010) but not in patients without an objective response (P=0.203). On multivariable analysis, factors associated with worse OS included: tumor triple negative status (HR 3.2; 95% CI, 1.8-5.5; P<0.0001), high histologic grade (HR 2.0; 95% CI, 1.3-3.1; P<0.01), absence of objective response to chemotherapy (HR, 2.7; 95% CI, 1.7-4.3; P<0.0001), and receipt of chemotherapy alone (HR, 1.5; 95% CI, 1.0-2.2; P=0.033). After propensity-score matching, patients who underwent resection (n=72) had better 5-year OS than patients who received chemotherapy alone (n=72) (56% vs 40%, P=0.02). Conclusion: Chemotherapy followed by hepatic resection is associated with improved OS compared to chemotherapy alone in patients with potentially resectable isolated BCLM. Selection of patients by response to medical therapy optimizes outcome.



P205

Identification and Characterization of Tumor Infiltrating Lymphocytes in Patients with Biliary Tract Cancers J.D. Beane,* S. Chaurasia, A. Srivastava, J. Tobin, S. Ankita, G. Yadav, M.P. Holtzman, A.H. Zureikat, J.F. Pingpank, D.L. Bartlett, U.S. Kammula. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Due to the aggressive tumor biology and subsequent dismal outcomes afforded by current therapies in patients with advanced biliary tract cancers, there is a need for novel treatments. Adoptive cell transfer using autologous tumor infiltrating lymphocytes (TIL) represents a personalized cancer immunotherapy strategy, targeting shared and unique tumor antigens expressed by a patient's tumor. The aim of our study was to determine if tumor reactive TIL could be generated against biliary tract cancers to be used as part of future adoptive cell transfer treatment strategy for these patients Methods: Seven consecutive patients with advanced biliary tract cancers underwent tumor resection at a single institution. Discrete 1 mm^3 tumor fragments were placed individually in wells of a 24-well culture plate containing complete media with human AB serum and recombinant interleukin 2 (6000 IU/mL). Remaining fresh tumor was processed by mechanical and enzymatic digestion to provide a single cell suspension of autologous tumor targets for TIL reactivity testing. TIL phenotype were characterized by FACS analysis and each TIL culture was screened for anti-tumor reactivity by co-culture with either autologous tumor cells or autologous monocytes to define background Results: Multiple TIL cultures (n=8-24 cultures/patient) were successfully generated in all 7 patients. The frequency of CD4+ and CD8+ T cells varied significantly across patients. Despite this phenotypic heterogeneity, TIL cultures with reactivity against autologous tumor were identified in all patients except for one based upon IFN-g release (Figure 1). Focused selection and expansion of these tumor

reactive TIL cultures was performed to numbers sufficient for clinical adoptive cell transfer. Conclusion: Tumor reactive T cells can be effectively isolated and expanded from resected tumors in patients with advanced biliary tract cancers. These findings have been used to develop a Phase II clinical trial to determine the safety and efficacy of adoptive transfer of autologous TIL in patients with advanced biliary tract cancers.

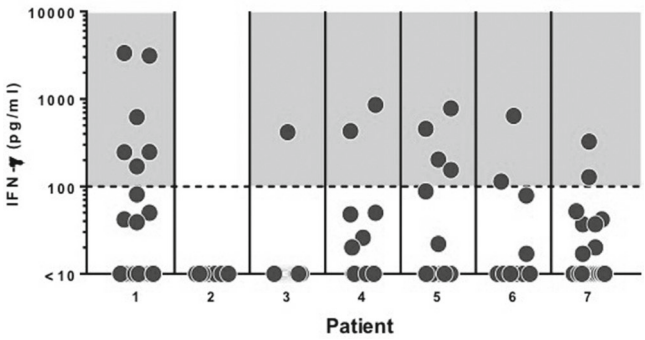


Figure 1. Multiple TIL cultures were generated from patients with advanced biliary cancer, and each TIL culture (blue dot) was screened for anti-tumor reactivity by co-culture with autologous tumor cells and measurement of IFN-g.

P206

Neoadjuvant Chemotherapy versus Upfront Resection in Ampullary Adenocarcinoma Stratified by Stage: A Retrospective Analysis Using the National Cancer Database S. Leonard-Murali,[1]* R. Shah,[2] T. Ivanics,[1] X. Han,[3] C.P. Steffes,[2] D.S. Kwon.[2] *1. Henry Ford Hospital, Department of Surgery, Detroit, MI; 2. Henry Ford Hospital, Division of Surgical Oncology, Department of Surgery, Detroit, MI; 3. Henry Ford Health System, Department of Public Health Sciences, Detroit, MI.*

Background: Outcomes of a neoadjuvant therapy (NAT) strategy to treat ampullary adenocarcinoma (AAC) are not clear. Upfront resection (UR) (typically pancreaticoduodenectomy) with or without adjuvant therapy (AT) is currently the standard of care. We looked to assess outcomes of NAT followed by radical surgery for AAC. Methods: The NCDB was queried for ampullary carcinoma patients from 2004-2015. Patients with Stage I to III AAC who underwent radical surgery were included, and separated into NAT with surgery and UR groups. Demographic/clinical/pathologic data and their associations to survival were analyzed with univariate and multivariate cox proportional hazard models. Overall survival was estimated from time of diagnosis using Kaplan-Meier curves and compared using log-rank tests (LRT) (see Figure 1). Statistical analyses were performed using R version 3.5.1 with significance established at $p<0.05$. Results: There was no difference in overall survival between the NAT (n = 47) and UR (n = 1521) groups, either as total groups (LRT p=0.2), or when stratified by stage (stratified LRT p=0.5). Rates of AT were higher in the UR group (p=0.038). Receiving AT was significantly associated with improved survival (hazard ratio (HR) = 0.648), while positive nodal status (HR = 2.06), stage 3 disease (HR = 1.542), age>65 (HR = 1.494), and male gender (HR = 1.241) were all significantly associated with decreased overall survival by multivariate analysis. Conclusions: NAT does not offer a survival advantage over UR either overall or for stage-specific disease. This finding extended even to stage III disease, where NAT would theoretically offer greatest benefit. This study suggests that a NAT strategy is not preferable to UR for treatment of resectable AAC, regardless of stage. Higher powered study of NAT for AAC with controls for AT is warranted before discarding a NAT strategy.

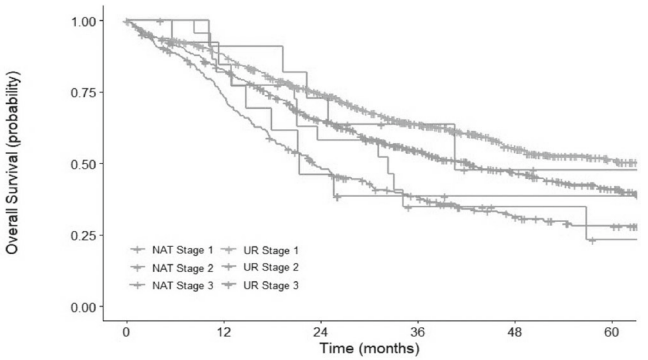


Figure 1: Kaplan-Meier curves of NAT (neoadjuvant therapy + surgery) vs UR (upfront resection) groups, stratified by stage of disease. Stratified log-rank test: p=0.5

P207

A Phase I Trial of Concurrent Immunotherapy and Irreversible Electroporation in the Treatment of Locally Advanced Pancreatic Adenocarcinoma R. Martin,* M. Donaldson, T. Hayat, C. O'Neill. *University of Louisville, Louisville, KY.*

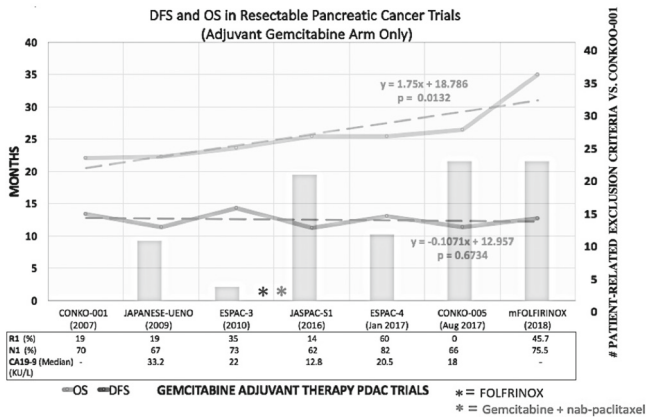
Background: Cytotoxic chemotherapy remains the mainstay of treatment for pancreatic adenocarcinoma; however, both the immunosuppressive effects and cumulative toxicity limit its long term benefits. Irreversible electroporation (IRE) is a surgical tumor disruptive therapy that has improved overall and disease free survival in locally advanced pancreatic cancers. IRE has also been proven to change the local immunologic milieu with recruitment of T regulatory cells. Based on IRE's immunologic effect we hypothesis that IRE with concurrent Nivolumab is safe and can improve progression free survival. Methods: This was a Phase 1 clinical trial (NCT03080974) to determine safety and tolerability of combination IRE and Nivolumab. Patients with Stage III locally-advanced unresectable PDAC received IRE followed by IV Nivolumab 240 mg between one to five days postoperatively, and then every 2 weeks for a total of 4 doses. Dose limiting toxicity and safety were recorded using Common Terminology Criteria for Adverse Events (CTCAE). Results: Ten patients, four males and six females, with a mean age of 59.0 years [38-67.8]. The mean tumor size was 33.3 millimeters [12-49mm]. All patients received dose 1 therapy on post-operative day 1 to 5 based on a stable surgical post-operative course, with 8 patients receiving all 4 doses and completing therapy. The most common grade 1-2 CTCAEs were surgical pain (90%), diarrhea (50%), fatigue (50%), abdominal bloating (40%), and anorexia (30%). Grade 3 CTCAEs included gastric ulceration/bleeding (n=1), fatigue (n=1) and persistent emesis (n=1). Two patients had grade 4 CTCAEs related to GI bleed from the surgery, and one of those patients had a liver abscess. There was no drug induced liver injury, dose limiting toxicity, or intolerance. Conclusion: Our data demonstrate that treatment with IRE and Nivolumab for patients with stage III pancreatic cancer is safe and well tolerated in the immediate post-operative period, with limited systemic toxicity. A multi-center phase II adjuvant trial is underway to improve progression with IRE and Nivolumab in patients with locally advanced pancreatic cancer.

P208

Elucidating the Causes of Improved Survival in Recent Randomized Adjuvant Pancreatic Ductal Adenocarcinoma (PDAC) Clinical Trials A. Alabd,[1]* O. Bolaji,[2] J. Ammori,[3] J. Hardacre,[3] J. Winter.[3] *1. Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA; 2. Christiana care Health System, Christiana, DE; 3. University Hospitals Cleveland Medical Center, Cleveland, OH.*

BACKGROUND: Overall survival (OS) has increased in recent PDAC adjuvant clinical trials, even when the chemotherapeutic agent is constant. While oncologists have taken notice, the root causes have not been examined. METHODS: All phase III adjuvant PDAC clinical trials were screened (n=16), and 7 were identified (2007– 2018) that included gemcitabine monotherapy treatment arms. Trends in OS and disease free survival (DFS) were plotted and analyzed over time using linear regression (quantified by the Y axis, left

side of the graph). Eligibility criteria were categorized as: 1) tumor-related factors (CA19-9 levels, pathological criteria) or 2) patient-related factors (medical comorbidities). Eligibility criteria were compared across trials. The number of new or distinct patient-related exclusion criteria in recent trials were compared to the earliest trial (CONKO-001), and quantified (histogram, Y axis on the right side of the graph). Of note, standard-of-care treatment for recurrent PDAC changed to multi-agent chemotherapy in 2011, as indicated by asterisks on the graph. RESULTS: OS improved over time in patients receiving only gemcitabine (slope=1.75 months, p= 0.01), while DFS remained constant (p= 0.7). CA19-9 values were relatively constant, with the exception of the Japanese trials. Pathologic features were also unchanged over time (except CONKO-001excluding R1 patients). Notably, recent trials had stricter inclusion criteria with respect to patient-related factors (i.e., more patients were excluded for medical reasons). CONCLUSION: OS of patients with resected PDAC has significantly improved, irrespective of adjuvant treatment. Consistent DFS (12 months) and cancer-related factors indicate that selection bias towards more favorable cancer biology in recent trials cannot account for this observation. However, recent trials included healthier patients, which may have had an effect. More likely, widespread adoption of effective multi-agent chemotherapy after 2011 likely had the greatest impact. These data provide indirect evidence that newer palliative chemotherapy regimens are impacting OS following recurrence of resected PDAC.



P209

Combined Hepatocellular-Cholangiocarcinoma (CHC): Contemporary Outcomes and Staging Challenges N. Parikh,[1]* P. Prieto,[1] H. Nathan.[2] *1. University of Rochester, Rochester, NY; 2. University of Michigan, Ann, MI.*

Introduction: CHC is a rare primary hepatic malignancy with features of both intrahepatic cholangiocarcinoma (ICC) and hepatocellular carcinoma (HCC). Its prognosis remains poorly characterized due to its uncommon incidence. Although CHC is staged according to the ICC system by the American Joint Committee on Cancer (AJCC), the prognostic relevance of this system for CHC is unknown. We used the National Cancer Database (NCDB) to characterize CHC outcomes and evaluate the prognostic utility of the AJCC 8th edition ICC staging system as applied to CHC. Methods: A retrospective analysis was performed using data from the NCDB on patients undergoing liver resection (LR) or liver transplantation (LT) for non-metastatic CHC, ICC, and HCC from 2004-2015. The Kaplan-Meier method was used to plot survival, and the log-rank test was used to calculate statistical significance. Multivariable Cox proportional hazards models were fit to the data, and staging system performance was assessed using c-statistics. Results: The analytic cohort included 25,209 patients with HCC, 5,246 with ICC, and 625 with CHC (Table). 441 (71%) CHC patients underwent LR, and 184 (29%) patients had LT. Overall prognosis for CHC patients was intermediate, between that for ICC and HCC. Median survival by histology was 35 months for ICC, 42 months for CHC, and 90 months for HCC. Overall 1, 3, and 5 year survival rates for CHC (76%, 41%, 22%) were lower than for HCC (85%, 55%, 33%, p<0.001), but higher than for ICC (77%, 36%, 17%, p=0.009). Post-LT survival rates for CHC at 1, 3, and 5 years (85%, 52%, 32%) were lower than for HCC (92%, 68%, 45%, p=0.002), but similar to ICC (83%, 47%, 28%, p=0.7). The AJCC 8th edition staging system had slightly poorer discrimination for CHC patients (Harrell's C = 0.57) than for ICC (0.60) patients. Conclusion: Surgically resected CHC has a prognosis slightly better than that for ICC. CHC survival outcomes after LT are inferior to those for HCC—LT for CHC should be avoided when preoperative distinction is possible. The current AJCC 8th edition staging for ICC is suboptimal for CHC, but the rarity of this disease may preclude developing a distinct and reliable staging system.

Median Survival Time from Diagnosis by AJCC Stage and Histologic Type

AJCC Stage	ICC (n=5,246)	CHC (n=625)	HCC (n=25,209)	p value
IA	66	70	125	<0.001
IB	46	53	84	<0.001
II	30	32	70	0.349
IIB	20	17	25	0.021

P210

RIP1 Kinase Promotes Macrophage Mediated Adaptive Immune Tolerance in Pancreatic Adenocarcinoma M. Hundeyin,* W. Wang, G. Miller. *New York University School of Medicine, New York, NY.*

Pancreatic adenocarcinoma (PDA) is a lethal disease with grim prognosis. It is characterized by local immunosuppression and resistance to immunotherapy. We have previously shown that the phenotype of tumor-associated macrophages (TAMs) largely regulates immunogenic or immune-suppressive T-cell programming in PDA, which ultimately affects tumor progression. However, the regulators of macrophage polarization in PDA and the optimal approach to macrophage-based immunotherapy remain uncertain. Receptor-interacting serine/threonine-protein kinase 1 (RIP1) is involved in diverse cellular functions including driving necroptosis and TLR signaling. We therefore postulated that RIP1 may have pleiotropic influences on suppressive macrophage polarization in cancer. Using murine $p48^{Cre}$;LSL-$KRas^{G12D}$ model of PDA, we found that RIP1 is upregulated in TAMs in PDA. In-vivo RIP1 inhibition conferred tumor protection and improved survival compared with controls. Mechanistically, RIP1 signaling programmed macrophages towards an immunosuppressive $CD206^{+}IL\text{-}10^{+}$phenotype, whereas inhibiting RIP1 promoted a highly immunogenic $MHCII^{hi}TNF\alpha^{+}IFN\gamma^{+}$ phenotype in a STAT1-dependent manner. Accordingly, RIP1 inhibition in TAMs promoted cytotoxic $CD8^{+}$ T cell activation and $CD4^{+}$ T cell differentiation towards a mixed Th1/Th17 phenotype. In addition, targeting RIP1 synergized with PD1- and ICOS-based immunotherapies in PDA-bearing mice and 3D organotypic models of human disease. Collectively, our work describes RIP1 as a novel checkpoint kinase that modulates tumor immunity in pancreatic cancer.

P211

Characterizing Tumor Stromal Architecture in a Spontaneous Mouse Model of Cholangiocarcinoma: A Robust Model for Evaluating Interventions Targeted at Re-engineering the Tumor Stroma L.I. Ruffolo,* K.M. Jackson, R. Ahmed, M. Doyley, B. Belt, D.C. Linehan, P. Prieto. *University of Rochester, Rochester, NY.*

Background: Cholangiocarcinoma (CCA) is the second most common primary hepatic cancer. Unfortunately, prognosis is poor due in part to resistance to chemotherapy. CCA is characterized by a dense fibro-inflammatory stroma. Additionally, tumor hypovascularity limit chemotherapeutic efficacy due to poor penetration of tissue. A murine model of CCA closely recapitulates the human disease. Here we characterize the transformation of the tumor stroma architecture, from onset to end-stage disease. Methods: Ultrasonography (US) was used to detect disease onset in mice with targeted $Kras^{G12D}$ and loss of p53 in the liver (Kras-p53). Infusion of microbubble contrast enhanced tumor detection in early disease. Tumors were imaged serially, comparing tumor and adjacent normal parenchyma. Hepatic perfusion was assessed throughout disease progression. Elastography was correlated with deposition of collagen and hyaluronic acid as measured through immunohistochemistry (IHC). Changes in markers for extracellular matrix metabolism were assessed with by RNA-seq and qRT-PCR analysis. Results: Disease was detectable at 1 mm in diameter. Volumetric analysis showed accelerated tumor growth overtime, with mean growth rate of 15.3 mm^3/week. Tumor perfusion decreased with progressive tumor size. Grouped perfusion between tumors was significantly decreased compared to normal liver (Figure 1). In-vivo tumor elastography demonstrated commensurate increases in stromal stiffness with disease progression. IHC demonstrated dense collagen and hyaluronic acid deposition in advanced disease. Genomic evaluation revealed statistically significant

increases in genes associated with hyaluronic acid, collagen metabolism, and markers of fibroblast activation (P<0.001). Conclusions: In this model, CCA progresses through a transformation of the normal hepatic parenchyma to stromal desmoplasia typical of human disease. US provides a robust in-vivo metric of perfusion. Tissue elastography demonstrated close fidelity with fibrosis. Taken together this model provides a novel platform for evaluating stromal re-engineering therapies.

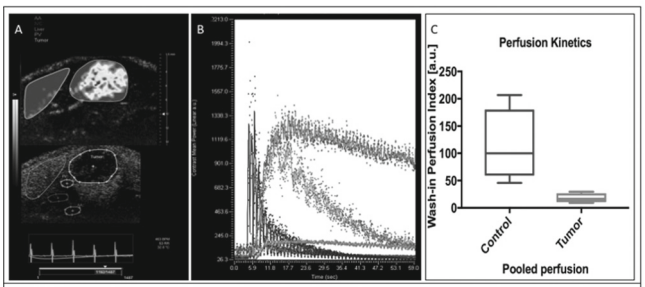


Figure 1: A) Representative B mode with microbubble contrast (bottom) and kinetic perfusion heat map (top). B) Corresponding perfusion kinetics in Aorta (red), Inferior Vena C ava (dark blue), Portal Vein (light blue), normal adjacent liver parenchyma (pink), and tumor (green). C) Grouped wash-in perfusion index comparing CCA tumors with adjacent normal liver parenchyma (P=0.0286).

P212

Neoadjuvant Therapy for Body and Tail Pancreatic Adenocarcinoma: Propensity Score Matched Analysis Using the National Cancer Data Base T. Ivanics,* S. Leonard-Murali, X. Han, C.P. Steffes, D.S. Kwon, R. Shah. *Surgery, Henry Ford Hospital, Detroit, MI.*

Introduction The role of neoadjuvant systemic therapy in the management of body and tail pancreatic ductal adenocarcinoma (PDAC) is unknown. The aim of our study was to investigate the outcomes associated with neoadjuvant therapy for early stage body and tail PDAC. Materials and Methods The National Cancer Database (NCDB) was queried for stage I and II body and tail PDAC between 2006-2014. Groups were defined according to treatment sequencing strategies into an upfront resection group (UR), resection followed by adjuvant therapy (R+AT), neoadjuvant therapy followed by resection (NAT+R), and neoadjuvant therapy followed by resection and adjuvant therapy (NAT+R+AT). Patients who underwent neoadjuvant therapy followed by resection were matched by propensity score with patients who underwent upfront resection. Overall survival was compared using Kaplan-Meier method and Cox proportional hazards regression model. Results 441 patients received neoadjuvant therapy followed by resection with or without adjuvant therapy compared to 1323 patient who underwent upfront resection with or without adjuvant therapy. NAT+R had lower pathologic stage, lymph node positivity and a higher rate of margin negative resections compared to the matched UR cohort. In the propensity matched cohort, the median survival (MS) was higher in the neoadjuvant (NAT+R/NAT+R+AT) group compared to the upfront resection (UR/R+AT) group (28.6 vs. 22.9 mos; p<0.001). When further stratified by treatment sequencing the MS was longer in a NAT+R+AT cohort compared to the R+AT group (36.0 vs. 25.3 mo; p<0.05) (Fig 1). However, there was no difference in MS between R+AT and NAT+R cohorts. On multivariable analysis, receipt of NAT represented an independent factor for survival (NAT+R+AT HR 0.41, 95% CI 0.32-0.54; NAT+R HR, 0.53, 95% CI, 0.44-0.64; R+AT HR 0.61, 95% C 0.53-0.70). Discussion There appears to be a survival benefit with neoadjuvant systemic therapy in patients with body and tail PDAC. A systemic perioperative treatment sequencing approach (NAT+R+AT) appears to have the greatest survival benefit.

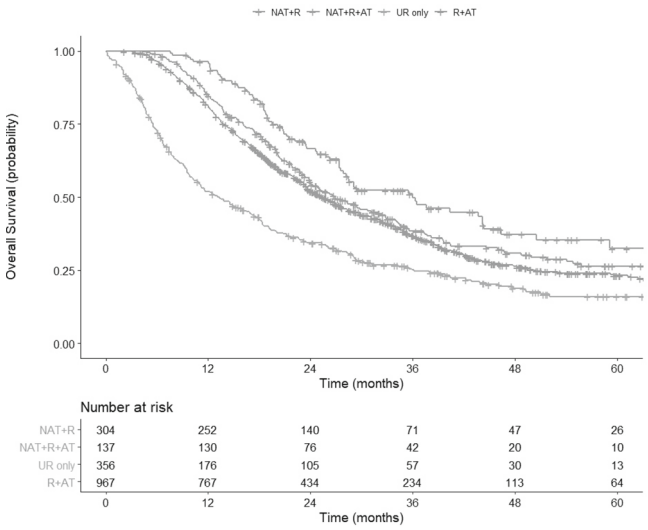
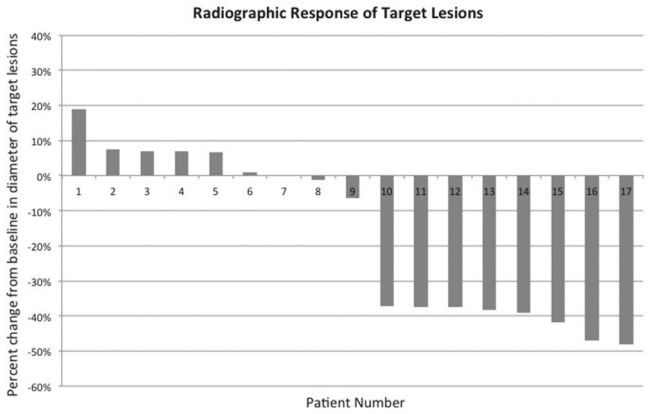


Figure 1. Kaplan-Meier curve for overall survival between patients of the upfront resection (UR) group with or without adjuvant therapy, as well as patients of the neoadjuvant therapy (NAT) group with or without adjuvant therapy.

P213

Neoadjuvant Capecitabine/Temozolomide (CAPTEM) for Locally Advanced or Metastatic Pancreatic Neuroendocrine Tumors M.H. Squires,[1]* K.K. Rossfeld,[1] B. Konda,[2] M. Shah,[2] M. Dillhoff,[1] S. Abdel-Misih,[1] T. Pawlik,[1] J. Cloyd.[1] *1. Division of Surgical Oncology, The Ohio State University Wexner Medical Center, Columbus, OH; 2. Department of Medical Oncology, The Ohio State University Wexner Medical Center, Columbus, OH.*

BACKGROUND: Recent evidence has demonstrated the efficacy of capecitabine and temozolomide (CAPTEM) for the treatment of metastatic well-differentiated pancreatic neuroendocrine tumors (PNETs). However, the role of CAPTEM in the neoadjuvant setting has not been established. METHODS: All patients with locally advanced or resectable metastatic PNETs who received CAPTEM with neoadjuvant intent between 2009-2017 were retrospectively reviewed. Radiographic response was assessed according to RECIST 1.1 criteria and predictors of response were measured by logistic regression. RESULTS: Seventeen patients with either locally advanced PNET (n=5) or pancreatic neuroendocrine hepatic metastases (n=12) underwent neoadjuvant CAPTEM therapy, receiving a mean number of 5 cycles (IQR, 3-8 cycles). Overall, 8 patients (47%) experienced a partial response (PR) whereas 9 (53%) had stable disease and no patients developed progressive disease (Figure). Thirteen (76%) patients underwent resection (pancreatectomy (n=7), pancreatectomy and liver resection (n=3), or major hepatectomy alone (n=3)); 3 (18%) declined surgery despite experiencing a PR, and 1 (6%) underwent an aborted pancreatoduodenectomy due to the finding of cirrhosis. Median PNET primary tumor size on final pathology was 7.1cm (IQR, 3.3-9.3cm), and the median Ki-67 index was 3.5% (IQR, 1-8%). Rates of PR were similar across WHO tumor grades (p=0.83): Grade 1 (4 of 7 patients, 57%), Grade 2 (3 of 8 patients, 38%), and Grade 3 (1 of 2 patients, 50%). At a median follow-up of 50.2 months for the cohort, the median progression-free survival for all patients was 42.5 months (95% CI: 17.5-67.5), and the 5-year overall survival was 65%. A decrease of >50% in the pre-treatment serum value of the tumor markers pancreatic polypeptide or pancreastatin was significantly associated with PR (p<0.001), while Ki-67 and tumor grade were not associated with response. CONCLUSION: Neoadjuvant CAPTEM is associated with a favorable radiographic response rate for locally advanced or metastatic PNET and facilitates selection of patients appropriate for surgical resection.



Radiographic response rates as measured by RECIST 1.1 criteria among patients (n=17) with locally advanced or resectable metastatic pancreatic neuroendocrine tumors (PNETs) treated with neoadjuvant capecitabine/temozolomide (CAPTEM)

P214

Fragmentation of Cancer Care in Patients with Hepatocellular Carcinoma is Associated with Worse Outcomes C.A. Hester,* N. Karbhari, N. Rich, A. Singal, A. Yopp. *Surgical Oncology, University of Texas Southwestern, Dallas, TX.*

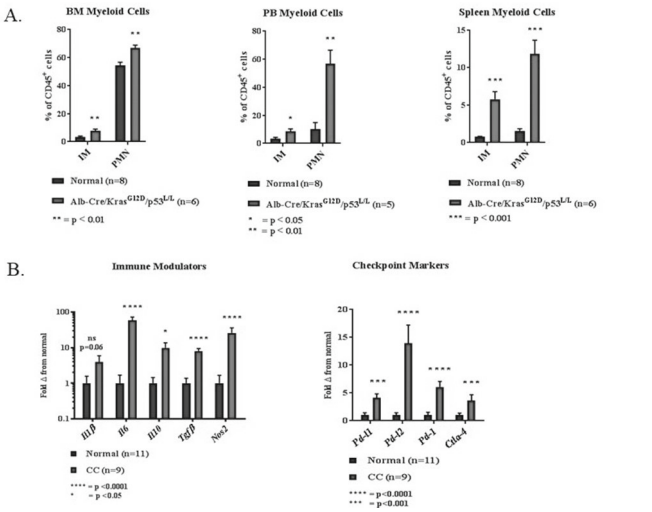
Background Fragmented cancer care, or care received from multiple institutions, increases health care costs resulting in a widening gap of cancer care disparities. However, there is a paucity of data associating fragmented care (FC) with outcome measures. We aimed to define clinicopathological factors associated with non-fragmented care (NFC) and FC and determine their association with outcome measures in hepatocellular cancer (HCC). Methods Patients with HCC were identified in the Texas Cancer Registry between 2004-2015. Clinicopathological variables were compared with chi-square analysis and ANOVA. Logistic regression and general linear model were used for multivariable analysis. Results We identified 4,329 patients: 3,144 (72.6%) and 1,185 (27.4%) in the NFC and FC cohorts. Compared to NFC, FC had larger tumors (52.6% vs 35.2% median size ≥ 4 cm, p<0.001) and more regional/metastatic stage (35.9% vs 26.7%, p<0.001). Patients were more likely to have NFC if they received initial curative therapy (45.7% vs 40.6%, p<0.001) or treatment at an ACS-accredited program (83.7% vs 76.9%, p<0.001) or safety net hospital (SNH) (57.2% vs 45.5%, p<0.001). FC was independently associated with an increased time to treatment (TTT) of 1.6 weeks (95%CI 1.0-2.3, p<0.001) compared to NFC. Median OS was 28 and 22 months for NFC and FC (p<0.001). FC was independently associated with worse OS (HR 1.1, 95%1.0-1.2). FC among early stage HCC patients receiving curative therapy was independently associated with increased TTT of 2.4 weeks (95%CI 1.3-3.5) compared to NFC. The median OS was 67 and 43 months for early stage NFC and FC (p<0.001). Early stage FC was independently associated with worse OS (HR 1.2, 95%CI1.0-1.4). Conclusion Nearly one quarter of all treated HCC patients experienced FC. FC was more common among patients initially treated with non-curative therapy or at a non ACS-accredited program or non-SNH. FC was independently associated with increased time to treatment and worse OS among all treated patients and early stage patients treated with curative therapy.

P215

The Tumor Microenvironment of Cholangiocarcinoma in a Spontaneous Mouse Model: Characterization and Potential Therapeutic Targets K.M. Jackson,* L.I. Ruffolo, R. Jewell, B. Belt, D.C. Linehan, P. Prieto. *Surgery, University of Rochester Medical Center, Rochester, NY.*

Background: Liver cancer remains one of the deadliest malignancies worldwide. Cholangiocarcinoma (CCA), the second most common liver primary, imparts a particularly dismal prognosis. The frequency of advanced disease mandates effective systemic therapies, but CCA classically displays robust resistance to standard treatments. The lack of pre-clinical models has hindered new treatment strategies. Targeted KRAS activation and loss of p53 (KRAS-p53) in mice lead to the spontaneous development of CCA. While these tumors demonstrate comparable histological features of human disease such as dense stroma and fibro-inflammatory reaction, the constitution of the tumor microenvironment (TME) has remained uncharacterized. Methods: Tissue acquired from human and mouse CCA underwent immunohistochemistry for immune and stromal markers. Blood, spleen, bone marrow, liver and tumor from KRAS-p53 mice and littermate controls were analyzed using flow cytometry. Myeloid cells were isolated and functional assays were performed. RNA-seq and RT-PCR were performed on tumor and normal liver samples. Results: Human tumors demonstrated pronounced immunosuppressive features. There was a significantly dense inflammatory myeloid infiltrate that included large populations of tumor associated macrophages (TAM) and neutrophils (TAN). Marked levels of TAM and TAN were also evident on flow cytometry of the KRAS-p53 tumors, and isolated cells from the tumors suppressed T cell proliferation. KRAS-p53 mouse CCA featured a dense fibro-inflammatory reaction featuring fibroblasts, collagen, and hyaluronic acid, as well as indicators of hypovascularity and hypoxia. PCR and RNA-seq revealed increased expression of cytokines associated with myeloid production and mobilization. The KRAS-p53 tumors also expressed significantly elevated levels of immunosuppressive checkpoint markers and soluble factors (Figure 1). Conclusion: The KRAS-p53 spontaneous mouse model of CCA results in tumors with a marked inflammatory immune infiltrate that recreates the highly immunosuppressive microenvironment. The model represents a novel tool to evaluate new therapies in this challenging disease.

Figure 1: A) Cholangiocarcinoma induces myelopoiesis in bone marrow, peripheral blood, and spleen of affected Kras-p53 mice. B) Significant increase in immunosuppressive soluble factors and checkpoint indicators in Kras-p53 mouse cholangiocarcinoma tumors.

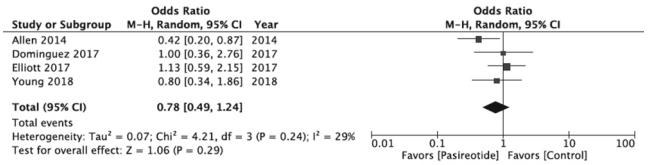


P216

Meta-Analysis on the Effect of Pasireotide for Prevention of Postoperative Pancreatic Fistula E.C. Dalton,* N. Petrelli, G. Tiesi. *Surgery, Christiana Care Health System, Wilmington, DE.*

Background: Pasireotide, a newer somatostatin analogue, was shown in a single institution randomized trial to decrease the incidence of postoperative pancreatic fistula (POPF) with routine prophylactic administration. More recent studies have not replicated these results. The aim of this study was to evaluate the efficacy of Pasireotide in preventing POPF after pancreatectomy. Methods: An online database search was performed for all prospective studies using postoperative Pasireotide administration compared to a control group of no somatostatin analogue. Primary outcome measured was clinically significant POPF (Grade B or 3 and higher). Secondary outcomes included length of stay (LOS), readmission rates and mortality. Pooled odds ratios (OR) and 95% confidence interval (CI) were calculated. Study quality and heterogeneity were assessed. Results: Four studies totaling 919 patients (418: Pasireotide; 501: control) were eligible for meta-analysis. There was no difference in age, sex, ductal dilation, gland texture or presence of cancer between groups. For all pancreatectomies, there was no difference between the incidence of POPF in the Pasireotide group versus the control group (OR 0.78; 95%CI 0.49-1.24, P = 0.29) [Fig. 1]. Similar results were seen for patients undergoing distal pancreatectomy as there was no significant difference in POPF with the 85 Pasireotide patients versus the 105 control patients (OR 0.62; 95%CI

0.28-1.35, P = 0.23). There was a trend to decreased incidence of fistula after Whipple procedure within the Pasireotide group (333 Pasireotide versus 396 control patients), however, this did not reach statistical significance (OR 0.75; 95%CI 0.49-1.14, P = 0.18). Readmission rates were significantly lower with Pasireotide (OR 0.61; 95%CI 0.44-0.85, P = 0.004). There was no difference in LOS or mortality between the groups. Conclusions: Despite a randomized control trial showing a decreased incidence of POPF with Pasireotide, meta-analysis did NOT replicate this finding. Pasireotide was associated with a decreased readmission rate, but further prospective studies are warranted to evaluate its utility after pancreatectomy.



P217

Robotic Versus Laparoscopic Hepatectomy: Comparison of Short-term Outcomes Using the NSQIP Database J.A. Lee,[1]* M.H. Al-Temimi,[2] L.A. DiFronzo.[1] *1. Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA; 2. Baylor University Medical Center, Dallas, TX.*

Background: Robotic surgery is generally associated with technical advantages over conventional laparoscopy. However, it is not clear if robotic hepatic resection is associated with better clinical outcomes than laparoscopic hepatectomy. Methods: The targeted hepatectomy file of the NSQIP database was surveyed for pure laparoscopic and robotic cases between 2014 and 2016. Multivariate logistic regression analysis was used to test the effect of both minimally invasive approaches on 30-day postoperative outcomes. These models were adjusted for predictors of case complexity (diagnosis, extent of resection and type of concomitant resections). Results: We identified 1980 (93.6%) laparoscopic and 137 (6.4%) robotic cases. Viral hepatitis (15% vs. 8.3%) and HCC (18.1% vs. 10.2%) were more common in the laparoscopic group (p<0.05). ASA≥3 (78.8% vs. 67.9%), secondary malignancy (48.2% vs. 37.2%), clean contaminated wound (98.5% vs. 94.2%), lysis of adhesions (11.7% vs. 6.8%), vascular repair/resection (2.2% vs. 0.7%) and lymph node dissection (10.2% vs. 3%) were significantly higher in the robotic group (p<0.05). Robotic cases were associated with a longer operative time (median, 201 min vs. 166 min), higher blood transfusion (15.3% vs. 8.7%) and more common organ/space infection (6.6% vs. 3.1%) (p<0.05); however the conversion rate was significantly lower in the robotic cohort (20.3% vs. 8.8%, P<0.001). Morbidity and mortality were not different between the two groups in bivariate and multivariate analysis (overall morbidity OR=1.45; 95% CI=0.94-2.22, major morbidity OR=1.05; 95% CI=0.59-1.88) Conclusions: Robotic liver resection is associated with longer operative time, a greater need for blood transfusion, and higher organ/space infection than laparoscopic hepatectomy. Hospital stay and morbidity were not significantly different, despite robotic surgery being associated with lower conversion rates

P218

Simultaneous Resection of Colorectal Cancer with Synchronous Liver Metastases: A Survey-Based Analysis C. Griffiths,[1]* J. Bogach,[1] M. Simunovic,[1] L. Ruo,[1] J. Hallet,[2] P. Serrano Aybar.[1] *1. McMaster University, Hamilton, ON, Canada; 2. Sunnybrook Health Sciences Centre, Toronto, ON, Canada.*

Background Decision to proceed with simultaneous or staged resection in synchronous colorectal cancer liver metastases varies greatly and is usually left to the involved surgeon. We examined practice intentions and determined barriers to performing simultaneous resection. Methods We developed and pilot-tested a tailored questionnaire. Members of the Society of Surgical Oncology and the College of Physicians and Surgeons of Ontario who provide colorectal cancer care were surveyed electronically. Four clinical scenarios of synchronous disease with gradually increased complexity determined practice intentions. Perceived outcomes and barriers were assessed on a 7-point Likert scale and compared between general and hepatobiliary surgeons using the Mann-Whitney U test for continuous variables and Chi-square test for categorical variables. Results: There were 184/1335 surgeons (14% response rate), including 50 general and 134 hepatobiliary surgeons. A high likelihood score for simultaneous resection (i.e., Likert score ≥5-7) varied among the four scenarios. The score for general and hepatobiliary surgeons, respectively, included the following: for minor liver and low complexity colon resection, 83% and 98% (p<0.001); for minor liver and rectal resection, 57% and 73% (p=0.042); for complex liver resection and low complexity colon resection, 26% and 24% (p=0.858); and, for complex liver and rectal resection, 11% and 7.0% (p=0.436). Hepatobiliary surgeons were more likely to perform simultaneous resections in their centres. All perceived that simultaneous resection increases post-operative morbidity (63%), but not mortality (69%). Among hepatobiliary surgeons, the most common barriers for simultaneous resections were patient comorbidities and extrahepatic disease, whereas general surgeons were more concerned about transfer to another facility. Conclusions Surgeon support for simultaneous resection increased with less complex surgery, and was higher among hepatobiliary versus general surgeons. Surgeons' perceived practice patterns and barriers to simultaneous resection will identify knowledge gaps, guide future clinical trials, and help establish disease care pathways.

P219

Simultaneous Versus Staged Resection for Synchronous Colorectal Cancer Liver Metastases: A Population-based Cohort Study J. Bogach,[1]* J. Wang,[1] S. Parpia,[1] M. Simunovic,[1] J. Hallet,[2] P. Serrano Aybar.[1] *1. McMaster University, Hamilton, ON, Canada; 2. Sunnybrook Health Sciences Centre, Toronto, ON, Canada.*

Background While considered safe, simultaneous resection of colorectal cancer and liver metastases is not performed routinely. We aimed to identify practice patterns, short and long-term outcomes of simultaneous vs. staged resection for synchronous colorectal cancer liver metastases. Methods We conducted a population-based cohort study of patients undergoing resection for synchronous colorectal cancer liver metastases from 2006-2015 by linking administrative healthcare datasets in Ontario, Canada. Resection of the primary cancer and liver metastases within six months was considered synchronous. Simultaneous (same hospital admission) and staged resections were compared. Outcomes were 90-day post-operative mortality, total length of hospital stay, overall survival (OS) and healthcare costs. Survival for the staged group was measured from the last surgical resection to death and estimated using Kaplan Meier. Cost analysis was undertaken from the perspective of a third-party payer. Results Of 2,738 patients undergoing colorectal and liver resection for cancer, 1,168 were synchronous, of which, 442 underwent simultaneous resection. The rate of simultaneous resections increased on average by 3% per year (p=0.02). Compared to staged resections, median total length of stay was shorter (8 vs. 11 days); 90-day post-operative mortality was higher (3.4% vs 1.2%); and readmission rate was higher (23% vs. 18%) for simultaneous resections. Median OS was worse with simultaneous resection (40 months, 95%CI 35-46 vs. 78 months, 95%CI 59-86), with 5-year OS of 37% (simultaneous) and 55% (staged). Mean overall costs were lower for simultaneous resections ($12,722 CAD vs. $16,455 CAD). Conclusion Simultaneous compared to staged resection for patients with synchronous colorectal cancer liver metastases is associated with higher 90-day readmission and postoperative mortality and worse survival. It was associated with shorter length of hospital stay and lower costs for the health cares system. Considering selection bias, randomized studies would be necessary to determine the role of simultaneous resection for synchronous disease colorectal cancer liver metastases.

P220

High CD73 Expression in Pancreatic Cancer is Associated with Accelerated Cell Cycle, Cell Adhesion and Worse Survival E. Katsuta,* L. Yan, S. Hochwald, K. Takabe. *Roswell Park Comprehensive Cancer Center, Buffalo, NY.*

Background: CD73 is a cell surface enzyme which converts ATP and ADP to adenosine together with CD39. High CD73 expression is associated with malignant potentials, including angiogenesis, immune suppression, tumor growth, and promoting metastasis in some types of malignancies. However, its role in pancreatic cancer remains unknown. This study aimed to clarify the role of CD73 in pancreatic cancer. Methods: CD73 was overexpressed in murine pancreatic cancer cell line, Panc02, for in vitro and in vivo study. Utilizing The Cancer Genome Atlas (TCGA), patients were classified into CD73 high and low expression group. Clinical factors and molecular signature were compared between these two groups. Results: CD73 overexpressed pancreatic cancer cells showed increased proliferation compared to control cells (p<0.001) with higher

G2 (p=0.004), S (p<0.001), and lower G1 phase proportion (p<0.001). Mice implanted with CD73 overexpressed cells had significantly shorter survival compared from control cells in murine carcinomatosis model (p=0.020). In TCGA cohort, there was no significant difference in clinicopathological features between CD73 high and low expressing groups. CD73 expression did not correlate with the expression of CD39 nor adenosine receptors (ADORA1, ADORA2A, ADORA2B and ADORA3). Correlation analysis and pathway analysis demonstrated that cell cycle and cell adhesion related genes were upregulated in CD73 high expression group, whereas there is no significant difference in angiogenesis related genes or immune suppressive related genes between these two groups. Patients with CD73 high expression group showed worse prognosis in both disease-free survival (DFS) and overall survival (OS) (p<0.001, p<0.001, respectively). These findings were reproduced in completely independent cohort, GSE28735 (OS: p=0.019). Multivariate analysis revealed that CD73 was the only independent prognostic factor for both DFS and OS (p=0.001 and p=0.005, respectively). Conclusions: High expression of CD73 associated with promoted cell cycle, increased cell adhesion and worse prognosis in pancreatic cancer in in vitro, in vivo and the patient cohort.

P221

Safety Net Hospital Status is Associated with Worse Oncologic Outcomes in Four Most Prevalent Solid Tumors C.A. Hester,* N. Karbhari, M. Augustine, J. Mansour, M. Leitch, P.M. Polanco, M. Porembka, S. Wang, R. Wooldridge, H. Zeh, D. Farr, A. Yopp. *Surgical Oncology, University of Texas Southwestern, Dallas, TX.*

Introduction: Racial/ethnic minorities have associated worse oncologic outcomes in many cancers and predominately receive their health care at safety net hospitals (SNHs). We hypothesize that patients receiving cancer care at SNHs have worse survival for the four most prevalent solid organ cancers: breast cancer (BC), colorectal cancer (CRC), lung cancer (LC), and prostate cancer (PC). Methods: Patients with the aforementioned cancers were identified in the Texas Cancer Registry (2004-2015). We compared system- and patient-level factors in patients diagnosed at non-SNHs, low-proportion SNHs (l-SNHs), and high-proportion SNHs (h-SNHs). H-SNH status and l-SNH status were defined as occupying the top 10% and 25% of the disproportionate share hospital index. Covariate-adjusted treatment use and DSS were compared among hospital categories. Results: H-SNHs disproportionately delivered care to young, uninsured, racial/ethnic minority patients who presented with more advanced disease compared to n-SNHs and l-SNHs across all four cancers. Compared to n-SNHs, h-SNHs had significantly decreased treatment receipt in stage-matched cohorts across all cancer types except early stage prostate cancer; l-SNHs had similar or increased treatment receipt. H-SNH status was independently associated with decreased odds of treatment receipt for PC (OR 0.53, 95%CI 0.49-0.56), CRC (OR 0.89, 95%CI 0.81-0.97), and LC (OR 0.94, 95% CI 0.90-1.00) but not BC (OR 1.09, 95%CI 1.02-1.18). L-SNH status had similar receipt of any treatment for CRC (OR 0.97, 95%CI 0.90-1.04) and LC (OR 1.03, 95%CI 0.98-1.09) and was independently associated with increased treatment receipt for BC (OR 1.42, 95% 1.33-1.51) and PC (OR 1.36, 95%CI 1.29-1.43). Among patients who were treated, h-SNHs had increased time to treatment compared to n-SNH and l-SNH for all cancers. L-SNH and h-SNH status were independently associated with worse DSS compared to n-SNH in all cancers. Conclusion: H-SNH status was associated with decreased treatment receipt for CRC, PC, and LC, but increased for BC compared to n-SNH status. L-SNH and h-SNH status were associated with worse DSS compared to n-SNH for all cancers.

1-year and 5-year disease specific survival stratified by cancer type

	1-year DSS	5-year DSS	p
Breast	.	.	<0.001
n-SNH	98.1%	91.4%	
l-SNH	97.3%	89.1%	
h-SNH	96.6%	85.5%	
Prostate	.	.	<0.001
n-SNH	99.1%	97.0%	
l-SNH	98.5%	95.3%	
h-SNH	97.8%	92.1%	
Colorectal	.	.	<0.001
n-SNH	87.4%	71.3%	
l-SNH	86.7%	68.6%	
h-SNH	84.0%	63.6%	
Lung	.	.	<0.001
n-SNH	57.2%	31.4%	
l-SNH	52.5%	25.5%	
h-SNH	49.6%	22.5%	

Table: 1-year and 5-year disease specific survival stratified by Breast, Prostate, Colorectal and Lung Cancers

P222

Pathologic Nodal Staging of Resected Pancreatic Adenocarcinoma Predicts Survival Regardless of Treatment Sequencing A. Lee,* L.R. Prakash, Y. Chiang, T.J. Vreeland, M. Kim, N. Ikoma, T. Aloia, J. Vauthey, J.E. Lee, M.H.G. Katz, C.D. Tzeng. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

INTRODUCTION Retrospective cohort studies have consistently shown lower rates of nodal positivity following neoadjuvant therapy (NT) compared to surgery-first (SF) sequencing for patients with resected pancreatic adenocarcinoma (PDAC). However, it is unclear whether post-NT pathologic nodal stage (ypNx) has similar survival implications compared to surgery upfront nodal stage (pNx). The primary aim of this study was to compare OS between NT and SF patients by nodal stage using the new American Joint Committee on Cancer 8th edition staging system (AJCC8). METHODS This was a retrospective cohort study using a prospectively maintained database at a single high-volume referral center, analyzing patients with resected PDAC from 2010-2016. Patients were staged using the current AJCC8 system, which was developed from a cohort of SF patients. Our patients were classified as SF vs. NT, and compared using Kaplan-Meier plots and log-rank tests. RESULTS Of 369 total patients, 94 (25.5%) underwent SF, and 275 (74.5%) underwent NT followed by surgery. Preoperatively, nearly all patients (98.9%) in the SF group had potentially resectable clinical stage, whereas NT patients had more advanced clinical stages (borderline resectable 30.9%, locally advanced 6.6%). Although SF patients had lower clinical stages at presentation, NT patients had lower rates of node-positivity on final pathology compared to SF (ypN0: 52.3% vs. pN0: 26.6%; ypN1: 28.4% vs. pN1: 30.8%; ypN2: 19.3% vs. pN2: 42.6%; p<0.001). For each comparable pathologic nodal stage, SF and NT groups had similar 5-year OS [pN0 (64.9%) vs. ypN0 (52.3%), p=0.339], [pN1 (34.8%) vs. ypN1 (28.3%), p=0.928], and [pN2 (13.6%) vs. ypN2 (16.4%), p=0.987]. CONCLUSIONS The new AJCC8 nodal staging system appropriately stratifies oncologic outcomes for each post-NT nodal stage for patients with resected PDAC. Pragmatically, despite presenting with more advanced clinical stage compared to SF patients, NT patients had lower rates of nodal metastases yet comparable OS when stratified by final pathologic nodal staging. These data provide further support for biologic and clinical downstaging of PDAC treated with NT.

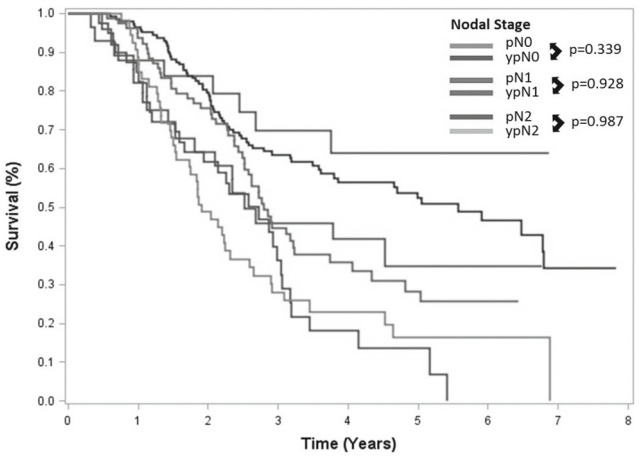


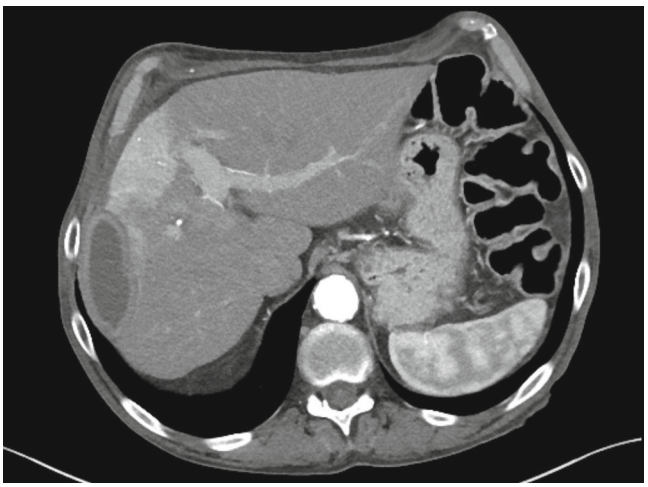
FIGURE: Patient survival stratified by treatment sequencing and pathologic nodal stage

P223

Radiation Spacer Placement to Facilitate Radiation Therapy in Unresectable Liver Tumors L. Yohanathan,* C. Hallemeier. *Hepatobiliary Surgery, Mayo Clinic, Rochester, MN.*

For primary and secondary liver tumors surgery provides curative intent therapy in the form of resection or transplantation depending on the etiology and distribution of disease. When surgery is not possible due to anatomic unresectability or conditional factors, other modalities have been employed i.e. chemotherapy and radiation. The ability to deliver full doses of radiation can be hindered by proximity of adjacent organs. Herein we describe our experience

with placement of customized biologic mesh spacers between the liver and adjacent viscera to facilitate full dose radiation treatment. Methods: Following IRB approval patients (pts) undergoing surgical placement of spacers were identified between 2015-2018. Demographics, clinical/operative parameters, radiation therapy details and follow-up were abstracted. Results: A total of 8 pts underwent spacer placement between 2015-2018 using 3 or 4mm thick biologic mesh constructed into a pouch. Median age was 64years (43-76). Two pts were male, six were female. Diagnoses were hepatocellular cancer (HCC,n=4), intrahepatic cholangiocarcinoma (n=1), colorectal liver metastases (n=2) and metastatic gastroesophageal adenocarcinoma (n=1). Three pts with HCC had cirrhosis with retained liver function (MELD=7). Five pts underwent a laparoscopic approach and 3 pts an open approach. Short term complications were seen in 2 pts. One with persistent abdominal pain relieved by aspiration of the spacer following radiation, and one pt with adhesion of small bowel over the spacer requiring reoperation for adhesiolysis before radiation. Median number of days from operation to radiation was 13 days (6-19) with expansion of the spacer with fluid in all. Radiation modality was photon in 5 pts, proton in 3 pts. The radiation dose was 50 to 60 Gy in 5 fractions (6 pts) and 67.5 Gy in 15 fractions (2 pts). Conclusion: For patients with unresectable tumors amenable to radiation therapy, placement of a spacer allows for safe administration of full doses of radiation and is a feasible strategy to address proximity of adjacent organs and critical structures. There is minimal morbidity in our limited experience, including in patients with cirrhosis.



Shown here is a picture of the expanded spacer between the liver and the colon adn pylorus of the stomach (video available for presentation)

P224

Differences in Outcome for Patients with Cholangiocarcinoma: Racial/Ethnic Disparity or Socioeconomic Factors? R.M. Lee,[2]* Y. Liu,[1] M.Y. Zaidi,[2] A.C. Gamboa,[2] C. Staley,[2] D.A. Kooby,[2] M.C. Russell,[2] K. Cardona,[2] S. Maithel.[2] *1. Biostatistics and Bioinformatics Shared Resource, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA.*

Background: Inequities in cancer survival are well documented. Whether disparities in overall survival (OS) result from inherent racial differences in underlying disease biology or socioeconomic factors (SEF) is unknown. Our aim was to define the association of race/ethnicity and SEF with OS in pts with cholangiocarcinoma (CCA). Methods: Pts with CCA of all sites and stages in the National Cancer Data Base (2004-14) were included. Racial/ethnic groups were defined as non-Hispanic White (NH-W), non-Hispanic Black (NH-B), Asian, and Hispanic. Income and education were based on census data for pts' zip code. Income was defined as high (≥$63,000) vs low (<$63,000). Primary outcome was OS. Results: 27151 pts were included with a mean age of 68 yrs; 51% were male. 78% were NH-W, 8% NH-B, 6% Asian, and 6% Hispanic. 56% had Medicare, 33% private insurance, 7% Medicaid, and 4% were uninsured. 67% had high income. 21% lived in an area where >20% of adults did not finish high school. NH-B and Hispanic pts had more unfavorable SEF including uninsured status, low income, and less formal education than NH-W and Asian pts (all p<0.001). They were also younger, more likely to be female and to have metastatic disease (all p<0.001). Despite this, NH-B race and Hispanic ethnicity were not associated with decreased OS. Male sex, older age, non-private insurance, low income, less education, non-academic facility, location outside the Northeast, higher Charlson-Deyo score, worse grade, larger tumor size, and higher stage were all associated with decreased OS (all p<0.001). On MV analysis, along with adverse pathologic factors, type of insurance (p=0.003), low income (p<0.001), and facility type and location of treatment (p<0.001) remained associated with decreased OS; non-white race/ethnicity was not. Conclusion: Disparities in survival exist in CCA, however they are not driven by race/ethnicity. Non-privately insured and low-income pts had decreased OS, as did pts treated at non-academic centers and outside the Northeast. This suggests that decreased ability to access and afford care results in worse outcomes, rather than biological differences amongst racial/ethnic groups.

P225

Association Between Travel Distance, Hospital Volume and Outcomes Following Resection or Transplantation for Hepatocellular Carcinoma E.W. Beal,* R. Mehta, J. Hyer, A. Paredes, K. Merath, M. Dillhoff, J. Cloyd, A. Ejaz, T. Pawlik. *The Wexner Medical Center at the Ohio State University, Columbus, OH.*

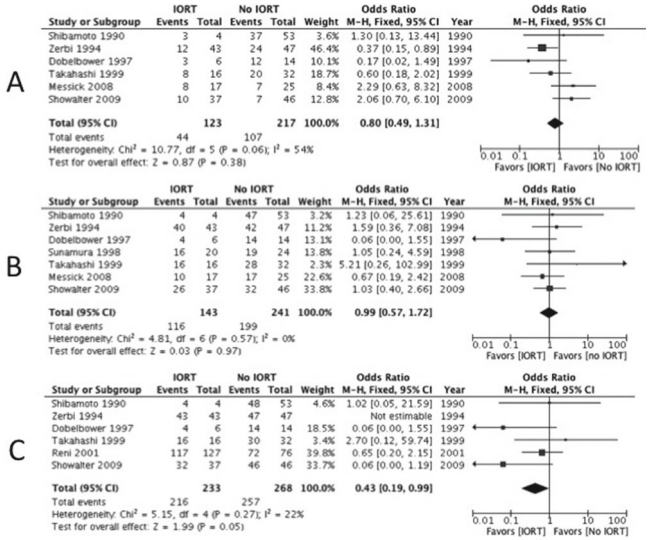
Background: Data on the impact of hospital/surgeon volume and travel distance on patient outcomes after major abdominal surgery remain poorly defined. We sought to characterize the relationship among travel distance, hospital volume and long-term outcomes after resection or transplantation for hepatocellular carcinoma (HCC). Methods: The 2004-2015 National Cancer Database was used to identify patients who underwent resection or transplantation for HCC. Patients were stratified according to travel distance and hospital volume quartiles and multivariable Cox regression models were utilized to examine the impact of travel distance, hospital volume and travel distance/hospital volume on overall survival (OS). Results: Among the 23,209 patients identified, procedures included liver transplantation (N=9,980, 43%), partial hepatectomy (N=5,234, 23%), or right (N=2,224, 10%) and left (N=1,164, 5%) hepatectomy. Stratifying data into quartiles, travel distance to surgical care was: ≤4.3 miles (mi), >4.3-10.1 mi, >10.1-29.3 mi, and ≥29.3 mi, while hospital volume was: 1-4, 5-9, 10-22, ≥ 23. On multivariable analysis, increased hospital volume was associated with improved OS (HR 0.57, 95% CI 0.46-0.71, p<0.001). In a separate multivariable model that controlled for factors except hospital volume, a longer travel distance was also associated with an improved OS (HR 0.77, 95% CI 0.61-0.96, p<0.025). Of note, the association of travel distance with OS seemed to be mediated through hospital volume as only hospital volume was associated with OS (HR 0.48, 95% 0.40-0.59, p<0.001) after controlling for both travel distance and hospital volume. Conclusions: Increased travel distance was associated with improved overall survival, however the association appeared to be mediated through the effect of increased hospital volume. The benefits of undergoing resection or transplantation for HCC at a high-volume hospital appear to outweigh the inconvenience of longer travel distances.

P226

Short- and Long-term Outcomes of Intraoperative Radiation During Pancreatectomy for Pancreatic Cancer: A Meta-analysis S. Cass, F. Macedo,* K. Kelly, D. Yakoub, A.S. Livingstone, D. Franceschi, N. Merchant. *Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL.*

INTRODUCTION: Despite the significant improvements over last decade, pancreatic cancer (PC) remains one of the most lethal malignancies. Even after resection, local failure rates are as high as 60%. Intraoperative radiation (IORT) has been introduced to enhance local control in PC, however remains highly controversial. METHODS: An online database search of MEDLINE was performed. Key bibliographies were reviewed. Studies comparing outcomes for patients with pancreatic cancer undergoing pancreatectomy with or without IORT were included. Odds ratios with corresponding 95% confidence intervals (CI) by random fixed effect models of pooled data were calculated. Primary endpoints were 1-year, 3-year and 5-year overall survival (OS). RESULTS: The initial literature review yielded 65 articles. Ten articles were included in the final analysis. A total of 696 patients were included in the analysis, 305 (43.8%) underwent IORT and 391 (56.2%) underwent pancreatic resection without IORT. Mean age was 61.2 years vs. 67 years (IORT vs. no IORT, respectively, p=0.180). Resection with IORT yielded similar 1-year OS [OR

0.80, 95% CI 0.49-1.31, p =0.380] (Fig. 1A), and 3-year OS [OR 0.99, 95% CI 0.57-1.72, p=0.970] compared to without IORT (Fig. 1B). There was a trend towards improved 5-year OS with IORT [OR 0.43, 95% CI 0.19-0.99, p =0.050] (Fig. 1C) when compared to those undergoing pancreatectomy without IORT. CONSLUSIONS: This is the first meta-analysis assessing the outcomes of patients with PC who underwent surgical resection with IORT. IORT did not present any short-term survival benefit compared with no IORT, however was possibly associated with superior long-term survival. These findings suggest a potential role for IORT in selected patients with resectable PC. Further evidence regarding local control and relapse rates after pancreatectomy with IORT is warranted.



P227

Role of Liver Resection in Selected Patients with Metastatic Breast Cancer: A Paradigm Shift Underway? F. Macedo,* R. Fayne, N. Song, D. Yakoub, D. Franceschi, A.S. Livingstone, N. Merchant. *Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL.*

INTRODUCTION: The value of liver resection (LR) in breast cancer liver metastases (BCLM) is controversial while prognosis without surgery remains poor. Recent evolution in systemic therapy has enabled surgical resection of metastatic lesions in several cancer populations with associated improved overall survival (OS). We sought to investigate the role LR in BCLM as a potential therapeutic option. METHODS: National Cancer Data Base (NCDB) was queried for patients with metastatic breast cancer to the liver diagnosed from 2010 to 2014. Actuarial estimates for OS were calculated using Kaplan-Meier methods. Log-rank and Cox multivariable regression analysis were performed to compare the outcomes of patients undergoing liver resection, systemic treatment, and those with multiorgan disease. RESULTS: A total of 9,244 patients with BCLM were included in the analysis. Median age was 58 years (IQR 49-68 years). Of them, 6,654 (72%) patients were Caucasians and 2,630 (28.5%) had metastatic disease confined to the liver. Only 2,671 (28.9%) patients underwent chemotherapy. Median OS was 18.3 months (IQR 5-37.7 months): 35.9 vs. 20.1 months (metastasectomy vs. no metastasectomy, p<0.001). Subgroup analysis demonstrated that resection was superior solely in ER+ tumors (41.7 vs. 25.2 months, p<0.002) and those with metastasis confined to the liver (69.7 vs. 35.2 months, p<0.001). Chemotherapy combined with LR was superior to chemotherapy alone (66.9 vs. 56.3 months, p=0.037) in patients with metastasis confined to the liver. After controlling for patient and tumor variables, LR (HR 1.724, 95% CI 1.135-2.620) was an independent predictor of improved survival. Age, grading, PR status, comorbidity status and African-American race negatively impacted OS. CONCLUSIONS: This is the largest series thus far assessing the role of LR in patients with BCLM. Liver resection combined with systemic treatment may result in improved OS compared to systemic treatment alone in patients with stage IV breast cancer confined to the liver. Resection should be considered in selected patients with isolated BCLM.

P228

Solid Pseudopapillary Neoplasms of the Pancreas: Surgical Resection and the Impact on Survival C.J. LaRocca,* A. Nguyen, P. Ituarte, L.G. Melstrom, S. Warner, B. Lee, G. Singh. *Surgery, City of Hope National Medical Center, Duarte, CA.*

Introduction: Solid pseudopapillary neoplasms (SPN) are rare pancreatic tumors. Much of the published data consists of single-center experiences. In this study, we used a population-based analysis to investigate factors predictive of survival. Methods: The Surveillance, Epidemiology, and End Results (SEER) database was queried to find patients who were diagnosed with SPNs from 1989-2014. The rank sum and Fisher's exact tests were used to perform bivariate analyses. The Kaplan-Meier method was used for survival studies. Univariate and multivariate regression analyses were used to identify variables associated with overall survival (OS). Results: The incidence is 0.1 cases per one million persons annually (age-adjusted based on 2000 census data). Of the 162 cases identified, 84% were female and the median age was 35 (range 8-71). 41% of patients were white, 29% were Hispanic, and 18% were black. The median tumor size was 5.2 cm and 12% of cases had distant metastatic disease at the time of diagnosis. 45% of tumors were in the tail of the pancreas, 26% were in the head, and 13% were in the body. 86% of patients underwent surgical resection. Median follow up was 50.5 months. Five-year OS was 90.6%. Surgical resection conferred a longer five-year OS when compared to those patients with unresected tumors (94.7% vs 66.1%, p<0.05). Receipt of surgical resection was not significantly associated with age, gender, race, marital status, insurance, or geographic region. Age (Hazard ratio [HR]=1.06), male gender (HR=3.59), distant metastatic disease at diagnosis (HR=37.29), and surgical resection (HR=0.13) were predictive of survival on univariate analysis (p<0.05). Race, geographic region, tumor size, and tumor location were not significantly associated with survival. On multivariate analysis, age (HR=1.05) and metastatic disease (HR=10.98) remained predictive of worse OS, and undergoing surgical resection (HR=0.14) continued to be associated with improved survival (p<0.05). Conclusion: Solid pseudopapillary neoplasms are uncommon pancreatic tumors with a good prognosis. Surgical resection resulted in a significant survival benefit and should be offered to patients whenever possible.

P229

Laparoscopic Pancreaticoduodenectomy: The Importance of Sustaining the Program Beyond the Early Learning Phase A. Paniccia,[1]* R. Torphy,[2] R. Schulick,[2] B. Edil.[2] *1. Surgery - Surgical Oncology, UPMC, Pittsburgh, PA; 2. University of Colorado, Denver, CO.*

Introduction: Total laparoscopic pancreaticoduodenectomy (TLPD) utilization continues to increase, nevertheless most centers are discouraged by the steep learning curve during the early adoption phase. We sought to conduct a qualitative analysis of an established TLPD program to describe its learning curve and compare early versus late outcomes. Methods: Patients undergoing TLPD between 2012 and 2017 at a tertiary referral center were identified in a prospectively maintained institutional database. Restricted cubic splines were employed to examine the functional relationship between increasing surgeon experience and outcomes. Parametric and non-parametric statistics were utilized to compare outcomes between early and late phases of the learning curve. Results: Ninety patients underwent a TLPD, 10% required conversion to laparotomy, no deaths occurred within 90-days. Statistical improvement in operative time (339.5 vs. 303 minutes, p<0.04) and rate of pancreatic fistula grade B (32% vs. 9.7%, p=0.03) occurred after 50 cases. Although statistical significance was not reached, other pancreatic specific metrics showed an undeniable trend toward improvement, including decreased rate of delayed gastric emptying (12% vs. 3%), bile leak (10% vs. 0%), postoperative bleeding grade ≥ 3 (6% vs. 3%), pseudoaneurysm (6% vs. 0%), Clavien-Dindo complication rate grade ≥ 3 (38% vs. 29%), median length of stay (11 vs. 9 days), and 90-day readmission rate (30% vs. 19%). Median estimated blood loss (300 mL vs. 300 mL), median number of lymph nodes harvested (18 vs. 19), R0 resection rate (98% vs. 96%), and patient characteristics, including age, sex, comorbidities, BMI and tumor size were similar in both phases. In addition, the cases of TLPD performed for PDAC increased in the late phase (36% vs. 68%, p=0.005). Conclusion: Herein, we define our institutional early phase learning curve as 50 cases and show a trend toward decreased pancreatic specific complications after this point. This analysis emphasizes the importance of understanding the learning curve prior to analyzing TLPD data, judging its merit, and comparing it to open pancreaticoduodenectomy outcomes.

P230

Assessing Pancreatic Cancer Survival Disparities Using the National Cancer Data Base G. Edwards,* X. Shu, M. Tan, K. Idrees, C. Bailey. *Surgery, Vanderbilt University Medical Center, Nashville, TN.*

Introduction: Little is known regarding the impact of treating facility type on socioeconomic-driven survival disparities in patients with pancreas adenocarcinoma (PAC). The primary aim of this study is to quantify disparities in overall survival (OS) associated with race, insurance status and type of treating facility for patients with PAC. Methods: A retrospective analysis was performed using the National Cancer Database. All patients diagnosed with PAC from 2004 to 2014 were included. Treating facility was classified as community cancer center (CCC; 100-500 cases/yr), comprehensive community cancer center (CPCC; >500 cases/yr), academic hospital (AH; teaching hospital with >500 cases/yr), or integrated network cancer center (INC; multi-center organization). Demographic and clinical factors were compared according to type of treating facility. Multivariable Cox proportional hazard analyses were used to assess the impact of race, insurance status, and facility type on OS. Results: Patients treated at an AH had improved OS compared to treatment at a CCC (HR 1.18, 95% CI 1.16-1.20;P<0.001), CPCC (HR 1.17, 95% CI 1.16-1.18;P<0.001), and INC (HR 1.14, 95% CI 1.12-1.16;P<0.001). Privately insured patients had improved OS compared to patients without private insurance (HR 1.03, 95% CI 1.01-1.03). However, insurance status disparities were mitigated according to type of treating facility ($P_{interaction}$=0.007). There was no difference in OS based on insurance status for patients treated at an AH, whereas patients without private insurance treated at non-AH had slightly worse OS (HR 1.03, 95% CI 1.02-1.04; P<0.001) compared to patients with private insurance. OS was improved for patients of other race (Hazard ratio [HR] 0.82, 95% Confidence interval [CI] 0.80-0.84; P<0.001) but was similar among black compared to white patients. Racial disparities were not mitigated according to type of treating facility ($P_{interaction}$=0.182). Conclusions: Other race, private insurance and treatment at AH were independently associated with improved OS in patients with PAC. Insurance-based, but not race-based, survival disparities are reduced at AH compared to other facilities.

P231

Surgical Resection of High-grade Non-functional Pancreatic Neuroendocrine Carcinoma is Associated with Improved Overall Survival in Node-Positive Patients J.P. Jiang,* E. Park, S.S. Kim, T.R. Donahue, M. Girgis. *David Geffen School of Medicine at UCLA, Los Angeles, CA.*

Introduction: Treatment guidelines have not clearly established the role of surgery in high-grade non-functional pancreatic neuroendocrine carcinomas (nf-PNEC). Currently, the 2010 North American Neuroendocrine Tumor Society consensus guidelines does not routinely recommend surgery in tumors beyond stage T1-2, N0. The objective of this study was to evaluate the effect of surgery on survival in high-grade nf-PNEC. Methods: The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database was used to identify patients with high grade nf-PNEC diagnosed between 2004-2015. Patients with additional malignancies were excluded. Data regarding patient demographics, cancer extent, therapeutic approaches, and survival were recorded. Tumor characteristics were evaluated using the American Joint Committee on Cancer 8th edition staging system. Results: 454 patients with high-grade nf-PNEC were identified. The median overall survival (OS) for the entire cohort was 10 months (IQR: 2,28 months). The average age was 63 (IQR: 54, 73). 152 (33.5%) patients underwent surgery. On univariate analysis, higher T-stage (T1-2: 35.2% vs. T3-4: 65.5%; p<0.001) was associated with nodal disease, and nodal involvement was not associated with worse survival (p=0.237). Multivariate Cox regression modeling showed that surgery (HR:0.30, p<0.001) was independently associated with improved survival. Negative predictors of survival included nodal involvement (HR:1.39, p<0.035) and distant metastases (HR:1.99, p<0.001). The median OS for node negative patients that underwent surgery was better than those who did not (100 vs. 9 months, p<0.001). Finally, patients with node positive disease that underwent surgery had better OS than those who did not (31 vs. 3 months, p<0.001) (Figure). Conclusion: These data suggest that surgery for node positive high-grade nf-PNEC is associated with prolonged OS. Although further studies need to elucidate this relationship, surgery should be considered in the treatment algorithm in patients with node positive high-grade nf-PNEC.

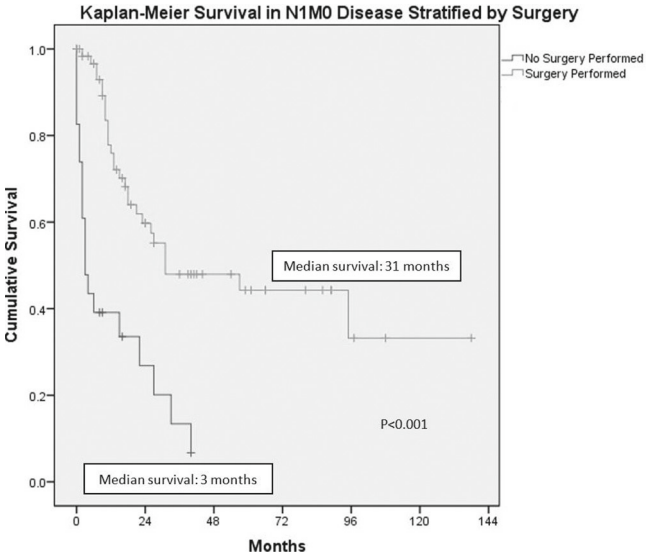


Figure. Kaplan-Meier survival function of N1M0 nf-PNEC stratified by surgery.

P232

Identifying Prohibitive Risk Factors for Resection in Non-Metastatic Pancreatic Neuroendocrine Tumors B.M. Heidenreich,[1]* J.M. Bader,[1] V.V. O'Connor,[2] D.W. Nelson.[1] *1. General Surgery, William Beaumont Army Medical Center, El Paso, TX; 2. Kaiser Permanenter Los Angeles Medical Center, Los Angeles, CA.*

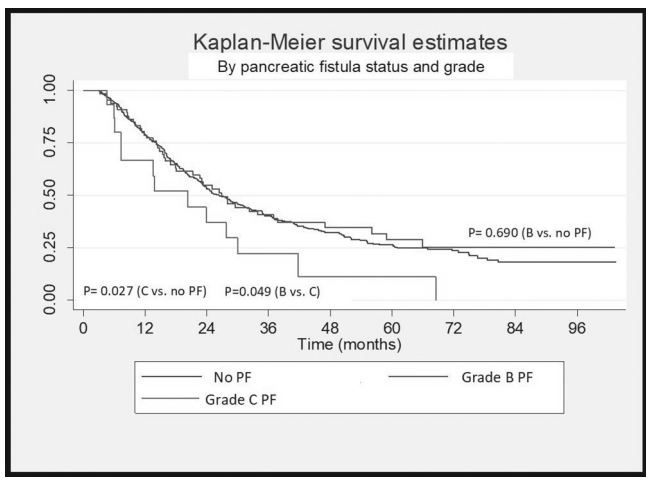
Introduction Patient comorbidities can influence recommendations for pancreatectomy in pancreatic neuroendocrine tumors (pNET). Prohibitive risks factors have not been well described. The purpose of this study is to identify potential patient and disease-related factors associated with prohibitive risk for resection. Methods Using the 2014-2016 ACS-NSQIP targeted pancreatectomy database, all patients undergoing formal resection for non-metastatic pNET were identified. Patient and disease-related characteristics were examined. Multivariable analysis was performed to determine risk factors for 30-day morbidity and mortality. Results 1,835 patients underwent formal pancreatectomy for non-metastatic pNET. Median age was 60 years. Patients were more frequently male (53.2%), Caucasian (83.6%), functionally independent (99.3%) and non-smokers (87.1%). The most frequent comorbidities included hypertension (50.3%) and diabetes (19.6%), and the majority of patients were ASA ≥3 (66.8%). Surgical resection consisted of 63.4% (n=1163) distal pancreatectomy, 34.9% (n=640) pancreaticoduodenectomy, and 1.7% (n=32) total pancreatectomy. The majority of tumors were malignant non-functioning pNET (69.5%), stage T1-3 (98.5%), with just 27.9% node positive cases. Overall 30-day morbidity and mortality were 27.3% and 1.2% respectively. The most common complications were deep organ space infections (16.4%) and sepsis (8.8%). Significant independent predictors of overall morbidity included BMI ≥30, ASA ≥3, and presence of preoperative biliary stent. However, only age ≥70 (OR 3.61; CI 1.47-8.87; p=0.005) and hypertension (OR 3.62; CI 1.01-12.94; p=0.05) were independently associated with increased 30-day mortality. Conversely, female sex and absence of biliary stent were associated with 78% and 80% reduction in likelihood of death within 30 days, respectively. Conclusion This series highlights multiple factors associated with early postoperative morbidity and mortality for patients undergoing pancreatectomy for non-metastatic pNET. Special consideration should be given to males, aged ≥70 with hypertension as these characteristics had significantly increased rates of death within 30 days.

P233

Impact of Post-Operative Pancreatic Fistula on Long-term Outcomes After Pancreatic Resection for Periampullary Adenocarcinoma

J.W. Bonaroti,[1]* M. Zenati,[1] A. Al-Abbas,[1] C. Rieser,[1] A.H. Zureikat,[1] B.A. Boone.[2] *1. Surgery, University of Pittsburgh, Pittsburgh, PA; 2. West Virginia University, Morgantown, WV.*

Introduction: The short-term morbidity associated with a post-operative pancreatic fistula (PF) is well established, however data regarding the long-term impact of PF are lacking. Limited studies examining outcomes present conflicting data and do not differentiate by PF grade. The goal of this study is to characterize long-term outcomes of PF after pancreatic resection for periampullary adenocarcinoma. Methods: A single institution study of all pancreatic resections, including pancreaticoduodenectomy and distal pancreatectomy, performed for periampullary adenocarcinoma from 2008 to 2016. PF was defined by ISGPF criteria. Kaplan-Meier survival analysis, logistic regression, and multivariate analysis (MVA) were used to evaluate the impact of PF on overall survival (OS), disease free survival (DFS), time to initiation of adjuvant therapy, and receipt of adjuvant chemotherapy (AC). Results: 767 patients were included; age 67.2 +/- 10.2 years and 47.5% female. Of those, 82 (10.7%) developed a Grade B (n=67, 8.7%) or C PF (n=15, 2.0%). Patients with a Grade C PF had decreased median OS when compared to no PF (20.33 vs 26.87 months, p=0.027) and compared to Grade B PF (20.33 vs. 26.87 months, p=0.049). PF patients also had a trend towards decreased median DFS when compared to the remaining cohort (9.13 vs 20.3 months, p=0.072). Patients with PF were less likely to receive AC than those without PF (59.5% vs 74.9%, p=0.003) and Grade C PF were less likely to receive AC than all others (26.7% vs 74.2%, p=0.0001). Patients with PF had longer median time to initiation of AC than those without PF (75 vs 61 days, p=0.002), and Grade C had a trend towards longer time to initiation of AC than all others (86 vs 62 days, p=0.083). On MVA, Grade C PF was independently associated with failure to receive AC (OR 0.18, CI (0.05,0.65); p=0.009). Conclusion: Patients who develop PF are less likely to receive AC and are more likely to have delay in time to receive AC. These factors are exacerbated in Grade C PF and likely contribute to decreased OS. Importantly, these findings validate the clinical significance of the updated ISGPS definitions of post-operative PF.



Overall survival in patients undergoing pancreatic resection for periampullary malignancy, stratified by post-operative pancreatic fistula. Grade C leak was associated with significantly worse overall survival when compared to Grade B leak and the remaining cohort.

P234

What is the Cure Rate After resection for Pancreatic Cancer?

A. Nevler,[1]* S.W. Keith,[1] J.R. Brody,[1] J. Winter.[2] *1. Thomas Jefferson University, Philadelphia, PA; 2. University Hospitals Cleveland Medical Center, Cleveland, OH.*

Background: Long-term outcomes for resected pancreatic ductal adenocarcinoma (PDA) are typically presented in terms of 5-year survival (~20%). Since many patients, who underwent curative-intent resection recur beyond this point, the chance of cure remains uncertain. Here, we attempt to estimate the cure rate through an integrated analysis of national administrative datasets. Methods: PDA survival rates from the SEER Cancer Database (1975-2012) were compared to age-stratified estimates from Social Security Life-Tables. A statistical model was utilized to explore how frequently patients experience a return to a normal life expectancy after pancreatic surgery for pancreatic cancer. The "Time-to-cure" was defined for each age group as the minimum survival interval after resection before a return to a normal life expectancy was observed for the group. This conditional interval represents the point where we can best estimate that a patient is statistically "cured" (i.e., life expectancy has returned to the norm). Therefore, the estimated "cure rate" equals the percentage of PDA patients who ultimately achieved a normal life expectancy after resection. Results: In the SEER PDA cohort, patients younger than 65 years of age rarely had a return to a normal life expectancy ("cure"), compared to age-matched controls (<1% of the time). Patients between 75 and 80 years experienced a renormalization of their life expectancy (statistical likelihood of "cure") more than 5% of the time. Octogenarian patients reached a normal life expectancy more than 10% of the time, which reflects the reduced, expected remaining life span of the elderly age-matched control group, compared to younger patients. For most PDA patients, the median "Time-to-cure" exceeded 12 years. Conclusions: Comparison of survival outcomes using the SEER and Social Security datasets reveals that renormalization of life expectancy, as a metric of PDA cure after resection, is an exceptionally rare event. These data underscore the unique aggressiveness of PDA and the systemic quality of the disease, even when diagnosed and treated at an early stage with "curative intent". In general, surveillance should continue well beyond 5 years after resection.

Estimated cure rates after resection for pancreatic cancer (N=5487, SEER) stratified by gender and age.

	Base Model (Assumption of fixed life expectancy of control patients)		
Age (Years)	Goal life expectancy (Years)*	Time to cure (Years)	Cure rate (%)
50-55	83.4	>25	<1%
55-60	84.3	25	<1%
60-65	84.9	21	<1%
65-70	85.7	15	1.6%
70-75	86.7	12	2.3%
75-80	88.1	8	5.7%
80-85	90.1	5.5	11.8%

*Available from Social Security Actuarial life tables.

P235

The Association Between Elevated CA 19-9 and Recurrence, Site of Recurrence, and Overall Survival in Upfront Resectable Pancreatic Cancer

B. Powers,[1]* J.K. Kim,[2] D.K. Deperalta,[1] T. Ogami,[2] J. Pimiento,[1] P.J. Hodul,[1] M.P. Malafa,[1] J. Fleming.[1] *1. Gastrointestinal Oncology, Moffitt Cancer Center, Tampa, FL; 2. University of South Florida School of Medicine, Tampa, FL.*

INTRODUCTION: Current practice guidelines for pancreatic adenocarcinoma (PDAC) recommend consideration of neoadjuvant therapy for patients with elevated CA 19-9. We sought to assess the association of preoperative elevated CA 19-9 (>1,000 U/ml) with outcomes in a cohort of patients with upfront resectable pancreatic cancer. METHODS: We used a single institution database of patients who underwent upfront resection for PDAC between 2007 and 2015. Patients with a bilirubin above 1.5 after decompression were excluded. A total of 144 resectable patients were analyzed. We used Chi-squared analysis for categorical variables and a Wilcoxon rank sum for continuous variables. Kaplan Meier curves, univariate and multivariate proportional hazards regression models were used to assess survival. RESULTS: 16 patients (11.1%) had elevated preoperative CA 19-9. There was no difference between elevated CA 19-9 and sociodemographic, pre-, peri-, and post-operative variables, including recurrence and site of recurrence (Table 1). Multivariable Cox regression showed that increased Charlson comorbidity index, increasing number of positive lymph nodes, perineural invasion, grade 3/4 Clavien complication and failure to complete adjuvant therapy were all predictors of increased mortality. CA 19-9 >1,000 (HR 1.30, 95% CI [0.73-2.34]) did not predict increased mortality in the multivariable model. CONCLUSION: While practice guidelines suggest neoadjuvant treatment for anatomically resectable PDAC with elevated CA 19-9, there was no association between elevated CA 19-9 and recurrence, site of recurrence, or overall survival in this cohort. Our findings do not suggest that elevated CA 19-9 alone should drive the decision for neoadjuvant treatment.

Table 1: Characteristics of Resectable PDACs by Pre-Operative CA 19-9 Level (n=144)

	Low CA 19-9	High CA 19-9	p-value
Number	128	16	
Sex			0.584
Female	47 (36.7)	7 (43.8)	
Male	81 (63.3)	9 (56.2)	
Age, y			0.443
<70	69 (53.9)	7 (43.8)	
≥70	59 (46.1)	9 (56.3)	
Race			0.552
White	117 (91.4)	15 (93.8)	
Black	4 (3.1)	1 (6.2)	
Other / Unknown	7 (5.5)	0 (0.0)	
Charlson Comorbidity Index			0.945
0-3	35 (27.3)	4 (25.0)	
4-5	58 (45.3)	7 (43.8)	
6+	35 (27.3)	5 (31.2)	
BMI (mean)	26.4	24.9	0.455
Operation			0.116
Whipple/total pancreatectomy	89 (69.5)	8 (50.0)	
Distal pancreatectomy +/- splenectomy	39 (30.5)	8 (50.0)	
Pathologic T Stage			0.859
1	9 (7.0)	1 (6.2)	
2	11 (8.6)	0 (0.0)	
3	63 (49.2)	9 (56.3)	
4	45 (35.2)	6 (37.5)	
Nodes Examined (mean)	19.5	18.3	0.767
Nodes Positive (mean)	2.8	2.1	0.849
R1 resection			0.639
No	117 (91.4)	14 (87.5)	
Yes	11 (8.6)	2 (12.5)	
Grade 3 / 4 Clavien Complication			0.129
No	107 (83.6)	16 (100.0)	
Yes	21 (16.4)	0 (0.0)	
Recurrence			0.708
No	42 (32.8)	6 (37.5)	
Yes	86 (67.2)	10 (62.5)	
Site of Recurrence			0.366
None	42 (32.8)	6 (37.5)	
Local	17 (13.3)	1 (6.2)	
Liver	30 (23.4)	3 (18.8)	
Lung	12 (9.4)	4 (25.0)	
Multi-site	15 (11.7)	2 (12.5)	
Other	12 (9.4)	0 (0.0)	

P236

Low Dose Doxorubicin Increases Clearance of Human Pancreatic Cancer Cells by Macrophages B. Goudreau,* J.B. Persily, S.J. Adair, S. Morioka, K.S. Ravichandran, J.T. Parsons, T.W. Bauer. *Surgery, University of Virginia, Charlottesville, VA.*

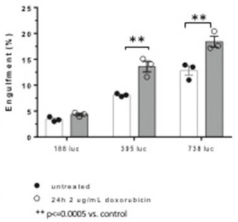
Objective: Doxorubicin (DOX) has been shown to increase human cancer cell surface expression of calreticulin (CRT), a proposed "eat me" signal, leading to increased phagocytosis by macrophages. The impact of DOX as an adjuvant therapy has not been well elucidated in pancreatic ductal adenocarcinoma (PDAC). We hypothesized that low dose DOX would increase expression of CRT on patient-derived PDAC cells, leading to increased phagocytosis by macrophages. Methods: Basal levels of CRT were assessed on patient-derived PDAC cell lines (395, 738, 188, 608, 449, and 366) via flow cytometry. CRT was measured after 24 hour exposure to DOX vs. control, at which time PDAC cells were used in an engulfment assay. In vitro engulfment was performed using mouse macrophages harvested via peritoneal washing. The macrophages were stained with CFSE and PDAC cells were stained with cypher, a pH sensitive dye. Treated and stained PDAC cells were incubated for 2 hours with stained macrophages. Samples were analyzed by flow cytometry to determine percent change in phagocytic engulfment measured by change in pH of PDAC cells. Results: Initial titration experiments determined 2ug/mL dose of DOX to be sublethal in the PDAC cell lines used. Flow cytometry demonstrated upregulation of CRT in 5 of the 6 PDAC cell lines after 24 hours of DOX treatment. Upregulation was unique to each cell line ranging from a 4-fold increase in 449 to a 60-fold increase in 395 (Fig.1A). In vitro engulfment assays showed a statistically significant increase in engulfment for 395 (8.1% to 13.6%, p= 0.0005) and 738 cells (12.8% to 18.4%, p= 0.0004) (Fig. 1B), which had previously demonstrated 60-fold (0.08% to 4.81%) and 5-fold (0.88% to 4.58%) increases in CRT expression with DOX treatment, respectively. 188 did not upregulate CRT after DOX treatment (0.36% to 0.19%) and also did not demonstrate a significant increase in macrophage engulfment (3.4% to 4.3%, p = 0.7555). Conclusions: Low dose DOX upregulates CRT on PDAC tumor cells in vitro leading to increased clearance by macrophages. Low dose DOX should be explored in vivo as an adjuvant therapy to stimulate PDAC cell clearance by innate immunity.

A

PDAC Cell Line	Basal Calreticulin (%)	Calreticulin 24H Doxorubicin Treatment (%)
395	0.08	4.81*
738	0.88	4.58*
188	0.36	0.19*
608	0.47	2.75*
449	0.57	1.78*
366	0.06	1.0*

* p<0.05 vs. control

B



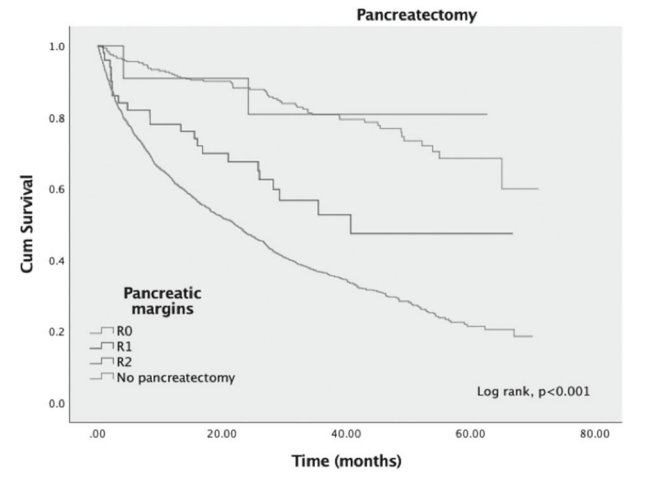
** p<=0.0005 vs. control

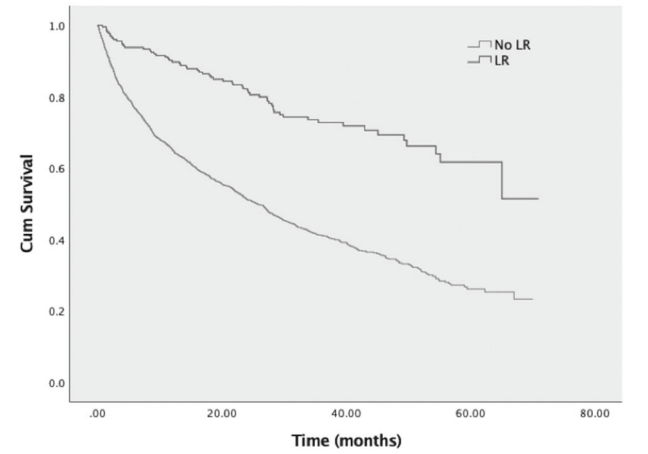
Figure 1. (A) Calreticulin Expression of PDAC Cell lines. Flow cytometry analysis of each PDAC cell line comparing treated and untreated levels of cell surface calreticulin is displayed. Treated cells were exposed to 2ug/mL doxorubicin for 24 hours. **(B) Engulfment of PDAC Cells.** Flow cytometry analysis to compare percent of macrophages with evidence of tumor cell engulfment of treated and untreated PDAC cells. Treated cells were exposed to 2ug/mL doxorubicin for 24 hours prior to initiation of the engulfment assay.

P237

Role of Liver Resection Among Patients with Pancreatic Neuroendocrine Liver Metastasis F. Macedo,* K. Kelly, S. Cass, D. Franceschi, D. Yakoub, A.S. Livingstone, S. Rodgers, V. Dudeja, N. Merchant. *Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL.*

INTRODUCTION: Recently, there has been a move towards decreasing the threshold for liver debulking for neuroendocrine liver metastasis (NELM). However, current data is equivocal and limited to small retrospective series. We sought to examine the long-term outcomes of patients with NELM from pancreatic neuroendocrine tumor (PNET) who underwent liver resection (LR) in a large nationwide cohort. METHODS: National Cancer Data Base (NCDB) was queried for patients with metastatic PNET to the liver diagnosed from 2010 to 2014. Actuarial estimates for overall survival (OS) were calculated using Kaplan-Meier methods. Logistic regression was used to assess factors associated with LR. Log-rank and Cox multivariable regression analysis were performed to compare the outcomes of patients undergoing LR. RESULTS: A total of 2,265 patients with NELM from PNET were included in the analysis. Median age was 62 years (range, 20-90 years). Of them, 1,765 (77.9%) patients were Caucasians and 1,290 (57%) were male. Median chromogranin level was 92 (0-890). 471 (20.8%) underwent resection of PNET. Median OS was 19.2 months (0-71 months) for those not undergoing pancreatectomy vs. 22.1 months for those undergoing pancreatectomy, p<0.001, respectively, Fig 1A). 230 (10.2%) patients underwent LR. Of those, median OS was 25.8 months for those undergoing LR vs. median survival not reached months in those that did not have LR (log rank, p<0.001, Fig 1B). Patients with poor comorbidity status (HR 2.624, 95% CI 1.085-6.342) and those undergoing chemotherapy were less likely to undergo LR (HR 3.491, 95% CI 1.145-10.639). After controlling for patient and disease-related factors, LR was independently associated with increased OS (HR 0.164, 95% CI 0.031-0.867, p=0.033). CONCLUSIONS: LR is associated with improved long-term survival in patients with NELM from PNET. Pancreatectomy may be advocated in selected group of patients with satisfactory functional status, however its survival benefits are yet unknown in those with extensive metastatic disease.





P238

Defining the Learning Curve for Robotic-Assisted Pancreaticoduodenectomy K. Meredith,[1]* T. Maramara,[1] J. Huston,[2] R. Shridhar.[3] *1. Surgical Oncology, Florida State University/Sarasota, Sarasota, FL; 2. Sarasota Memorial Institute for Cancer Care, Sarasota, FL; 3. Florida Hospital Cancer Institute, Orlando, FL.*

Background: The expansion of robotic-assisted surgery is occurring quickly though little is generally known about the "learning curve" for the technology with utilization for complex pancreatic procedures. The purpose of this study is to define the learning curve for robotic-assisted pancreaticoduodenectomy with respect to operative time, conversion rates, and morbidity. Methods: We have prospectively followed all patients undergoing robotic-assisted pancreaticoduodenectomy and compared operations performed at our institutions by a single surgeon in successive cohorts of 10 patients. Our measures of proficiency included: operative times, conversion rates, and complications. Statistical analyses were undertaken utilizing Spearmann regression analysis and Mann-Whitney U-test. Significance was accepted with 95% confidence. RESULTS: We identified 66 patients (40 (60.6%) male: 26 (39.4%) female) with a median age of 71(43-88) who underwent robotic assisted pancreatiduodenectomy. Thirty-eight (57.6%) were adenocarcinoma, 14 (21.2%) were neuroendocrine, 9 (13.6%) were IPMN, and 5 (7.6%) were other. The Median estimated blood loss was 150 (25-600), and not significantly different between any 10-patient cohort (p=0.32). R0 resections was performed in 65 (98.5%) of patients. The median lymph node harvest was 17 (10-31). A significant reduction in operative times was noted following the completion of 20 procedures (681±151 minutes vs 412±43 minutes (p=0.001) and further reduced with the subsequent 46 cases 375±63 minutes p≤0.001. There were 3 (4.5%) conversions to open (2 lack of progression, 1 tumor adherence to SMV). Complications occurred in 25 (37.9%) patients. There was a significant reduction in complications seen after case 31 (p=0.04). Additionally, a reduction in grade 3-5 complications were seen after case 46 (p=0.04). Pancreatic leaks occurred in 14 (21.2%) patients and did not differ among individual cohorts. There were no in-hospital mortalities. CONCLUSIONS: For surgeons eager to perform robotic assisted pancreaticoduodenectomies, the learning curve appears to begin near proficiency after 20 cases for operative time and 31 cases for a decrease in complications.

P239

Identifying and Correlating Circulating Tumor Cells and Cell-Free DNA in Pancreatic Ductal Adenocarcinoma K. Baugh,* M. Navarro Cagigas, W. Fisher. *Surgery, Baylor College of Medicine, Houston, TX.*

Introduction: We report preliminary results of a prospective observational study on CTCs and circulating free DNA in patients undergoing treatment for pancreatic ductal adenocarcinoma (PDAC). Methods: Prospective observational study of PDAC patients with enrollment beginning in August 2018. Patients were consecutively enrolled based upon pre-determined eligibility criteria. Peripheral blood samples were collected from each participant at baseline prior to any treatment and then before and after each treatment modality when applicable. Isolation and identification of CTCs from whole blood was performed using cell density differentials and immunofluorescent staining. While circulating free DNA was identified using enhanced hybrid capture target enrichment techniques. Healthy age and gender matched individuals were identified and used as controls. Results: 8 samples were obtained from 5 PDAC patients; 3 were resectable, 1 locally advanced, and 1 metastatic. Prior to treatment, CTCs were isolated in 100% (5) of patients with corresponding isolation and enrichment of cell free DNA in 60% (3 of 5) patients. In resectable patients, surgery resulted in a 83% decrease from a baseline of 8.4 cells/ml to 1.4 cells/ml. Among the isolated CTCs, two distinct subtypes were identified on staining. An epithelial subtype with a classic pattern of CK and EpCAM expression, accounting for 59% of CTCs and a mesenchymal subtype, characterized by loss of EpCAM expression and weak CK staining, indicating epithelial to mesenchymal transition in 41% of CTCs. Studies examining sequence homology between isolated DNA from CTCs, cell free DNA, and the primary tumor are on-going. Conclusion: Circulating tumor cells and cell free DNA can be effectively isolated from the peripheral blood of PDAC patients signifying potential as biomarkers.

P240

Claudin-1 Targeted Fluorescence In Vivo Imaging of Pancreatic Cancer for Surgical Guidance T. Lwin,[2]* S. Amirfakhri,[3] H. Hollandsworth,[2] F. Filemoni,[3] S. Batra,[1] R. Hoffman,[4] P. Dhawan,[1] M. Bouvet.[2] *1. University of Nebraska Medical Center, Omaha, NE; 2. University of California San Diego Medical Center, San Diego, CA; 3. VA Medical Center San Diego, San Diego, CA; 4. Anticancer Inc, San Diego, CA.*

Introduction: A critical problem in surgical treatment of pancreatic cancer is difficulty in intra-operative visualization of the primary tumor and detection of peritoneal metastases if present. Claudins are tight junction proteins whose aberrant expression plays a role in cancer cell dissociation and invasion. In the present study, we evaluated claudin-1 as a potential tumor specific probe for fluorescence guided surgery Materials and methods: The claudin-1 antibody was conjugated to LICOR-IRDye800CW (LI-COR, Lincoln, NE). BxPC3 pancreatic cancer cells were injected into flanks of nude mice. Tumors were allowed to grow for 4 weeks. Tumors fragments (2 mm^3) were grafted onto the pancreatic tail of recipient mice to create an orthotopic xenograft model of pancreatic cancer. After the tumors developed for 4 weeks, 75 ug of Claudin-800 dye was injected into the tail-vein. Mice were imaged with the LI-COR Pearl Trilogy imaging system 72 hours after injection. After imaging, necropsy of individual organs was performed and fluorescence evaluated. The tumor was bivalved and 15 mm sections were taken for fluorescence scanning as well as hematoxylin and eosin staining. Results: Images obtained after fluorescent antibody injection showed that claudin-800 clearly labeled the tumor at 72 hours (FIgure 1). There was signal in the liver consistent with nonspecific hepatic accumulation as well as weaker signal in the kidneys and spleen. Cross-sectional fluorescence imaging showed that the fluorescence

probe was able to permeate deep into the tumor. Conclusions: The use of a claudin-1 antibody conjugated to LICOR-IRDye800CW (Claudin-800) can selectively label pancreatic cancer in an orthotopic xenograft mouse model. The nonspecific hepatic accumulation is likely due to the hydrophobic nature of the fluorophore. The fluorescence probe had good central penetration into the tumor. Claudin-1 and other additional claudins could be a potentially useful marker to target invasive pancreatic cancer for fluorescence-guided surgery Reference: Singh AB, Sharma A, Dhawan P. Claudin family of proteins and cancer: an overview. J Oncol. 2010;2010:541957.

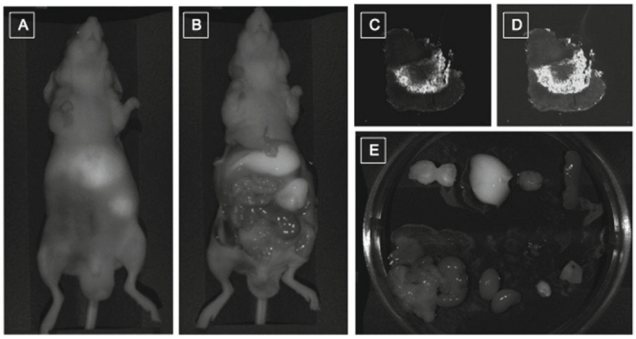


Figure 1. Fluorescence in-vivo imaging using claudin-800 fluorescent probe using bxpc3 human pancreatic cancer in an orthotopic xenograft nude mouse model. (A) There is a fluorescence signal detectable at the liver and the tumor that is visible through the skin in non-invasive views. (B) Laparotomy confirms the fluorescence localization at the liver and the tumor. (C) 30 uM sections were obtained and slides were viewed under fluorescence imaging showing good tumor penetration. (D) Heat map image shows the highest intensity deep within the tumor. (E) Organ necropsy shows weak non-specific signal additionally at the kidney and spleen.

P241

Survival and Cost Associated with Adjuvant Chemotherapy and Chemo-Radiotherapy After Pancreas Cancer Resection N. Vela,[1]* L. Davis,[2] S. Cheng,[3] A. Hammad,[2] Y. Liu,[3] D. Kagedan,[1] L. Bubis,[1] C. Earle,[4] L. Paszat,[4] S. Myrehaug,[4] A. Mahar,[5] N. Mittmann,[3] N. Coburn.[4] *1. University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Research Institute, Toronto, ON, Canada; 3. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada; 4. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 5. University of Manitoba, Winnipeg, ON, Canada.*

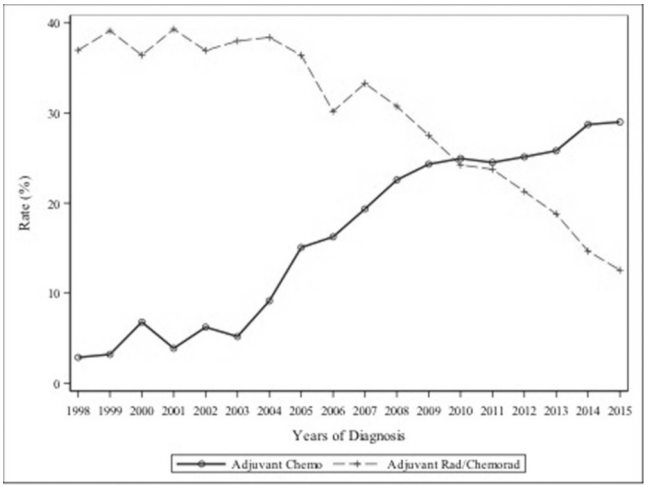
Background: Pancreas cancer is expensive to treat, and the effectiveness of adjuvant chemotherapy (CT) and chemoradiation (CRT) following resection is debated. We compared both survival and healthcare costs by adjuvant therapy after curative-intent pancreaticoduodenectomy (PD) for pancreas adenocarcinoma (PC). Methods: All patients with resected PC in Ontario, Canada diagnosed 2004 to 2014 were identified and linked to administrative healthcare databases. Stratified Kaplan—Meier survival curves and log-rank test compared survival across treatment groups. Costs were assessed from the perspective of Ontario's single-payer healthcare system and compared between CT and CRT. A one-year time horizon was used from the date of surgery. Results: 677 PC patients met all inclusion/exclusion criteria and underwent curative-intent PD with 77% receiving CT and 23% CRT. Median survival after resection was 21.7 and 18.9 months for CT and CRT groups, respectively. Patients receiving CRT were less likely to have high comorbidity burden (ADG >10), but were similar across other demographics. CRT patients were more likely to have margin positive disease. In a subgroup of 489 patients with margin negative disease, median survival in the node negative patients (n=156) was 28.0 months for CRT and 24.7 months for CT (p=0.8297, logrank). Median survival in the node positive patients (n=333) was 20.6 months and 21.8 months for the CRT and CT patients, respectively (p=0.9856, logrank). The median total one-year cost for CT was $52,575 (USD); CRT was $68,216 (Table 1). Conclusion: Patients who underwent adjuvant CT and CRT after PD for PC had similar overall survival, but healthcare expenditures were significantly higher in the CRT group.

Cost component	CT Median $USD	CRT Median $USD
Radiotherapy		
Equipment and supplies	0	1816
Physicist	0	962
Therapy planning	0	1195
Therapy delivery	0	14,170
Other physician payments	0	178
Chemotherapy		
Chair time	3092	2474
Chemotherapy drugs	2152	1146
Supportive drugs	145	228
Other healthcare costs		
ED	473	297
Cancer clinic	12,595	11,974
Other clinic	2204	2887
Inpatient stay	18,621	21,091
Home care	2118	2187
Physician billing	7235	6781
TOTAL MEDIAN COST	52,575	68,216

P242

The Effect of ESPAC-1 on Changing Paradigms of Pancreatic Cancer Treatment L.K. Winer,* A.R. Cortez, K. Wima, M.C. Morris, T.C. Lee, S.A. Shah, S.A. Ahmad, S.H. Patel. *University of Cincinnati, Cincinnati, OH.*

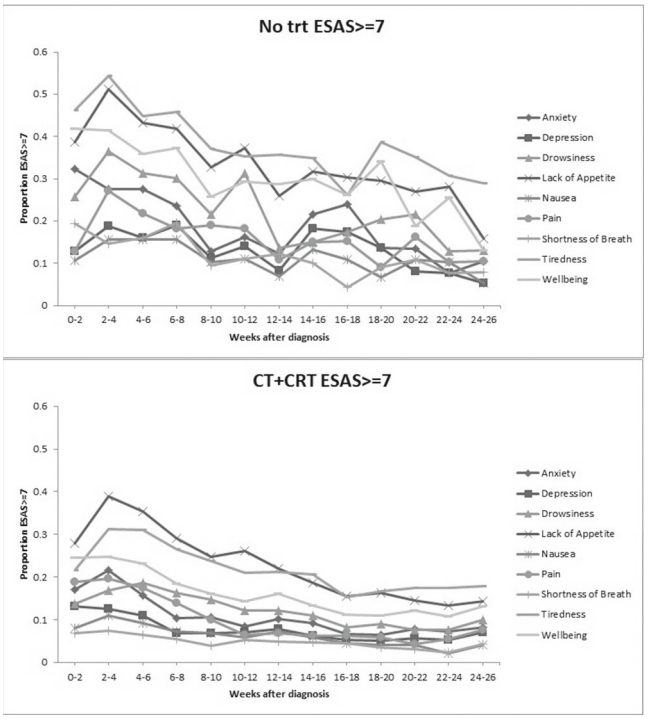
Background: In 2004, the European Study Group for Pancreatic Cancer (ESPAC)-1 concluded that adjuvant chemotherapy (CT) provided a significant survival benefit for patients with pancreatic ductal adenocarcinoma (PDAC). In contrast, adjuvant radiation did not improve survival. We performed this study to determine if the results of ESPAC-1 impacted treatment strategies and how long it took for practice patterns to change. Methods: The National Cancer Database was used to identify patients with stage 1-3 PDAC who underwent resection between 1998 and 2015. Patients diagnosed between 2004 and 2015 were categorized into adjuvant CT and chemoradiation (CRT) groups. Univariate and multivariate analyses were conducted to determine predictors of adjuvant CRT use. Results: Between 1998 and 2015, adjuvant CT use increased from 2.9% to 29.0%, while adjuvant CRT decreased from 37.0% to 12.6%. One year prior to ESPAC-1's publication, 38% of patients received adjuvant CRT. By 2010, this declined to 24.2% as adjuvant CT utilization surpassed that of CRT. For PDAC patients diagnosed between 2004 and 2015, adjuvant CT (n=9,203) and CRT (n=8,199) were compared to evaluate predictors of adherence to ESPAC-1 in the modern era. Adjuvant CT and CRT groups were similar in terms of race, income, and education (all p >0.05). However, adjuvant CRT patients were younger, had private insurance, received treatment at non-academic centers, and had clinical stage 2 or 3 PDAC with larger tumors, node positive disease, and R1 resections (all p<0.0001). On multivariate analysis, R1 resection was the strongest independent predictor of adjuvant CRT use (OR 1.93, CI 1.73-2.14, p<0.0001). Conclusion: Following ESPAC-1, adjuvant CT utilization increased and adjuvant radiotherapy decreased in the United States. This paradigm shift occurred 6 years after the publication of the final ESPAC-1 results. Moreover, we found that the majority of adjuvant CRT patients were treated at non-academic centers and for microscopically positive disease, consistent with current consensus guidelines. Prospective studies are underway to further delineate the role of and specific PDAC population best suited for adjuvant radiation.



P243

Symptom Burden of Unresected Pancreatic Adenocarcinoma: An Analysis of 10,719 Patient-Reported Outcomes S. Tung,[1]* M. Mavros,[2] L. Davis,[2] J. Hallet,[2] A. Mahar,[3] L. Bubis,[1] A. Hammad,[2] H. Zhao,[4] C. Earle,[2] L. Barbera,[2] N. Coburn.[2] *1. University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 3. University of Manitoba, Winnipeg, MB, Canada; 4. Institute of Clinical Evaluative Sciences, Toronto, ON, Canada.*

Background: Pancreatic adenocarcinoma (PA) is a debilitating disease, with the vast majority of patients not amenable to curative-intent surgical resection and data on symptom burden are scarce, but necessary to support them. Using population-based screening, we sought to identify symptom burden and trajectories following PA diagnosis and examine factors associated with high symptoms. Methods: We linked administrative healthcare datasets to conduct a retrospective cohort study of patients registered to a Regional Cancer Center with PA, not undergoing resection, 2010-2015, who reported ≥1 Edmonton Symptom Assessment System (ESAS) score in the year following diagnosis. The ESAS is a validated tool measuring 9 common cancer symptoms. Primary outcome was severe patient-reported symptoms defined ≥7/10. Overall prevalence of monthly severe symptoms was determined for each symptom, and presented graphically for the first 6 months. Multivariable modified Poisson regression identified factors associated with reporting of severe symptoms. Results: A total of 10,719 symptom assessments from 2,161 patients were analyzed. The mean age of the patients was 66.7 years and 47% were female; median survival was 7 (IQR 3-12) months. Most common severe symptoms were tiredness (54.6%), anorexia (53.6%), overall wellbeing (45.5%), and drowsiness (37.1%). Factors independently associated with severe symptoms were female sex, comorbidities, and shorter survival from diagnosis. Older age, recent receipt of chemoradiation, and residence in a semi-rural community were independently associated with lower risk of severe symptoms. Patients receiving cancer-directed treatment (chemotherapy or chemoradiation) reported less severe symptoms (Figure). For both groups, the severity of symptoms started decreasing 1 month after diagnosis and plateaued 4 months after diagnosis. Conclusions: The prevalence of severe symptoms in patients with unresected PA was high, but potentially modifiable. We identified patient-factors with increased risk of severe symptoms to target for future interventions. This information is important for patient counseling and design of supportive care strategies.



P244

Socioeconomic Status Does Not Impact Clinical Outcomes for Localized Pancreatic Adenocarcinoma When Treated at a High-Volume Cancer Center B. Powers,[1]* L.D. Rothermel,[1] A. Dhahri,[1] D.K. Deperalta,[1] T. Ogami,[2] J.K. Kim,[2] J.B. Permuth,[1] J. Pimiento,[1] P.J. Hodul,[1] M.P. Malafa,[1] D.A. Anaya,[1] J. Fleming.[1] *1. Moffitt Cancer Center, Tampa, FL; 2. University of South Florida School of Medicine, Tampa, FL.*

Introduction: Multiple administrative database studies have concluded that low socioeconomic status, defined by race and insurance status, are associated with worse outcomes for pancreatic adenocarcinoma (PDAC). No studies to date have assessed the impact of socioeconomic deprivation (SED) on PDAC using detailed clinicopathologic data. We hypothesized that with accurate staging, receipt of standard of care treatment obviates disparities due to SED. Methods: We performed a retrospective cohort study using PDAC patients who underwent resection between 2007-2015 to examine the relationship between the Area Deprivation Index (ADI) and PDAC outcomes. The ADI is a publicly-available, validated dataset that ranks census blocks on socioeconomic disadvantage, which comprises income, education, employment, and housing quality data based on the 2013 American Community Survey. State-level ADI decile was determined by patient address at diagnosis and divided into terciles of disadvantage (low, moderate, high). We used one-way ANOVA and univariate and multivariate Cox regression for statistical analysis. Results: We identified 307 resected PDAC patients; 289 had ADI data for analyses. Patients with low, moderate, and high SED comprised 117 (40.5%), 101 (34.9%) and 71 (24.6%) of the cohort. We found no association between SED and comorbidity, resectability, pathology, complications, completion of adjuvant therapy, or site of recurrence (Table 1). On multivariate Cox analysis, increasing comorbidity, lymph node positivity, perineural invasion, and failure to receive neoadjuvant therapy or complete adjuvant therapy, increased mortality. Importantly, moderate and high SED were not associated with increased mortality (OR 1.22, 95% CI 0.88-1.69) and (OR 1.25, 95% CI 0.87-1.80). Conclusions: While nearly one-quarter of surgical PDAC patients at our institution are from high SED neighborhoods, they had no difference in resectability, site of recurrence, or survival. These results suggest that while we serve patients from socioeconomically diverse neighborhoods, access to standard of care treatment obviates SED disparities in PDAC.

Table 1: Biology and Outcomes of Resected PDACs by Area Deprivation Index (n=289)

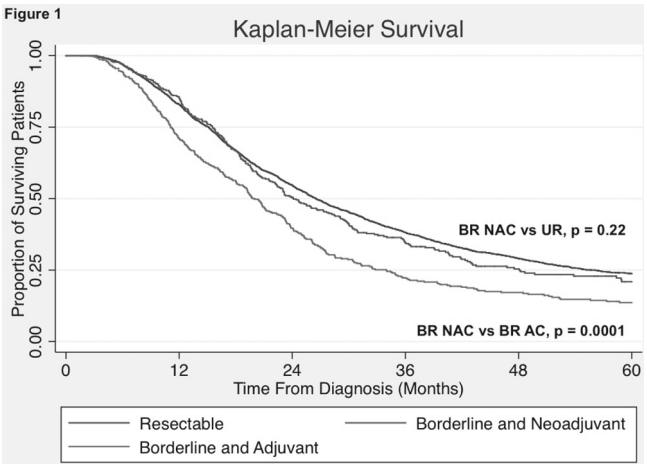
	Low SE Deprivation	Moderate SE Deprivation	High SE Deprivation	p value
Charlson Comorbidity Index				0.418
0-3	31 (26.5)	23 (22.8)	13 (18.3)	
4-5	60 (51.3)	47 (46.5)	42 (59.2)	
6+	26 (22.2)	31 (30.7)	16 (22.5)	
Preoperative Resectability				0.552
Resectable	80 (68.4)	62 (61.4)	47 (66.2)	
Borderline	37 (31.6)	39 (38.6)	24 (33.8)	
Neoadjuvant Therapy				0.458
No	80 (68.4)	61 (60.4)	47 (66.2)	
Yes	37 (31.6)	40 (39.6)	24 (33.8)	
Operation				0.593
Whipple/total pancreatectomy	90 (76.9)	79 (78.2)	59 (83.1)	
Distal pancreatectomy	27 (23.1)	22 (21.8)	12 (16.9)	
Nodes Positive				0.083
0	51 (43.6)	48 (47.5)	24 (33.8)	
1-3	47 (40.2)	37 (36.6)	28 (39.4)	
4+	19 (16.2)	16 (15.9)	19 (26.8)	
Grade 3 / 4 Clavien Complication				0.415
No	102 (87.2)	83 (82.2)	63 (88.7)	
Yes	15 (12.8)	18 (17.8)	8 (11.3)	
90 Day Mortality				0.387
No	115 (98.3)	96 (95.1)	69 (97.2)	
Yes	2 (1.7)	5 (4.9)	2 (2.8)	
Completion Adjuvant Therapy				0.639
No	37 (32.7)	38 (38.0)	22 (31.9)	
Yes	76 (67.3)	62 (62.0)	47 (68.1)	
Site of Recurrence				0.083
None	35 (32.1)	30 (32.6)	14 (23.0)	
Local	16 (14.7)	9 (9.8)	3 (4.9)	
Liver	27 (24.8)	20 (21.7)	17 (27.9)	
Lung	10 (9.2)	16 (17.4)	11 (18.0)	
Multi-site	14 (12.8)	10 (10.9)	8 (13.1)	
Other	7 (6.4)	7 (7.6)	8 (13.1)	

P245

Survival After Neoadjuvant Chemotherapy in Borderline Resectable Disease is Similar to That of Upfront Resectable Pancreatic Adenocarcinoma A. Chawla,* G. Molina, L. Pak, J. Wang. *Surgical Oncology, Dana-Farber Cancer Institute, Needham, MA.*

Introduction: The purpose of this study was to evaluate the benefits of neoadjuvant chemotherapy (NAC) in patients with borderline resectable (BR) pancreatic adenocarcinoma (PDAC) and compare its survival to a similar cohort of patients with upfront resectable (UR) disease. Methods: We used the 2004-2015 National Cancer Database to evaluate patients with PDAC treated with both curative-intent pancreatectomy and chemotherapy. UR patients were defined those with clinical T1 and T2 PDAC localized to the pancreas with no evidence of vessel involvement. BLR patients were defined as those who had clinical evidence of arterial or venous involvement. Clinical and pathologic data were obtained. Univariate and multivariate Cox regression analyses were performed for overall survival (OS) using known prognostic clinical and pathologic variables. Kaplan Meier method was used for survival analysis. P values <0.05 were considered significant. Results: In 985 patients with BLR who underwent curative-intent pancreatectomy, those treated with NAC compared to those treated with AC had a higher node negative rate (55.6% vs 24.1%, p<.001), achieved a higher rate of margin negative resection (78.2% vs 55.1%, p<.001), and had better OS (Figure 1). Independent predictors of OS for BLR patients included age, tumor size, tumor differentiation, margin status, lymph node involvement and the use of NAC. Out of3952 UR patients treated with chemotherapy, only 13.1% received NAC as compared to 49.3% of BLR patients treated with NAC. In comparison to the UR cohort, patients with BLR disease were older, had more comorbidities, and had larger tumor size. On final pathology, patients with BLR PDAC had worse tumor grade and had a higher rate of margin positive resection. Despite this, BLR patients treated with NAC had higher rate of lymph node negative disease compared to those with UR disease (39.6% vs 34.7%, p<.001). In addition, BLR patients treated with NAC performed as well as UR patients in terms of survival (Figure 1). Conclusions:Use of NAC in BLR PDAC leads to survival outcomes similar to that of patients with UR PDAC.

Figure 1



P246

Radiomic Analysis on Preoperative Imaging Identifies Patients with High-risk Hepatocellular Carcinoma G.C. Wilson,* R. Cannella, G. Fiorentini, C. Shen, B. Amir, A. Furlan, A. Tsung. *Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

BACKGROUND: Microvascular Invasion (MVI) is a negative prognostic factor for hepatocellular carcinoma (HCC). Radiomic texture analysis quantifies the microscopic features of tumor imaging. The aim is to determine if radiomics can predict biologic aggressiveness in HCC and identify tumors with MVI. METHODS: Single-center, retrospective review of HCC patients undergoing resection/ablation with curative intent from 2009-2017. DICOM images from preoperative MRIs were analyzed with texture analysis software based on the largest tumor cross-section as the region of interest. Texture analysis parameters extracted included mean pixel intensity (MPI), standard deviation, kurtosis, skewness, entropy, mean of positive pixel on T1, T2, arterial phase and portal venous phase (PVP) images. Multivariate logistic regression analysis evaluated factors associated with MVI. Kaplan-Meier methods were used for survival analysis RESULTS: MVI was present in 52.2% (n=133) of HCCs. Disease free survival was worse in MVI-positive HCC with a median survival of 14.8 mos, 95% CI=9.8–19.8 compared to MVI-negative HCC with median survival of 28.7 mos, 95% CI=25.2–32.2 (p=0.012). Texture analysis parameters associated with MVI included T1 MPI (OR=0.98 95%CI 0.96–1.0, p=0.068), T1 skewness (OR=3.4, 95%CI 0.89–13.3, p=0.075), T1 kurtosis (OR=1.75, 95%CI 0.95–3.2, p=0.074), T2 entropy (OR=3.8, 95%CI 1.1–13.0, p=0.034), and PVP entropy (OR=4.3, 95%CI 1.2–15.1, p=0.025). Tumor characteristics associated with MVI included tumor size (OR=1.33, 95%CI 0.98–1.8, p=0.067), tumor grade (OR=3.02, 95%CI 0.83–11.03, p = 0.093), and minimal liver fibrosis (OR=0.19, 95%CI 0.03–1.1, p=0.064). On multivariate analysis, only T1 MPI (OR=0.97, 95%CI 0.95–0.99, p=0.043) and PVP entropy (OR=4.7, 95%CI 1.37–16.3, p=0.014) were associated with tumor MVI. Area under ROC curve was 0.83 for this final model as depicted in Figure 1. CONCLUSION: Tumor entropy and MPI are both associated with MVI in HCC. Texture analysis on preoperative imaging correlates with microscopic features of HCC and provides the basis for a digital biopsy.

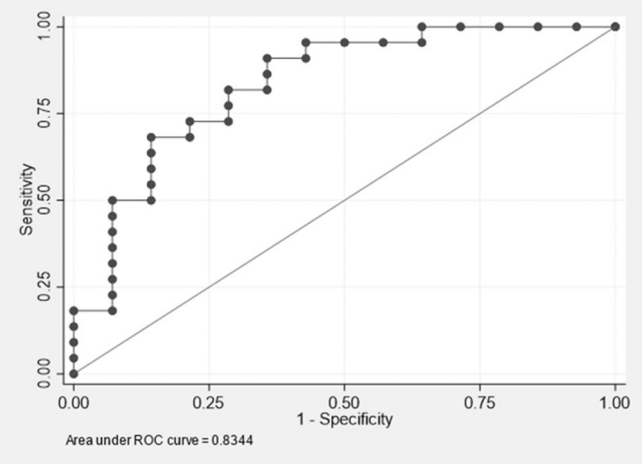


Figure 1: Receiver operating characteristic (ROC) curve of final multivariate model for microvascular invasion

P247

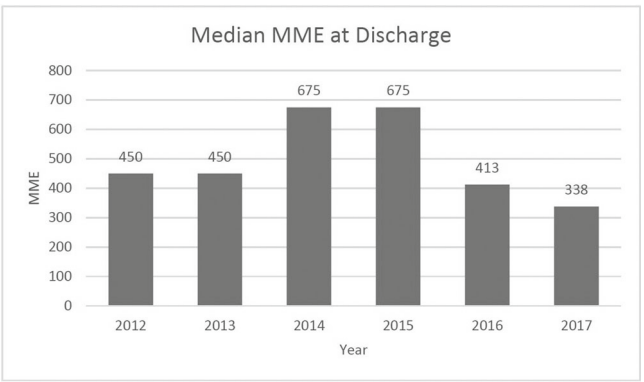
Predictive Value of Preoperative Fine Needle Aspiration Biopsy in the Identification of IPMN-Associated Adenocarcinoma T. Hughes,* L.R. Prakash, J. Lee, M. Bhutani, B. Weston, W. Ross, H. Wang, E. Koay, A. Maitra, F. McAllister, J.E. Lee, T. Aloia, J. Vauthey, C.D. Tzeng, M.H.G. Katz, M. Kim. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

The identification of high grade dysplasia (HGD) or invasive cancer in pancreatic intraductal papillary mucinous neoplasms (IPMNs) by preoperative fine needle aspiration (FNA) largely directs recommendations for surgical resection. We sought to determine the fidelity of preoperative FNAs to accurately identify and discriminate IPMNs with HGD and adenocarcinoma (CA) from LGD/MGD at a high-volume cancer center. A retrospective review identified 136 patients who underwent resection for IPMN from 2005-2018. Preoperative FNA biopsy was performed for 122 patients and final pathology assessment for the presence of LGD/MGD, HGD and invasive cancer was compared to preoperative FNA pathology results. Among 122 patients, FNA identified CA in 38, HGD in 11, LGD/MGD in 19, no atypia in 23 and non-diagnostic samples in 31. Symptoms, worrisome features and high-risk stigmata prompted resection in patients without HGD or CA on biopsy. Of the patients with FNA demonstrating CA, 27/38 were confirmed on final pathology (PPV 71%); 9/38(23.7%) and 2/38(5.3%) were downgraded to HGD and LGD/no atypia, respectively. Neoadjuvant therapy was given to 4 patients that were downgraded from CA to HGD, LGD or benign. Among 11 patients with HGD on FNA, final pathology demonstrated HGD in 3(27.3%), CA in 5(45.5%) and LGD/MGD in 3(27.3%), yielding a PPV of 27.3% and a NPV of 54.5%. Among 19 patients with LGD/MGD on preoperative FNA, 13(68.4%) were upgraded to HGD or CA with 6(31.5%) confirmed as LGD/MGD/no atypia. The PPV and NPV of LGD/MGD FNA were 26.3% and 31.6%. For 54 patients with non-diagnostic samples or no atypia, a final diagnosis of HGD or CA was identified in 29(53.7%). Preoperative FNAs demonstrating adenocarcinoma reliably identify candidates for surgical resection. HGD associated with IPMN may identify candidates for surgical resection but may also result in resection for a significant number of patients with lower grade lesions. FNA yielding LGD/MGD/no atypia does not accurately stage IPMNs in the setting of worrisome features, high risk stigmata or patient symptoms and should not be used to exclude such patients from consideration for surgical selection.

P248

Analysis of Narcotic Prescribing Practices After Hepatectomy at a Tertiary Academic Medical Center R.A. Erali,* M. Share, G. Russell, T. Pu, R. Howerton, C. Clark, E. Levine, K.I. Votanopoulos, P. Shen. *Surgical Oncology, Wake Forest University, Winston-Salem, NC.*

Intro Opioid related deaths and addictions have made perioperative pain management after major surgical procedures a topic of discussion. Recent trends have emphasized decreasing opioid exposure through regional anesthesia and standardized recovery pathways. Methods Analysis of patients undergoing hepatectomy for neoplastic disease was performed from January 2012 through December 2017. Patients were excluded if they were on opioids preoperatively. Postoperative narcotics were prescribed for 161 patients undergoing a total of 169 operations. Repeated measures of analysis of variance were employed. Results Median age of patients was 60 years old with 54% male gender. 21% of patients underwent major hepatectomy and 47% underwent minimally invasive resection. Median length of stay was 5 days (range, 1-24 days). All 169 admissions received narcotics at discharge with median morphine milligram equivalents (MME) being 450 (range, 100-4050). No independent predictors for amount of narcotics prescribed at discharge were found among any variables included in our analysis: age, gender, preop ECOG status, comorbidities (diabetes, cardiac, chronic obstructive pulmonary disease, or asthma), blood loss, extent of hepatic resection, operative time, length of stay, preoperative chemotherapy or use of regional anesthesia. Sixty patients (35.5%) received a refill prescription with a mean MME of 852.9 ± 894.6. Thirteen patients (7.6%) received a second refill (3 total prescriptions) with a mean MME of 400 ± 86.6. There was no significant correlation between amount of narcotics prescribed at discharge and refills ordered (p=0.93). The median MME prescribed at discharge peaked in 2014 and 2015 and significantly decreased consecutively in 2016 and 2017 (p=<0.05) (see chart). Discussion The range of narcotics prescribed after hepatectomy varied greatly and no predictive factors for amount were identified. In addition patients receiving more narcotics at discharge did not have less need for refills. Over time the amount of narcotics prescribed at discharge significantly decreased, likely due to multimodality acute pain protocols. Standardization of discharge pain prescriptions is needed.



Median MME at Discharge, by Year

P249

Multimodality Neoadjuvant Therapy Increases Normalization of Carbohydrate Antigen 19-9 (CA19-9) in Patients with Pancreatic Cancer A. Krepline,* C.N. Clarke, K. Christians, P. Ritch, B. George, A. Khan, N. Kulkarni, C. Hagen, B. Erickson, W. Hall, M. Aldakkak, D. Evans, S. Tsai. *Surgery, Medical College of Wisconsin, Milwaukee, WI.*

Introduction: We previously demonstrated normalization of CA19-9 levels in response to neoadjuvant therapy is a favorable prognostic marker. We analyzed trends in CA19-9 decline in response to sequential neoadjuvant therapy. Methods: We identified patients with localized pancreatic cancer who had pretreatment CA19-9 levels >35 U/mL, total bilirubin <2 mg/dL, and received neoadjuvant therapy consisting of 2 months of chemotherapy followed by 50.4 Gy chemoradiation. CA19-9 was assessed after chemotherapy and after chemoradiation (preop) and were classified as normal (nl) or elevated (hi) based on a cutpoint of 35 U/mL. Patients were classified into 4 groups based on CA19-9 response to chemotherapy and chemoradiation: A (nl/nl), B (nl/hi), C (hi/nl), D (hi/ hi) Results: For the 103 patients, Table 1 summarizes changes during neoadjuvant therapy. Following chemotherapy, the median change in CA19-9 was -51% (IQR:49); 26 (25%) patients achieved a normal CA19-9 and 77 (75%) did not. Of 26 patients who normalized their CA19-9 levels after chemotherapy, 16(62%) had a pretreatment CA19-9 level between 35-100. Of the 77 patients with elevated CA19-9 after chemotherapy, 21 (27%) further normalized their CA19-9 levels with chemoradiation (Grp C) and 56 (73%) did not (Grp D). Of 21 Grp C patients, 14 (66%) had a CA19-9 level between 35-100. After neoadjuvant therapy, the median preop CA19-9 was 47 (IQR:112) U/mL. Of 103 patients, 77 (75%) underwent

surgical resection, 18 (90%), 5 (83%), 20 (95%), and 34 (61%) in Grp A, B, C, and D, respectively (p=0.003). The preop CA19-9 was higher than the pretreatment CA19-9 in 6 (6%) patients of which 4 (66%) were not resected. In an adjusted logistic regression, elevated preop CA19-9 was associated with an 88% decreased odds of surgical resection (95%CI: 0.03-0.48, p =0.002). Conclusion: CA19-9 monitoring during neoadjuvant therapy demonstrated normalization in CA19-9 in 20% of patients after chemotherapy and an additional 21% following chemoradiation. Patients with higher CA19-9 are less likely to achieve normalization, and extended neoadjuvant therapy may be an option to augment CA19-9 response.

Changes in CA19-9 During Sequential Neoadjuvant Therapy

Group	A (n=20)	B (n=6)	C (n=21)	D (n=56)	Total (n=103)	p-value
CA19-9 After Induction Chemotherapy	Norm	Norm	Elevated	Elevated		
CA19-9 after Chemoradiation	Norm	Elevated	Norm	Elevated		
Median Pretreatment CA19-9 (IQR)	69 (100)	149 (757)	120 (636)	470 (700)	293 (628)	<0.001
Pretreatment CA19-9 range, n(%)						<0.001
35-100	14 (70)	2 (33)	7 (33)	6 (11)	29 (28)	
101-250	3 (15)	2 (33)	6 (29)	8 (14)	19 (18)	
251-750	2 (10)	0	3 (14)	26 (46)	31 (30)	
750+	1 (5)	2 (33)	5 (24)	16 (29)	24 (23)	
Median % change after induction chemo (IQR)	-63 (33)	-90 (28)	-49 (52)	-45 (56)	-51 (49)	0.005
CA19-9 range induction chemo, n(%)						<0.001
Normal (<=35)	20 (100)	6 (100)			26 (25)	
35-100			14 (67)	13 (23)	27 (26)	
101-250			4 (19)	16 (29)	20 (19)	
251-750			2 (10)	19 (34)	21 (20)	
750+			1 (5)	8 (14)	9 (9)	
Median % change after chemo and chemoradiation	-70 (38)	-55 (34)	-83 (24)	-32 (89)	-51 (44)	<0.001
CA19-9 range after 2nd therapy, n (%)						<0.001
Normal (<=35)	20 (100)		21 (100)			
35-100		4 (67)		26 (46)	30 (29)	
101-250		2 (33)		14 (25)	16 (16)	
251-750				12 (21)	12 (12)	
750+				4 (7)	4 (4)	
Median Preoperative CA19-9 (IQR)	18 (10)	55 (91)	23 (14)	113 (209)	47 (112)	<0.001
Completed all neoadjuvant therapy and surgery, n (%)	18 (90)	5 (83)	20 (95)	34 (61)	77 (75)	0.003

P250

Improving Postoperative Outcomes of Older Frail Surgical Patients with Hepatopancreatobiliary Cancer J.W. Harris,* A. Tin, R. Downey, A. Shahrokni, M.I. D'Angelica. *Surgery, Memorial Sloan Kettering, New York, NY.*

Introduction: Increased life expectancy over the last century has resulted in a growing population of older adults. Age remains one of the most important risk factors for cancer development. Older frail patients with hepatopancreatobiliary (HPB) cancers have poorer outcomes compared to older fit patients. Thorough geriatric assessment in addition to perioperative geriatric comanagement may improve outcomes of older frail patients in the non-oncologic surgery setting. We aimed to report our experience with geriatric comanagement of frail versus fit older surgical patients with HPB cancers. Methods: From 2015 to 2017, the majority (>80%) of patients age 75+ undergoing minor/major hepatectomy, pancreaticoduodenectomy (PD), or distal pancreatectomy (DP) were referred to a Geriatrics service for perioperative care. Patients completed geriatric assessment (GA) with the score of 0-12 (Frail ≥4). Outcomes collected included Clavien-Dindo classification grade ≥ 3, readmission, urgent care visit, death by postoperative day 30, and prolonged length of stay (LOS) (greater than upper quartile). Groups were compared using Fisher's exact test. Results: In total, 180 patients (median age 79; 42% male) underwent HPB procedure GA. Table 1 shows the most prevalent geriatric deficits identified. 54% (n=98) and 46% (n=82) were defined as fit and frail, respectively. Fit and frail patients had similar rates of major complications (11% vs. 18%, p=0.2), readmission (7.1% vs. 13%, p=0.2), urgent care visit (12% vs. 17%, p=0.4), and LOS greater than upper quartile (20% vs. 27%, p=0.4). One patient, considered fit, died within 30 days of surgery. Conclusions: This hypothesis generating study suggests that thorough geriatric assessment and perioperative geriatric comanagement of older frail HPB cancer patients is feasible and may improve outcomes to levels experienced by older fit patients. Medical and psychosocial optimization of frail patients prior to oncologic surgery should be further evaluated in larger prospective studies.

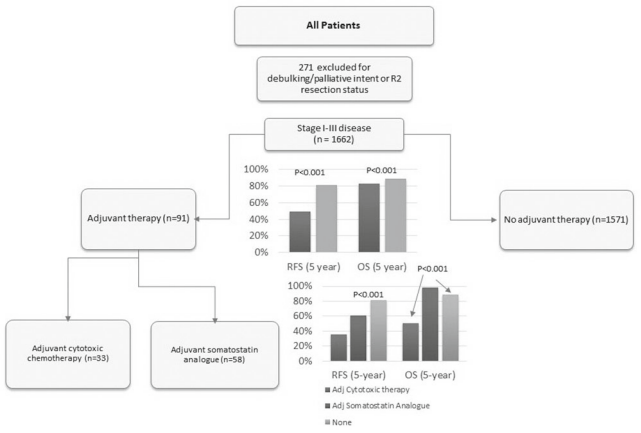
Frequency (proportion) of patients with the most prevalent geriatric deficits based on grouped procedure (N=168 as unresectable patients excluded).

	Minor hepatectomy (N=42; 25%)	Major hepatectomy (N=21; 13%)	Pancreaticoduodenectomy (N=85; 51%)	Distal pancreatectomy (N=20;12%)
Distress Thermometer Score > 4 (N=166) (score range 1-10)	25 (60%)	12 (57%)	47 (56%)	12 (63%)
Geriatric Depression Score > 1 (N=167) (score range 0-4)	23 (55%)	11 (52%)	47 (56%)	8 (40%)
Social Activity Limitation Score >8 (score range 3-15)	20 (48%)	10 (48%)	45 (53%)	7 (35%)
Social Support Score < 16	24 (57%)	5 (24%)	34 (40%)	6 (30%)
Activities of Daily Living Score < 13 (score range 0-14)	18 (43%)	9 (43%)	33 (39%)	8 (40%)
> 5 Medications (N=154)	12 (33%)	8 (40%)	32 (41%)	7 (37%)
Instrumental Activities of Daily Living Score < 15 (score range 0-16)	16 (38%)	8 (38%)	25 (29%)	6 (30%)
Karnofsky Performance Status Score < 80	12 (29%)	5 (24%)	27 (32%)	6 (30%)
Weight Loss of > 10 pounds (N=162)	8 (21%)	5 (26%)	29 (35%)	5 (25%)
Timed-up-Go Score > 10 seconds (N=159)	13 (33%)	7 (37%)	14 (17%)	2 (10%)
Fall in the Past Year (N=166)	9 (21%)	2 (10%)	18 (21%)	5 (28%)
Cognitive Problem based on Mini-Cog (Score < 2) (N=158) (score range 0-5)	7-18%)	2 (11%)	8 (10%)	1 (5%)

P251

Does Adjuvant Therapy Following Resection of Gastroenteropancreatic Neuroendocrine Tumors Improve Outcomes? An Analysis of the U.S. Neuroendocrine Tumor Study Group J. Barrett,[1]* A.G. Lopez-Aguiar,[2] G. Poultsides,[3] F. Rocha,[4] A. Crown,[4] T. Pawlik,[5] R. Fields,[6] R.Z. Panni,[6] K. Idrees,[7] C.S. Cho,[8] A. Fisher,[1] S. Weber,[1] S. Maithel,[2] D. Abbott.[1] *1. University of Wisconsin, Madison, WI; 2. Emory University, Atlanta, GA; 3. Stanford University, Palo Alto, CA; 4. Virgina Mason, Seattle, WA; 5. The Ohio State University, Columbus, OH; 6. Washington University, St. Louis, MO; 7. Vanderbilt University, Nashville, TN; 8. University of Michigan, Ann Arbor, MI.*

Introduction: Lack of high-level evidence supporting adjuvant therapy for patients with resected gastroenteropancreatic neuroendocrine tumors (GEP NETs) provides an opportunity to evaluate its non-standard of care use. Data from the US Neuroendocrine Tumor Study Group were used to evaluate adjuvant therapy and recurrence-free (RFS) and overall (OS) survival in this population. Methods: Patients with primary GEP NETs who underwent curative-intent resection at eight institutions between 2000 and 2016 were identified; those with residual disease were excluded. 91 patients (of 1,662) received adjuvant therapy. RFS and OS were estimated and compared between adjuvant cytotoxic chemotherapy and somatostatin analogue cohorts. Results: In resected patients, 33 received cytotoxic chemotherapy, and 58 received somatostatin analogues. 5-year RFS/OS was 49% and 83%, respectively. In contrast, patients not receiving adjuvant therapy demonstrated higher 5-year RFS/OS of 81% and 89%, respectively (p<0.001). On subset analysis, cytotoxic chemotherapy RFS/OS was 36% and 61%, respectively, lower than the no therapy cohort (p<0.001). RFS with somatostatin analogue therapy (compared to none) was lower (p<0.001), while OS was not different. Multivariable analysis demonstrated that adjuvant cytotoxic therapy was negatively associated with RFS/OS after controlling for patient comorbidities and tumor-specific characteristics (RFS p = 0.001, OS p<0.003). Conclusions: Our data, reflecting the largest reported experience to date, demonstrate that adjuvant therapy for resected GEP NETs is negatively associated with RFS/OS. Selection bias enriching our treatment cohort for individuals with unmeasured high-risk characteristics likely explains some of these results; future studies should focus on subsets of patients who may benefit from adjuvant therapy.



P252

Adjuvant Chemo-Radiotherapy for Resectable Pancreatic Head Cancer: The Real Benefit of Radiation Therapy A. Masi.* *Surgery, SUNY Downstate Medical Center, Brooklyn, NY.*

Background: Adjuvant chemotherapy for pancreatic head cancer offers a survival benefit compared with surgical procedure alone. However, the use of adjuvant radiotherapy combined with chemotherapy remains poorly defined. The aim of this study is to elucidate in which subset of patients radiotherapy offers the maximum benefit. Methods: We retrospectively investigated the US National Cancer Data Base and evaluated patients who underwent pancreaticoduodenectomy and adjuvant treatment for adenocarcinoma from 2004 to 2014. Differences between two groups, Chemotherapy Group (CH), and Chemoradiotherapy Group (CH-RT) were analyzed, and comparison was performed to identify the beneficial effect of radiation. Study end point was overall survival. Results: Population study included 3228 patients, 1647 were in Group CH and 1581 were in Group CH-RT. The two groups were well matched in demographic profile including age, race distribution, co-morbidities (Charlson/Deyo Score), pathological stage, grading and status of resection margins. Multivariable Cox proportional hazard regression model demonstrated lymphovascular invasion (HR 1.257), pathological grade (HR 1.271), positive node (HR 1.450), positive surgical margin (1.075) and elevated CA 19-9 (HR1.118) associated with overall survival. Kaplan-Meier analysis demonstrated superior survival for CH-RT group compared to CH group in patients with positive node (mean OS 30.4 months vs 26.9 months, $p < .005$), surgical margin R1 (mean OS 27.0 months vs 19.4 months, $p < .005$), grade poorly/undifferentiated (mean OS 37.0 months vs 17.8 months, $p < .005$), positive lymphovascular invasion (mean OS 30.2 months vs 25.8 months, $p < .005$) and CA19-9 greater than 100 ng/ml (mean OS 31.8 months vs 28.0 months, $p < .005$). Conclusions: Adjuvant chemo-radiotherapy offers a survival benefit more than chemotherapy alone for resectable pancreatic adenocarcinoma that presents with more aggressive features including poorly differentiated, positive margins, lymphonode positive, presence of lympho-vascular invasion and elevated CA19-9.

Mean overall survival (months)

Variable	CH	CH-RT	p- Value
Lymph-node negative	39.8	38.0	NS
Lymph-node positive	26.9	30.4	<.005
Surgical Margin R0	32.6	35.1	NS
Surgical Margin R1	19.4	27.0	<.005
Grade 1	36.2	36.6	NS
Grade 2	33.0	34.0	NS
Grade 3	25.9	30.0	<.005
Grade 4	17.8	37.0	<.005
Lympho-vascular invasion absent	36.2	35.8	NS
Lympho-vascular invasion present	25.8	30.2	<.005
CA19-9 < 37 ng/ml	35.1	34.4	NS
CA19-9 37 - 100 ng/ml	32.5	36.3	NS
CA19-9 >100 ng/ml	28.0	31.8	<.005

P253

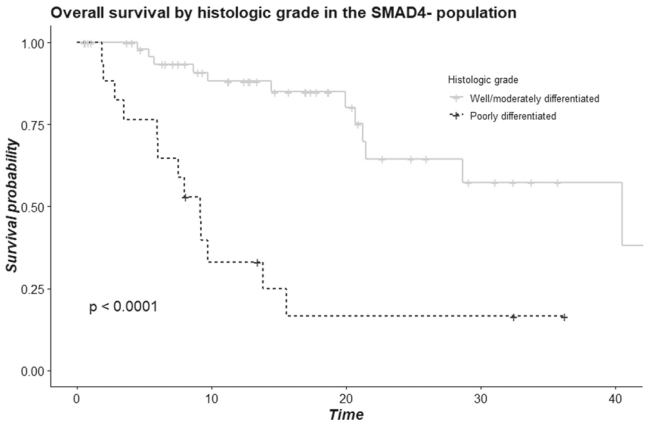
Neoadjuvant Radiation Does Not Improve Survival in Patients with Pancreatic Cancer Undergoing Neoadjuvant Chemotherapy Followed by Pancreatectomy F. Macedo,* O. Picado, K. Kelly, D. Yakoub, D. Franceschi, A.S. Livingstone, V. Dudeja, N. Merchant. *Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL.*

BACKGROUND: Pancreatic adenocarcinoma (PDAC) carries a dismal prognosis. Neoadjuvant chemoradiation therapy (NACR) has been introduced to enhance the outcomes of patients with resectable and borderline resectable PDAC, however the role of radiation therapy remains largely unknown. METHODS: The National Cancer Database (NCDB) was queried for patients with stage I-III PDAC who underwent surgical resection from 2004 to 2014. Patients undergoing NACR were compared to those undergoing neoadjuvant chemotherapy (NAC) alone. The association between clinical characteristics and overall survival (OS) was assessed using the Kaplan-Meier method and multivariable Cox regression model. RESULTS: Of 3,133 patients, 2,351 (75%) patients underwent NACR and 782 (25%), NAC alone. Most patients were Caucasians (84%), with Charlson-Deyo comorbidity score 0 (68%), treated at academic institutions (67%) and underwent pancreaticoduodenectomy (74%). Median number of lymph nodes examined (LNE) and number of positive nodes (NPN) were significantly decreased in NACR (13 vs. 16, $p < 0.001$ and 0 vs. 1, $p < 0.001$, respectively). Rates of margin positivity were similar between 2 groups (NACR, 15% vs. NAC, 17%, $p = 0.545$). OS was also similar in NACR compared to NAC alone [median OS 25.7 months (95% CI 24.4 – 26.7) vs. 25.1 months (95% CI: 23.9 – 27.5)] and 5-year OS 20% vs. 22%, $p = 0.616$, respectively). CONCLUSION: NACR is associated with lower rates of lymph node positivity at resection. However, this did not translate in survival or margin positivity benefit over patients who received NAC alone. Further evidence with prospective trials is warranted to confirm these findings.

P254

Poorly Differentiated Histologic Grade is Associated with Worse Overall Survival in SMAD4 Negative Pancreatic Ductal Adenocarcinomas E.J. Park,* J.P. Jiang, A. Dann, S.S. Kim, L. Damoto, J. King, O.J. Hines, H.A. Reber, T.R. Donahue, M. Girgis. *DGSOM UCLA, Los Angeles, CA.*

Objective: The purpose of this study was to investigate the influence of transcription factor SMAD4 in overall survival following surgical resection of pancreatic ductal adenocarcinoma (PDAC). Methods: The immunohistological (IHC) SMAD4 status of 125 surgically resected PDAC specimens at Ronald Reagan UCLA Medical Center from June 2014 to December 2017 were determined prospectively and retroactively correlated with clinicopathologic characteristics and overall survival. Institutional Review Board approval was obtained. Results: SMAD4 loss occurred in 62% of patients, and was associated with higher incidence of lymphovascular invasion, peripancreatic involvement, and nodal involvement. SMAD4 status was not associated with recurrence patterns or overall survival (OS). On multivariate Cox proportional hazards survival analysis, poorly differentiated histologic grade was the sole predictor of worse survival in the SMAD4 negative population (adjusted HR = 8.2, $p<0.0001$). In the SMAD4 positive population, histologic grade was associated with survival on univariate analysis, but lost significance when adjusted for other prognostic factors (adjusted HR = 3.5, $p=0.07$). Median OS for SMAD4 negative/well-moderately differentiated patients and poorly differentiated patients was 40.5 months and 9.2 months respectively. Conclusion: In this large cohort of resected PDAC, SMAD4 status was not a predictor of overall survival; however, histologic grade independently predicted overall survival in the SMAD4 negative population. Our analysis identified a subpopulation of PDAC patients characterized histologically as SMAD4 negative and poorly differentiated with a particularly poor prognosis with median OS of 9.2 months. Preoperative determination of SMAD4 and histologic status may serve to optimize treatment strategies for this group of patients.



P255

Transarterial Radioembolization and Portal Vein Embolization as Pre-Operative Strategies in Highly Selected Patients with Primary and Metastatic Hepatic Malignancies J. Pedó Freitas,* M.A. Alvarez, S.M. Husain, J.L. Deneve, P.V. Dickson, D. Shibata, E. Glazer. *Surgical Oncology, University of Tennessee Health Science Center, Memphis, TN.*

Background: The treatment of hepatic malignancies confined to the liver (non-transplantable hepatocellular carcinoma [HCC], intrahepatic cholangiocarcinoma [ICC], neuroendocrine tumors [NET] and colorectal hepatic metastases [CRHM]) is challenging. Patients who will not have adequate future liver remnant after resection have high rates of post resection liver failure unless they undergo successful portal vein embolization (PVE). There are few published studies concerning resection after transarterial radioembolization (TARE). The purpose of this study was to understand the natural history of this patient population. We hypothesized that TARE is effective as a bridge to resection in highly selected patients where PVE failed. Methods: This was a retrospective case-control study from 2008 to 2018. The population consisted of non-liver transplant eligible patients who underwent TARE, PVE, or liver resection; they were propensity matched based on co-morbidities, etiology of liver disease, Child-Pugh Score, and ECOG performance status. Statistical analyses were performed with chi-square. Results: Of the 196 patients, the average age was 57.8±12.6 years and 148 underwent liver resection. There were 119 male patients (60.7%). There were 137 Caucasian patients (CC, 70%) and 59 African American patients (AA, 30%). There were 61 HCC, 31 ICC, 65 CRHM, and 12 NET patients. 28 patients had otherdiagnoses (other). HCC patients were more likely to undergo TARE (36.4%), than ICC (20%), CRHM (23.6%) or NET (9.1%, P= 0.043). While AA patients were more likely to undergo any embolization procedure compared to CC patients (47% vs 31%, P=0.03), they were less likely to undergo PVE (P=0.018). Prior to liver resection, CRHM patients were more likely to undergo PVE (80%) than HCC (10%), ICC (10%) and NET (0%) patients (P=0.029). TARE was a bridge to resection for 9 patients: HCC (n=3), ICC (n=2), CRHM (n=2), NET (n=1), and other (n=1). Conclusions: We identified 9 out of 196 patients where TARE was used to bridge patients to resection. In highly selectcases, TARE may be an option to help patients reach resectable status.

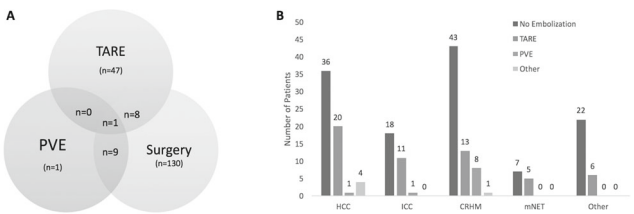
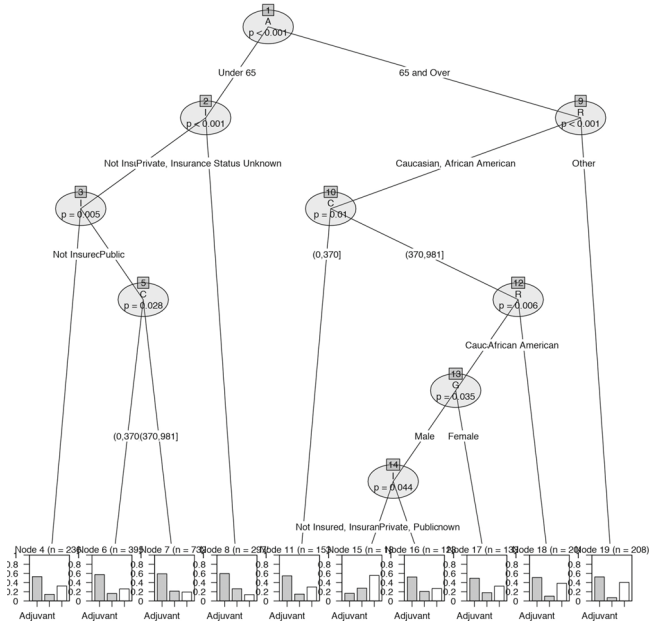


Figure 1. A) Distribution of the patient population according to treatment. **B)** Bar chart of patients according to diagnosis and type of embolization procedure

P256

Not All are Treated Equally: A National Analysis of Treatment Disparities in Pancreatic Cancer J. Bergquist,* E.B. Habermann, M.J. Truty. *Mayo Clinic, Rochester, MN.*

Background: Curative-intent surgery together with systemic chemotherapy are required to maximize survival for patients with localized pancreatic cancer. However, a relatively small number of patients undergo such complete therapy. We sought to study how therapy and outcomes vary across a diverse national cohort and to identify populations at high risk of undergoing sub-optimal therapy. Methods: The National Cancer Data Base (NCDB) 2004-2014 was reviewed for patients with early stage (I/II) PDAC. Treatment with surgery, chemotherapy, and therapeutic sequence were determined. Conditional inference trees were created utilizing available demographic variables (race, gender, age, and insurance status) to identify groups at high risk of non-treatment. Results: 41,205 patients were included, of which 20,057 (48.6%) underwent curative-intent surgery and 25,021 (60.7%) underwent systemic chemotherapy. On conditional inference tree analysis, age was the most important factor associated with surgical and chemotherapy treatment. There were a wide range of surgical treatment rates, from Caucasian patients under 65 with private insurance undergoing curative intent surgery in 65.6% of cases, to Caucasians age 65 and older without insurance who only underwent surgery in 25% of cases. Similar variability levels were observed in chemotherapy treatment with age again being the most important factor, followed by insurance status, node status, gender, and race. Age was again the strongest predictor of therapy sequence, but neoadjuvant treatment rates were higher in patients with elevated CA 19-9 although the rate was lower among African Americans with elevated CA 19-9. Conclusion: Only about half of patients with seemingly resectable pancretic cancer actually underwent curative-intent surgery. Rates of surgical therapy vary widely by patient demographics. Substantial disparities persist in treatment patterns for resectable pancreatic cancer nationally and efforts should be made to address these disparities.



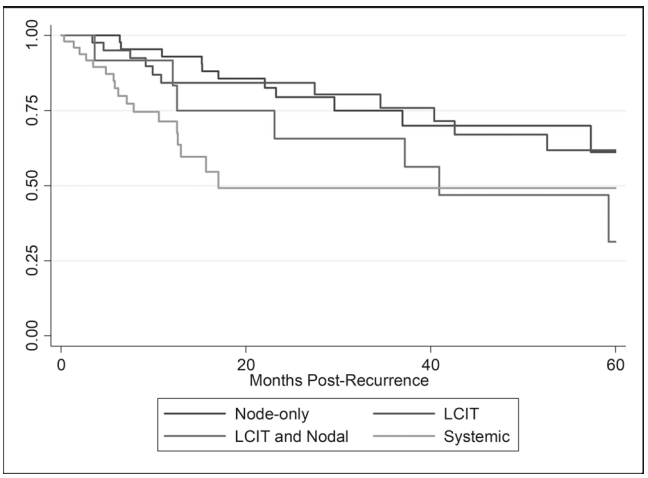
Conditional Inference Tree Plot for Therapy Sequence

P257

Recurrence Patterns and Survival Following Observation After a Positive Sentinel Lymph Node (SLN) Biopsy in Patients with Melanoma E. Bartlett,* A.Y. Lee, P.M. Spanheimer, D. Bello, M.S. Brady, C.E. Ariyan, D. Coit. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: In melanoma, 2 prospective randomized trials failed to demonstrate a survival benefit for completion lymphadenectomy (CLND) after a +SLN biopsy. Uncertainty persists regarding recurrence patterns and regional control in patients undergoing observation. Methods: Patients with a +SLN but without CLND were identified from a prospective melanoma

database (1995-2018). Recurrences were classified as node-only, local and in-transit (LCIT), LCIT and nodal, or systemic (inclusive of synchronous nodal or LCIT). Clinicopathologic characteristics and melanoma-specific survival (MSS) were analyzed using Cox regression. Results: Of 370 included patients, 159 (43%) recurred at a median follow-up of 33 months. The sites of first recurrence were node-only (13.8%), LCIT (11.9%), LCIT and nodal (3.5%), and systemic (13.5%). The median time to node-only recurrence was 8 months, versus 12 for LCIT, and 13 for systemic. 3-yr post-recurrence MSS was 75% (95%CI 56-87%) for node-only, 76% (95%CI 57-87%) for LCIT, 66% (95%CI 32-86%) for LCIT and nodal, and 49% (95%CI 29-66%) for systemic recurrence (p=0.006, Figure 1). Ultrasound surveillance detected the initial recurrence in 22 patients (14%), 13 of whom had node-only recurrence. Of those with node-only recurrence, 80% (41/51) underwent a therapeutic lymphadenectomy, and none experienced loss of regional control (median post-recurrence follow-up of 12 months). Age, thickness, ulceration, satellitosis, lymphovascular invasion, number of +SLNs, and nodal disease burden (<0.1, 0.1-1, >1mm) were associated with MSS in the whole cohort (p<0.05 each). In a multivariate analysis, increasing thickness (HR 1.07, p=0.03), ulceration (HR 3.35, p<0.001), and number of +SLNs (HR 1.63, p=0.01) remained independently associated with MSS. Discussion: Node-only recurrences were detected in 14% melanoma patients observed following a +SLN biopsy. Although follow-up remains limited, loss of regional control has not been observed in these patients. Node-only recurrence is associated with a relatively favorable MSS, supporting the use of observation to identify those patients who might benefit from lymphadenectomy.



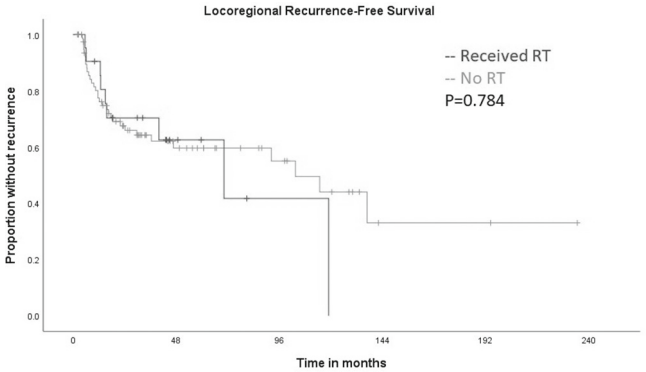
Post-recurrence Melanoma-Specific Survival Stratified by Site of Initial Recurrence.

P258

Adjuvant Radiation Does Not Affect Locoregional Control Following Resection of Melanoma Satellitosis or In-Transit Disease

A. Yaney,[1]* K.K. Rossfeld,[1] T. Wu,[2] E. Wuthrick,[1] D. Agnese,[1] A. Terando,[1] J.H. Howard.[1] *1. The Ohio State University Wexner Medical Center, Columbus, OH; 2. The Ohio State University College of Medicine, Columbus, OH.*

Introduction: Adjuvant radiation therapy (RT) may reduce recurrence after lymphadenectomy for regionally metastatic melanoma. The objective of this study is to evaluate whether RT is associated with improved locoregional (LR) recurrence rates for resected melanoma satellitosis and in-transit (IT) disease. Methods: Data were collected on patients treated surgically for melanoma satellitosis or IT disease from September 1996 to December 2017. Categorical and continuous data were compared using Fisher's exact tests or independent Student T tests, respectively. Kaplan-Meier curves were used to assess recurrence-free survival (RFS). Results: 103 patients were identified. 21 patients (20.4%) received adjuvant RT while 82 (79.6%) did not receive RT. There was no significant difference in age (59 in RT vs 56; p=0.343), sex (76% male in RT vs 57%; p=0.137), Breslow depth (4.45 mm in RT vs 4.55 mm; p=0.935), ulceration (45% in RT vs 54% p=0.607), lymphovascular/neural invasion (65% in RT vs 49%; p=0.311), completion lymphadenectomy rates (43% in RT vs 32%; p=0.439) or receipt of adjuvant systemic therapy (42% in RT vs 34%; p=0.597). The median radiation dose was 30 Gy (range 25-60 Gy) and the median dose per fraction was 5 Gy (range 2-6 Gy). Median follow up in the RT group was 3.5 years and 3.7 years in the non-RT group. 81% of patients who underwent RT suffered a complication, most commonly dermatitis and one case of RT associated lymphedema. LR recurrence occurred in 9 patients (43%) treated with adjuvant RT and 32 patients (39%) in the non-RT group (p=0.805). Median LR RFS was 5.8 years in the RT group and 8.6 years in the non-RT group (Figure 1, p=0.784). On multivariable analysis, there were no independent predictors of LR RFS. Ulceration was the only independent predictor of overall survival (HR 3.8, 95% CI 1.6-9.4). Conclusion: The locoregional failure rate following resection of melanoma satellitosis or in-transit disease is not improved with the addition of adjuvant radiation. Further investigation is needed to identify effective adjuvant therapies for LR control with this pattern of disease in cutaneous melanoma.



P259

Should All Merkel Cell Carcinoma be Treated with Multimodal Therapy?

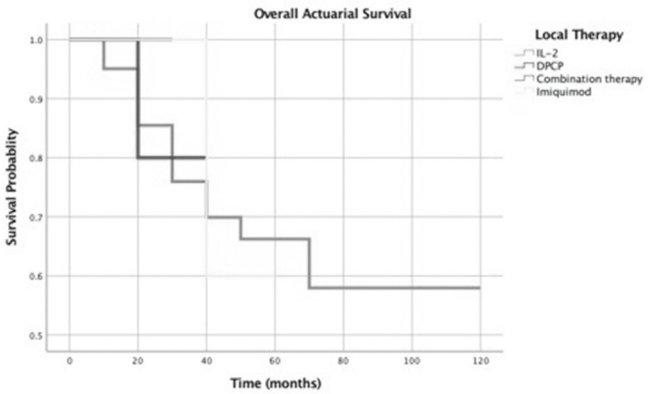
M. Landry, A. Arroyave,* R.E. Heidel, A. Ward, J.M. McLoughlin, J.M. Lewis. *surgery, UTMCK, Knoxville, TN.*

Introduction Merkel Cell Carcinoma (MCC) is a rare and aggressive cutaneous malignancy. Historically mortality has been high. We examined the impact of multimodal treatment and Merkel cell oncoprotein antibody seropositivity on outcomes. Methods After IRB approval, a retrospective review of a prospectively maintained database of patients with MCC from 2014 to 2018 was performed. The Merkel cell polyomavirus antibody (McAB) titer levels were measured and documented serially along with patient demographics including TNM staging, adjuvant therapy, type of surgery, and clinical outcomes (recurrence, adverse events, and overall survival). Results From 2014 – 2018, 29 patients with complete data were analyzed. At presentation 18(62%) were stage I, 3(10.3%) were stage II, and 8(27.5%) were stage III or IV. There were 26 (89.6%) survivors at time of analysis with a mean follow-up of 15.8 months (3.4 -45.3). Twenty-four patients (82.6%) underwent wide excision, and 27(93.1%), 9(32.1%), and 6(20.7%) underwent radiotherapy, immunotherapy, and chemotherapy, respectively. Of patients undergoing excision, 12(50%) had sentinel lymph node biopsy, with 4(33.3%) positive results. Overall, 11(36.6%) patients were treated with multimodal therapy, Sixteen (53.3%) patients underwent radiotherapy therapy alone for treatment, 2(6.6%) underwent immunotherapy alone, and 1(3.3%) patient pursued surgical resection only. Patients receiving radiotherapy alone were 1.25 times more likely to die compared to those receiving multimodal therapy (p=0.68; CI95% 0.09-15.6). All patients who received triple modality therapy at time of review were alive. Overall, there were 7(25%) recurrences. Nineteen (63.3%) patients were evaluated for McAB, with 14(73.68%) antibody negative and 5(26.31%) positive. Four (80%) treated McAB positive patients' titers decreased to baseline, with no recurrences. Two (14.28%) McAB negative patients have recurred. Conclusions Our patient population had higher than expected overall survival. Antibody positivity correlated with positive outcome and treatment effect, however more data is required for ongoing analysis. Multimodal therapy may positively impact overall survival.

P260

Local Therapies for In-Transit Melanoma: An Evidence-Based Algorithm A. Nadler,* N.J. Look Hong, F. Wright. *General Surgery, Sunnybrook Health Sciences Centre, Toronto, ON, Canada.*

INTRODUCTION: This study describes the largest experience to date outlining outcomes with interleukin-2 (IL-2), diphencycprone (DPCP), combination therapy (IL-2, Retin A, imiquimod; CT), and imiquimod for local therapy for in-transit melanoma. The aim of the study is to describe outcomes and create an evidence-based algorithm for management. METHODS: Retrospective review of a prospectively managed database was completed at a tertiary cancer center. Data was collected for patients with in-transit melanoma receiving IL-2, DPCP, CT, or imiquimod from 2008 to 2018. Demographics, primary tumor characteristics, in-transit characteristics, and outcomes were extracted. The primary outcome was overall survival and secondary outcomes included toxicity and complete pathologic response (pCR). RESULTS: The cohort was comprised of 92 patients with a median age of 70 (range 29-94) and 40% were female. Sixty-six of the patients started treatment with IL-2, 10 with DPCP, 12 with CT, and 4 with imiquimod. At baseline, groups differed by location of primary (lower extremity most common for IL-2, DPCP, and CT, head and neck most common for imiquimod; p=0.01) and median number of in transit lesions (IL-2 12, DPCP 5, CT 8, imiquimod 2; p=0.01). With a median follow-up time of 42 months, cumulative one-year overall survival was 82%, with the best survival in the group initiated on CT. pCR was achieved in 35 patients (53%), including 39% initiated on IL-2, 20% on DPCP, 58% on CT, and none on imiquimod (p=0.02). Of patients who switched therapies, 33% responded to IL-2, 43% to DPCP, and none to CT. Forty-seven percent of patients experienced toxicity, including 35% on IL-2, 80% on DPCP, 67% on CT, and all patients on imiquimod (p<0.01). All toxicities were CTCAE grade 1 or 2. Discontinuation of therapy due to toxicity was required in none of the patients on IL-2, CT, or imiquimod, but 25% of patients on DPCP (p=0.022). At completion of follow-up, 23% of patients had progressed to systemic therapy. DISCUSSION: IL-2 or combination therapy should be first line topical therapies for in-transit melanoma, given encouraging pCR rates and minimal toxicity. DPCP should be considered if progression occurs on first line therapies.



Overall actuarial survival for local therapies for in-transit melanoma.

P261

Predictive Genetic Profiles for Regional Lymph Node Metastasis in Primary Cutaneous Melanoma: A Case Matched Pilot Study A. Nye,[1] J. Collins,[2] C. Porter,[1] M. Montes de Oca,[1] K. George,[3] C. Stafford,[4] C.M. Schammel,[5] S. Horton,[5] S.D. Trocha.[6]* *1. University of South Carolina, Greenville, SC; 2. Institute for Oncologic Research, Greenville, SC; 3. Furman University, Greenville, SC; 4. Medical University of South Carolina, Charleston, SC; 5. Pathology, Pathology Associates, Greenville, SC; 6. Greenville Health System, Greenville, SC.*

Background: Melanoma confers an estimated lifetime risk of 1 in 50 for 2016. Clinicopathologic staging and sentinel lymph node biopsy (SLNB), have been the standard of care for T2 and T3 lesions. Molecular biomarkers identified in the primary lesion suggestive of metastatic potential may offer a more conclusive prognosis of these lesions. Methods: Our purpose was to investigate molecular mutations in primary melanoma that were predictive for micrometastasis as defined by +SLN in a case controlled manner: nine patients with -SLN and nine with +SLN. Results: The two cohorts were statistically identical as shown by a t-test for age (p=0.17), race (p=0.18), Breslow depth (p=0.14), Clark level (p=0.33), host response (p=0.17), ulceration (p=0.50), satellite nodules (p=0.17), lymphovascular invasion (p=0.50), and mitotic activity (p=0.09). While no single gene was significantly associated with SLN status, multivariate analysis using classification and regression tree (CART) assessment revealed two unique gene profiles that completely represented regional metastases in our cohort as defined by SLN (+): PIK3CA (+) NRAS (-) and PIK3CA (-) ERBB4 (-) TP53 (+) SMAD4 (-). These profiles were identified in 89% of the patients with +SLN; none of these profiles were identified in the –SLN cohort. Conclusion: We identified two unique gene profiles associated with +SLN that do not overlap other studies and highlight the genetic complexity that portends the metastatic phenotype in cutaneous melanoma.

P262

Association Between Neighborhood Socioeconomic Status and Stage at Diagnosis of Cutaneous Melanoma D.S. Swords,* J.M. Bleicher, C.L. Scaife, T.L. Bowles, J.R. Hyngstrom. *Surgery, University of Utah, Salt Lake City, UT.*

Introduction: In melanoma, stage at diagnosis is a powerful determinant of prognosis. Lower socioeconomic status (SES) is associated with advanced stage. Previous studies were limited by their dichotomization of stage and use of SES measures defined at nongranular, large geographic levels. We examined the association between neighborhood SES and stage using composite measures of SES in the Surveillance, Epidemiology, and End Results (SEER) database and the National Cancer Database (NCDB). Methods: This study evaluated patients diagnosed with invasive melanoma in 2010-2015. In SEER data, the primary predictor of stage was a composite census tract-level SES variable that is unavailable in standard SEER data. In NCDB Data, the predictor was a 7-value SES scale created from zip code-level income and education levels. Associations between SES and stage were evaluated using multivariable multinomial models. Adjusted rates of the stage distribution within SES groups were obtained using marginal standardization. Results: SEER cohort included 93,242 patients; 42% were female, median age was 61, and 91% were non-Hispanic White (NHW). NCDB cohort included 175,629 patients; 42% were female, median age was 60, and 96% were NHW. The NCDB cohort had higher stage (64% stage I, 17% II, 13% III, 6% IV) vs. the SEER cohort (77% stage I, 11% II, 7% III, 4% IV), reflecting referral of higher stage cases to CoC-accredited facilities. In both cohorts, there were significant, graded relationships between decreasing SES and higher stage (Table). In SEER data, lowest SES patients had 40% higher risk of stage II, 60% higher risk of stage III, and 230% higher risk of stage IV (vs highest SES patients). In NCDB data, lowest SES patients had 30% higher risk of stage II, 40% higher risk of stage III, and 170% higher risk of stage IV (vs highest SES patients). Conclusions: Population- and hospital-level data demonstrate a robust, graded association between lower SES and increased risk of advanced stage melanoma at diagnosis. Greater understanding of the mechanisms underlying this disparity is needed. Interventions that increase access to timely diagnostic care in low SES areas may be warranted.

Adjusted Rates of Stage at Diagnosis by Neighborhood Socioeconomic Status in 2010-2015 SEER and NCDB Data*

Predictor variable	2010-2015 SEER Cohort**			
Census tract-level SES	Stage I N=72,378 Adjusted % (95% CI)	Stage II N=10,213 Adjusted % (95% CI)	Stage III N=6,893 Adjusted % (95% CI)	Stage IV N= 3,758 Adjusted % (95% CI)
Quintile 1 (Lowest SES)	70.7 (69.8, 71.6)	13.7 (13.0, 14.4)	9.2 (8.6, 9.8)	6.4 (5.9, 7.0)
Quintile 2	73.2 (72.5, 73.9)	12.5 (12.0, 13.1)	9.0 (8.5, 9.4)	5.3 (5.0, 5.7)
Quintile 3	76.2 (75.7, 76.8)	11.3 (10.9, 11.7)	7.9 (7.6, 8.3)	4.6 (4.3, 4.9)
Quintile 4	78.1 (77.6, 78.6)	10.7 (10.3, 11.1)	7.4 (7.1, 7.8)	3.8 (3.6, 4.0)
Quintile 5 (Highest SES)	81.6 (81.2, 82.0)	9.6 (9.3, 9.9)	5.9 (5.7, 6.2)	2.8 (2.7, 3.0)
	2010-2015 NCDB Cohort***			
Zip code-level SES	Stage I N=113,184 Adjusted % (95% CI)	Stage II N=29,108 Adjusted % (95% CI)	Stage III N=22,157 Adjusted % (95% CI)	Stage IV N=11,180 Adjusted % (95% CI)
1 (Lowest SES)	57.1 (55.4, 58.8)	19.5 (18.8, 20.2)	15.2 (14.8, 15.5)	8.2 (6.7, 9.8)
2	58.2 (56.3, 60.1)	19.0 (18.3, 16.0)	15.1 (14.2, 16.0)	7.8 (6.7, 8.8)
3	59.7 (58.0, 61.4)	18.4 (17.5, 19.2)	14.1 (13.3, 14.9)	7.9 (6.6, 9.1)
4	62.1 (60.4, 63.8)	17.2 (16.7, 17.6)	13.5 (12.7, 14.3)	7.2 (6.3, 8.1)
5	64.1 (62.1, 66.1)	16.4 (15.8, 17.0)	12.8 (12.1, 13.6)	6.7 (5.7, 7.6)
6	66.6 (64.7, 68.5)	16.1 (15.3, 16.9)	11.7 (10.9, 12.6)	5.6 (4.7, 6.4)
7 (Highest SES)	69.6 (67.9, 71.3)	14.7 (14.1, 15.4)	10.9 (10.0, 11.7)	4.8 (4.2, 5.5)

*The referent group for statistical comparisons in both the SEER and NCDB analyses was patients in the highest SES groups. Bold values for other SES groups represent statistically significant differences at P < 0.05, and all comparisons were significant.
**The multivariable analysis of SEER data adjusted for age, sex, race/ethnicity, personal cancer history, marital status, histology, and year of diagnosis. Insurance status was considered an intermediate variable and was not adjusted for.
***The multivariable analysis of NCDB data adjusted for age, sex, race/ethnicity, Charlson-Deyo comorbidity score, personal cancer history, histology, and year of diagnosis. This analysis included census division as a cluster variable. Insurance status and evaluation at multiple Commission on Cancer-accredited facilities were considered intermediate variables and were not adjusted for.

P263

Indocyanine Green Lymphangiography: An Alternative to Blue Dye Detection for Sentinel Lymph Node Biopsy in Cutaneous Malignancies of the Head and Neck R.I. Neves,[1]* C. Parham,[2] C. Pameijer.[1] *1. Surgery, Penn State Cancer Institute, Hershey, PA; 2. Penn State Health Hershey Medical Center, Hershey, PA.*

Introduction: Sentinel lymph node biopsies (SLNB) are standard for staging of invasive cutaneous melanoma (CM). Preop lymphoscintigraphy (LS) with ^{99}Tc and intraop use of a blue dye (BD) is used to identify the SLN. SLNB for CM occurring in the head and neck (HN) region can be challenging due to multiple draining LN basins, small size of LNs, and anatomic challenges of nodal removal. In addition, the proximity of the primary site to draining LN basins may preclude accurate tracer identification of the SLN. Also, previous studies have demonstrated complications with the use of BDs including anaphylactic reactions, wound infections, and inconsistent identification of SLNs. Our objective is to evaluate the SLN detection in HN malignancies with the use of intraop Indocyanine Green (ICG) lymphangiography. Methods: Ten consecutive cases of primary CM of the HN without clinically evident regional metastasis undergoing SLNB with ICG and identification by the SPY-PHY Fluorescence Imaging Technology (Stryker Corp., Kalamazoo, MI, USA) in association with a preop LS with Spect-CT were evaluated. A total of up to 1mL of ICG was injected intradermally around the primary lesion. The SLNs were confirmed through an enhanced fluorescence white light images in real-time and subsequently with Gamma probe and pathological identification. Results: All SLNs identified preop by LS with Spect-CT were correctly identified by the SPY-PHY system. In all cases, visual localization of the lymphatic drainage in the skin helped to detect the LN basin. Very bright appearance of the SLN has made identification easier and dissection from nearby structures safer. Confirmation via Gamma probe and pathological evaluation were 100%. There were no complications at the injection sites in any patients. Conclusion: In this pilot case series, the ICG lymphangiography via the SPY-PHY system proved as a safe and reliable alternative to BD localization in SLNB of HN CM. It showed easier SLN visualization and detection compared to BD injection and possibly a decreased complication profile. Longer term studies are needed to accurately assess false negative rates.

P264

Clinical Impact of Shave Biopsy on Surgical Management of Cutaneous Melanoma L. Petit,[1]* J.M. Lyons, III.[2] *1. Louisiana State University Health Science Center, New Orleans, LA; 2. Our Lady of the Lake Regional Medical Center, Baton Rouge, LA.*

Introduction: Sampling of suspicious pigmented lesions using a shave biopsy technique has not been universally recommended due to its potential to transect and possibly understage the index lesion. However, this method is routinely used in clinical practice. We aimed to determine the ability of preoperative shave biopsy to predict final T-stage and the impact of this technique on definitive surgical treatment and outcomes. Methods: We reviewed records of patients with cutaneous melanoma who had undergone a preoperative biopsy and were subsequently referred to surgical oncology at our institution for definitive surgical management between 2012 and 2017. Results: 196 patients diagnosed with cutaneous melanoma were identified. 103 lesions were thin (<1mm). 73 lesions were intermediate thickness (1-4mm). The mean Breslow's depth was 1.1mm. Lesions were located in the head and neck (15%), trunk (30%), and extremities (55%). 163 (83%) had shave biopsies performed by 35 separate referring dermatologists. Following surgical excision, residual melanoma was only observed in 22% (36/163) of specimens. Greater postop Breslow's depth was noted in 16% (20/163), and a higher T-stage in 9% (15/163). While 19 patients warranted an additional operation to manage their disease, only 2 (1%) required this because of discordant pre and postoperative staging. Patients who underwent a shave biopsy (n=163) were compared to patients who underwent other biopsy types including excisional, punch, or incisional biopsies (n=25). The prevalence of patients with a greater postoperative Breslow's depth did not significantly differ between these two groups, and was 10.4% (n=17) for shave biopsy and 8.0% (n=2) for other (p=1.00). When comparing the preoperative and postoperative TNM staging, a substantial agreement was observed as measured by weighted kappa across all observations [k=0.76, 95% CI (0.69, 0.84)]. Conclusion: In our experience, preoperative shave biopsies adequately reflect the Breslow's depth and T-stage of cutaneous melanoma in the vast majority of cases. When discordance is observed it rarely results in additional surgery. Shave biopsies can safely be used to determine definitive surgical planning.

P265

Molecular Mutations and Their Association with Site of First Recurrence in Patients with Melanoma M. Hill,* E. O'Halloran, S. Murthy, S. Reddy, J. Farma. *General Surgery, Fox Chase Cancer Center, Bala Cynwyd, PA.*

Introduction: In patients with high risk, metastatic, and recurrent melanoma, molecular testing is now being routinely performed to identify treatment targets. NRAS and BRAF have been identified as two common mutations, but their prevalence among different recurrence patterns is not well established. The aim of this study was to determine the rate of NRAS and BRAF mutations among patients with recurrent melanoma and determine the effect they have on disease free (DFS) and overall survival (OS). Methods: A retrospective review was performed to identify all patients with melanoma who had molecular profiling performed. Clinico-pathologic characteristics, mutations, and recurrence patterns were identified. Patients were categorized into one of five recurrence categories based on the site of first recurrence: in-transit or satellite, local, regional, distant, or simultaneous local and distant recurrence. DFS and OS were compared for each recurrence pattern with BRAF and NRAS mutations. Results: Two hundred forty patients had molecular profiling performed; of these, 109 patients had recurrence. Twenty-seven (24.8%) patients were found to have a BRAF mutation and 37 (33.9%) had NRAS. Thirty (27.5%) patients had in-transit or satellite metastasis as their site of first recurrence; 15 (50%) had a NRAS mutation and 5 (16.7%) had a BRAF mutation. Patients with in-transit metastasis as their site of first recurrence had greater odds of having a NRAS mutation (OR 2.59, p=0.032). DFS was noted to be significantly shorter among patients with this recurrence pattern and a NRAS mutation compared to a BRAF mutation (15.5 months versus 69.4 months (p= 0.02). OS was clinically but not statistically different (47.7 months versus 89.6 months (p=0.1). Among the other sites of first recurrences, no difference was noted

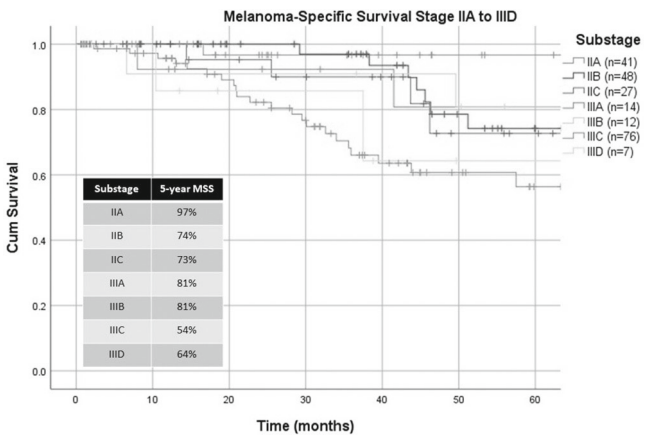
in DFS or OS. Conclusions: In patients with melanoma, those with in-transit metastasis as their site of first recurrence are more likely to have an NRAS mutation. These patients have a dramatically shorter DFS and OS compared to those with BRAF mutations. This large difference has significant implications in patient counseling and emphasizes the need for NRAS targeted therapy.

P266

Substage-Specific Survival in Acral Lentiginous Melanoma

A.Y. Lee,[1]* E. Friedman,[1] J. Sun,[2] A. Potdar,[2] H. Daou,[2] N.E. Farrow,[3] C. Farley,[5] J. Vetto,[4] D. Han,[4] M. Tariq,[5] R. Shapiro,[1] G. Beasley,[3] C. Contreras,[6] I. Osman,[1] M. Lowe,[5] J. Zager,[2] R. Berman.[1] *1. Surgery, New York University, Mount Kisco, NY; 2. Moffitt Cancer Center, Tampa, FL; 3. Duke University, Durham, NC; 4. Oregon Health and Science University, Portland, OR; 5. Emory University, Atlanta, GA; 6. University of Alabama, Birmingham, AL.*

Introduction: Decreased survival rates in acral lentiginous melanoma (ALM) compared to non-acral melanomas are thought to be secondary to late presentation, but this has only been studied in smaller cohorts. We sought to characterize clinicopathologic features and analyze melanoma-specific survival (MSS) by substage in a large cohort of ALM patients. Methods: A retrospective review of the US Melanoma Consortium database, a large prospectively-collected database from 6 academic centers, was performed. Primary ALMs treated between 2000 and 2017 were included. Clinicopathologic data included age, sex, race, AJCC 8th edition stage and MSS. Results: We identified 434 patients with primary ALMs with median follow-up of 33 months. Median age at diagnosis was 66 years (range 22-97). Self-identified race was available for 426 patients, of whom 355 (83%) were non-Hispanic White, 52 (12%) were Black, 12 (3%) were Hispanic, and 5 (1%) were Asian/Pacific Islander; 53% were female. Median thickness was 1.8mm (range in situ - 19.0mm). Ulceration was present in 160 (37%) and any mitoses in 268 (58%). At presentation, 20 patients (5%) were pathologic stage 0, 150 (34%) stage I, 116 (27%) stage II, 109 (25%) stage III, and 5 (1%) stage IV. An additional 34(8%) patients had incomplete staging due to lack of information about ulceration and/or nodal status. Five-year MSS was excellent in patients with stage 0 (100%, n=20) to IIA (97%, n=41); however, stage IIB (74%, n=48) was notably similar to IIC (73%, n= 27) (Figure 1), and lower than expected based on recent AJCC stage IIB data (5-year MSS 87%). Stage IIIC patients had 5-year MSS of 54%; 86% of IIIC deaths occurred within 3 years of surgery while 80% of IIB/IIC deaths occurred after 3 years. Conclusions: Contrary to prior reporting, a significant number of our cohort presented with early stage disease. At 5 years, stage IIB/IIC patients have worse MSS than IIIA/IIIB, suggesting that T3b or higher T category is associated with poor MSS even in the absence of nodal metastases. Melanoma-specific death often occurred after 3 years for stage IIB/C patients and should be considered when tailoring surveillance strategies for acral melanomas.

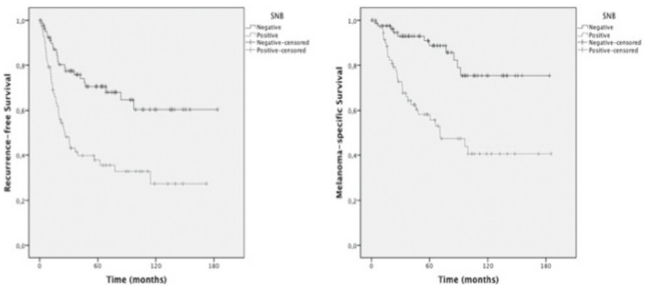


P267

Prognostic Impact of Sentinel Node Status in T4 Melanoma Patients

E. Bertolli,[2]* A.S. Jafelicci,[2] E. Doria Filho,[4] M.P. de Macedo,[1] C.A. Pinto,[1] V.F. Calsavara,[3] J.P. Duprat Neto.[2] *1. Pathology - AC Camargo Cancer Center, São Paulo, Brazil; 2. Skin Cancer Department - AC Camargo Cancer Center, São Paulo, Brazil; 3. Epidemiology and Statistics Department - AC Camargo Cancer Center, São Paulo, Brazil; 4. Surgical Oncology Residence Program - AC Camargo Cancer Center, São Paulo, Brazil.*

Background: Although sentinel node biopsy (SNB) is the main tool for nodal staging in melanoma patients, its role in patients with thick primary lesions is still controversial, mainly due to the risk of systemic disease. Objectives: To evaluate the impact of SNB in T4 melanoma patients and its clinical implications Patients and methods: Retrospective analysis of patients with thick melanomas who underwent SNB in a single institution from 2000 to 2015. Recurrence-free survival (RFS) and Melanoma-specific survival (MSS) were assessed by Kaplan Meier curves, non-parametric logrank test, and by Cox single and multiple regressions. Results: Among 1213 patients who underwent SNB from 2000 to 2015, 158 presented with T4 primary lesions (13.02%). There were 60.8% male patients and mean age was 55.6 years (range 5 – 86, SD 17.43) and mean follow up was 65.3 months. SNB was positive in 47.5% of patients and all of them underwent completion lymph node dissection. The only characteristic of primary lesion that was statistically related to SNB positivity was lymphatic invasion [OR 8.0 (CI 95% 1.722 – 37.1620; p 0,006]. There were 8 local relapses, all of them in patients initially considered as SNB negative. SNB positivity was statistically related to RFS [logrank < 0.0001 – HR 5.005 (CI 95% 2.066 – 12.125); p < 0.0001] and MFS [logrank < 0.0001 –HR 4.211 (CI95% 1.479 – 11.9880); p 0,007]. Conclusions: SNB result impacts in prognostic even in T4 melanoma patients. Until there is no adjuvant treatment available for high-risk stage II patients, SNB should be offered to patients with thick primary lesions for better staging and risk stratification of these patients.



Kaplan Meier curves for A) Recurrence-free survival and B) Melanoma specific survival in T4 melanoma patients who underwent sentinel node biopsy at AC Camargo Cancer Center from 2000 to 2015

P268

Comparative Analysis of Acral Melanoma in Chinese and Caucasian Patients

K. Huang,[1]* Y. Xu,[2] R. Joseph,[3] S.P. Bagaria,[3] S. Misra,[1] Y. Chen.[2] *1. General Surgery, Brandon Regional Hospital, Brandon, FL; 2. Fudan University Shanghai Cancer Center, Shanghai, China; 3. Mayo clinic florida, Jacksonville, FL.*

Background Acral melanoma (AM) is the most common subtype of melanoma in Chinese and least common in Caucasians. It is unclear if outcomes differ between Chinese and Caucasians diagnosed with AM. We sought to compare the patient characteristics and survival between Chinese and Caucasians diagnosed with AM utilizing two large institutional databases located in China and the US. Methods Retrospective review of a Chinese-based and US-based institutional databases identified patients diagnosed with AM from 2009 to 2015. Clinicopathologic data, including age, gender, race, pTMN staging, location, Max diameter, Breslow thickness, Clark level, Histology, ulceration, Sentinel lymph node status, surgical approach and adjuvant therapy, were collected and analyzed. The primary outcome measured was disease-specific survival (DSS). Results Overall, 281 consecutive Chinese AM patients and 62 Caucasian AM patients were identified. The Chinese group presented with more advanced disease compared with Caucasians: thicker Breslow depth (median 3.0 mm vs. 1.2 mm), more ulcerated disease (64.8% vs 29%) and advanced stages (stage II/III 83.9% vs 37.1%), compared to those in the US.

No significant difference was identified in terms of age at diagnosis, gender, location, histologic subtypes and node positive rate. The 5-year DSS rate was 63.3% vs. 72% (P=0.23). When stratified by stage, the lack of significance in DSS between Chinese and Caucasians persisted. In multivariate analysis, Breslow thickness (P=0.04), ulceration(P=0.02) and positive sentinel lymph nodes (p=0.002) predicted worse DSS. The hazard ratio for Chinese vs. Caucasian was 1.61 (0.74-3.50, 95% CI; P=0.23). Conclusion This study represents the first comparison of Chinese and Caucasian patients diagnosed with AM. There appears to be no difference in survival between the two racial groups, therefore suggesting that the biological course of AM is likely similar between Chinese and Caucasians. These data support the implementation of clinical trials of AM that include both Chinese and Caucasian cohorts.

Analysis of factors associated with disease specific survival in AM patients from FUSCC and Mayo Clinics

Variable	Univariate analysis		Multivariate analysis	
	Hazard Ratio(95% CI)	P Value	Hazard Ratio(95% CI)	P value
Age	1.02(1.00-1.04)	0.06		
Gender(Male vs. Female)	1.47(1.13-1.91)	0.004*	1.66(0.94-2.93)	0.08
Pathologic stage				
(0/I vs. III)	0.16(0.06-0.41)	<0.001*	1.50(0.32-7.05)	0.61
(II vs. III)	0.52(0.32-0.84)	0.01*	2.17(0.84-5.58)	0.11
Location (Volar vs. Subungual)	1.11(0.65-1.89)	0.69		
Breslow thickness(mm)	1.05(1.03-1.10)	0.03*	1.04(1.03-1.09)	0.04*
Clark Level				
(I/II/III vs. IV/V)	0.34(0.15-0.75)	0.01*	0.83(0.35-1.96)	0.67
(unreported vs. IV/V)	0.44(0.24-0.84)	0.01*	0.56(0.19-1.67)	0.30
Histology				
(Nodular vs. Acral lentiginous)	0.99(0.24-4.05)	0.99		
(superficial spreading vs. Acral lentiginous)	0.24(0.03-1.73)	0.16		
Ulceration (Yes vs. No)	4.25(2.17-8.30)	<0.001*	3.09(1.20-8.00)	0.02*
SLN biopsy (No vs. Yes)	0.19(0.03-1.44)	0.12		
SLN biopsy status	3.13(1.95-5.03)	<0.001*	4.40(1.70-11.36)	0.002*
Surgery (amputation vs. WLE)	1.20(0.91-1.58)	0.19		
Adjuvant therapy (yes vs No)	0.79 (0.59-1.06)	0.12		

P269

Upregulation of CD4+/CD8+ Lymphocyte Activity Following Intratumoral Anti-PD-1 Injection R.J. Hendrix,* J. Chuprin, N. Condron, M. Brehm, G. Whalen. *University of Massachusetts Medical School, Worcester, MA.*

Background: Subsets of CD4+/CD8+ lymphocytes possess unique cytokine profiles which vary in response to specific environmental stimuli. These cytokines regulate cell growth, cell differentiation, and play an integral role in immunomodulation. Blockade of programmed cell death protein 1 (PD-1) could produce functional changes in CD4+/CD8+ lymphocytes which translate to a heightened state of activity and an enhanced immune response. Methods: Lymphocytes were isolated following injection of intratumoral (IT) anti-PD-1 at 10mg/kg (n=5) or IT PBS solution (n=5). Using the techniques of intracellular cytokine staining, CD4+/CD8+ lymphocyte production of intracellular interleukin-2 (IL-2), tumor necrosis factor alpha (TNF-a), and interferon (IFN-n) was determined. Generation of cytokines was assessed in an unstimulated state, a moderately stimulated state (exposure to anti-CD3/anti-CD28 beads), and a highly stimulated state (exposure to PMA/Ionomycin). Analysis was performed using FlowJo (v.10.0, FlowJo LLC). Results: The proportions of CD4+/CD8+ lymphocytes were similar between mice treated with IT anti-PD-1 and IT PBS, respectively (CD4+: 76.9% v 70.4% ; CD8+: 19% v 24.8%). In the unstimulated model, treatment with IT anti-PD-1 resulted in increased proportions of CD4+/CD8+ lymphocytes producing IFN-n(CD4+: 70.4% v 61.6% ; CD8+: 71.4% v 60.9%) and TNF-a(CD4+: 10.4% v 9.5% ; CD8+ 13.6% v 7.3%). There was no difference in production of IL-2 (Table 1). After moderate stimulation with anti-CD3/anti-CD28 beads, there were no differences in cytokine expression for either group compared to the unstimulated baseline state. In the highly stimulated state after exposure to PMA/Ionomycin, production of all cytokines was increased. However, the response was greatest after IT injection of anti-PD-1: IFN (CD4+: 76.4% v 63.1% ; CD8+: 78.1% v 58.4%), TNF (CD4+: 39.0% v 28.5% ; CD8+: 21.0% v 11.9%), and IL-2 (CD4+: 16.2% v 9.8% ; CD8+: 78.1% v 58.4%). Conclusion: Intratumoral injection of a PD-1 inhibitor produces a heightened CD4+/CD8+ immune response as measured by generation of intracellular IL-2, TNF-a, and IFN-n. This functional upregulation may contribute to enhanced antitumor immunity.

Table 1. Cytokine Profiles of CD4+/CD8+ Lymphocytes After Intratumoral (IT) Injection in Unstimulated, Moderately Stimulated, and Highly Stimulated States

	CD4+ IL-2	CD4+ TNF-α	CD4+ IFN-γ	CD8+ IL-2	CD8+ TNF-α	CD8+ IFN-γ
Unstimulated						
IT anti-PD-1	1.6	10.4	70.4	0.0	13.6	71.4
IT PBS	1.7	9.5	61.6	0.7	7.3	60.9
Anti-CD3/Anti-CD28						
IT anti-PD-1	1.6	25.1	80.6	0.7	15.6	82.0
IT PBS	1.1	23.5	88.7	0.4	16.6	87.5
PMA/Ionomycin						
IT anti-PD-1	16.2	39.0	76.4	4.5	21.0	78.1
IT PBS	9.8	28.5	63.1	1.3	11.9	58.4

*All values recorded as % of lymphocytes

P270

Merkel Cell Carcinoma in Patients in Very Old Patients: A Population-Based Analysis of Treatments and Outcomes. E. Jost,[1]* J. Mckinnon,[1] E. Thiboutot,[2] A. Bouchard-Fortier.[1] *1. Surgical Oncology, University of Calgary, Calgary, AB, Canada; 2. Universite Laval, Montreal, QC, Canada.*

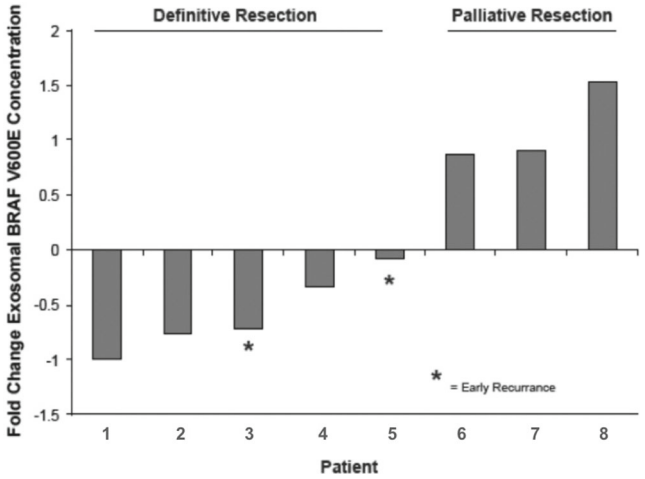
Introduction: Merkel Cell Carcinoma (MCC) is a rare neuroendocrine malignancy of the skin more prevalent in older patients. Evidence supporting treatment in patients older than 85 years is lacking due to the paucity of studies that specifically address this age group. In this study we sought to describe the clinical characteristics, treatment patterns and oncologic outcomes of patients ≧85 years with newly diagnosed MCC. Methods: This is a population-based cohort of all patients ≧ 85 years evaluated for MCC between 1982 and 2015 in Alberta. Patient data was obtained from a provincial cancer registry. Chart reviews were performed to abstract patient demographics, tumour characteristics, treatment, and outcome measures. Results: A total of 212 patients were diagnosed with MCC during the study period, of which 48 patients were ≧ 85 years old (mean age: 89.7 years). At diagnosis, most of the patients in this group had T1 primary tumours (91.3%), were clinically node-negative (64.7%) and without evidence of distant metastasis (100%). Biopsy was the only treatment provided to 18 (37.5%) patients. A total of 26 (54.2%) patients underwent excision of their MCC, of whom only 6 underwent lymph node surgery. Adjuvant radiotherapy (RT) was given to 7 (27.9%) patients, and 4 (8.3%) underwent palliative RT. No patients received chemotherapy during the study period. At a median follow-up of 9.0 months, 19 (41.3%) of patients developed locoregional recurrences, of which, 7 (36.8%) were treated with RT alone as opposed to 5 (26.3%) with surgery. Median disease-free survival and overall survival were 6.0 and 16.5 months respectively. MCC was noted to be the cause of death for only 3 patients (6.7%). Conclusions: This study suggests that patients ≧ 85 years with MCC are undertreated according to current guidelines with only 54.2% of patients getting definitive surgery and 20.8% undergoing RT. Despite conservative treatment, most of these patients did not die of MCC-related causes. Further study is required to help inform the choice of multimodality therapies order to improve quality and delivery of care in elderly patients.

P271

Blood-based Assays for BRAFV600E: Comparison of ctDNA and Exosomes in Melanoma and Papillary Thyroid Cancer G.G. Kasumova,[1]* W.A. Michaud,[1] M. Hazar-Rethinam,[1] B. Nadres,[1] M. Kim,[1] V. Gunda,[1] S. Amin,[1] D.T. Frederick,[1] S. Parangi,[1] R.J. Sullivan,[1] R.B. Corcoran,[1] D.J. Panka,[2] C.C. Lubitz,[1] G. Boland.[1] *1. Massachusetts General Hospital, Boston, MA; 2. Beth Israel Deaconess Medical Center, Boston, MA.*

Introduction: BRAFV600E mutations are present in half of patients with papillary thyroid cancer (PTC) and two-thirds of patients with melanoma. Blood-based assays allow for serial, quantitative analysis to monitor treatment effects and serve as a potential biomarker of tumor burden and disease recurrence. The aim of this study was to compare the detection of BRAFV600E using blood based biomarkers of tumor derived fragmented or cell-free DNA (ctDNA) and exosomes, circulating microvesicles, to standard tissue analysis. Methods: Melanoma and thyroid cancer cell lines, as well as patient plasma with confirmed BRAFV600E were used for analysis. CtDNA was isolated using the QIAamp circulating nucleic acid kit. Exosomal vesicles and RNA were isolated using serial ultra-centrifugation or exoRNeasy serum/plasma

kits. CtDNA and cDNA from extracted exosomal RNA were analyzed using droplet digital PCR. Results: In vitro, BRAFV600E mutations were detected in both melanoma (N=3) and thyroid cell lines (N=3), cell-line derived exosomes, and ctDNA released from tumor cells. In patients with stage IV melanoma, BRAFV600E was detected in both ctDNA and exosomal cDNA (N=2). In addition, in patients with melanoma, exosomal BRAFV600E levels corresponded with tumor burden pre- and post-treatment, with decreased levels following definitive resection (N=5) and increased levels following palliative resection N=3) (Figure 1). Furthermore, BRAFV600E levels from ctDNA could predict visceral recurrence of melanoma prior to radiographic recurrence. However, in patients with thyroid cancer and tissue confirmed BRAF mutation (N=17), ctDNA analysis and exosomal RNA did not detect BRAFV600E at any stage of disease. Conclusions: In melanoma, BRAFV600E can be monitored both in vitro and peripheral blood derived ctDNA and exosomes, and is reflective of tumor burden and response to therapy. However, these blood based biomarkers do not appear to be promising in the detection of papillary thyroid cancer in patient samples, reflecting underlying differences in mechanisms of tumor shedding and the need for alternative biomarker assays for PTC.

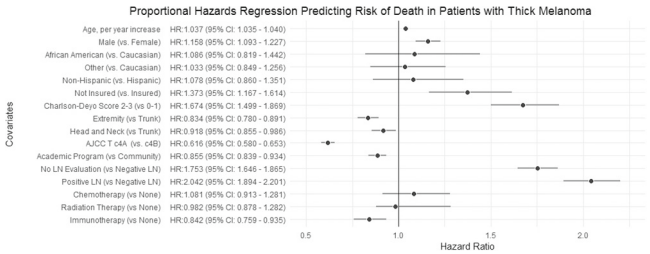


Fold change in exosomal BRAFV600E concentration following definitive (patients 1-5) or palliative (patients 6-8) resection.

P272

To Do or Not to Do? Regional Lymph Node Evaluation in Patients with Thick Melanoma E.L. Ryon,* O. Picado, M. Moller, N. Goel, S.B. Kesmodel. *University of Miami, Miami, FL.*

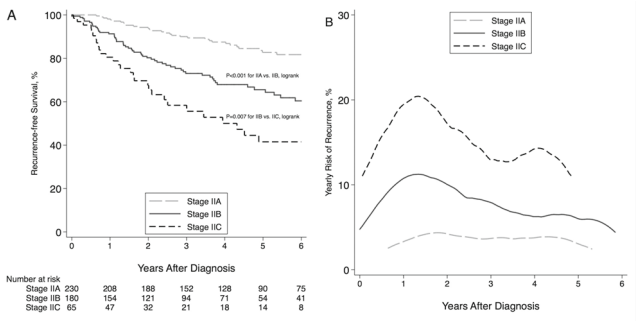
INTRODUCTION: Sentinel lymph node biopsy in patients with thick melanoma is controversial. We examine regional lymph node evaluation (RLNE) in patients with T4 melanoma and the impact on treatment and overall survival (OS). METHODS: Patients with clinical T4N0M0 melanoma were selected from the National Cancer Database (2004-2015). Clinical characteristics were compared between treatment groups. Logistic regression analysis was used to identify factors associated with RLNE and treatment. Survival analysis was performed using Kaplan-Meier method and Cox regression model. RESULTS: 14,286 patients with clinical T4N0M0 melanoma were identified; 10,020 (70.2%) had RLNE with positive LNs identified in 2,713 (27.1%). Mean age was 67.2 years and most were male (65.2%), Caucasian (97.1%) and treated at academic centers (46.2%). RLNE was more likely in males (OR: 1.41, 95% CI: 1.29–1.54, p<.001), patients with extremity (OR: 1.16, 95% CI: 1.05–1.29, p<.001) or non-ulcerated primaries (OR: 1.16, 95% CI: 1.06–1.26, p<.001), or patients treated at academic centers (OR: 1.54, 95% CI: 1.42–1.67, p<.001). Immunotherapy use was more common in patients undergoing RLNE (13.9% vs 3.4%, p<.001) and was associated with positive LNs (OR: 2.50, 95% CI: 2.19–2.86, p<.001). The median follow-up was 51 months. The 5-year estimate of OS for patients treated with RLNE was 56.8% and without was 32.7%. Independent factors associated with better OS were non-ulcerated (HR: 0.62, 95% CI: 0.58–0.65, p<.001), extremity (HR: 0.83, 95% CI: 0.78–0.89, p<.001) or head/neck (HR: 0.92, 95% CI: 0.86–0.99, p<.001) primaries, treatment at an academic center (HR: 0.89, 95% CI: 0.84–0.93, p<.001), and immunotherapy use (HR: 0.84, 95% CI: 076–0.94, p<.001). (Figure 1) CONCLUSIONS: RLNE was performed in the majority of patients with thick melanoma. Use of immunotherapy was more common in those who underwent RLNE and was associated with nodal involvement and better OS. RLNE in patients with thick melanoma is important for prognosis and to risk stratify patients for use of adjuvant therapy and enrollment on clinical trials.



P273

Patterns of Recurrence in Stage II Cutaneous Melanoma
J.M. Bleicher,[1]* D.S. Swords,[1] T.L. Bowles,[2] J.R. Hyngstrom.[1]
1. General Surgery, University of Utah, Salt Lake City, UT;
2. Intermountain Medical Center, Salt Lake City, UT.

Introduction: Optimal adjuvant and surveillance strategies for resected Stage II melanoma patients are unknown. The NCCN recommends considering imaging surveillance in stage IIB-IIC but not stage IIA. Adjuvant therapy is not recommended for stage IIA, and observation vs. interferon is recommended for stage IIB-IIC. We aimed to review institutional recurrence rates, patterns, and detection methods in patients with stage II melanoma. Methods: Retrospective review of prospectively followed patients with resected AJCC 8th edition stage II cutaneous melanoma from 2000-2015 was performed. Eleven patients were excluded due to missing data. Recurrence-free survival (RFS) was calculated using the Kaplan-Meier method. Dynamic changes in substage-specific recurrence risk over time were evaluated by calculating yearly hazards of recurrence. Recurrences were classified as local/in transit, regional, and distant. Recurrences were classified as detected by the patient, imaging, or physician exam. Results: Of 475 patients, 48.4% were stage IIA, 37.9% IIB, and 13.7% IIC. Median follow-up was 3.7 years (interquartile range 1.8, 6.1). Five-year RFS was 82.7% (95% confidence interval [CI] 76.0%, 87.7%) in stage IIA, 64.4% (95% CI 55.5%, 71.9%) in IIB, and 41.5% (95% CI 26.7%, 55.7%) in IIC (Figure A). Risks of recurrence were highest in the 2nd year after diagnosis for stages IIB-IIC, but were consistent over time for stage IIA (Figure B). Of 130 recurrences, 16.9% were local/in transit, 33.1% were regional, and 50.0% were distant. Recurrence type did not vary based on stage (P=0.67, chi-square). Of 109 patients with data on method of recurrence detection, 63.3% were patient detected, 25.7% were detected in imaging surveillance, and 11.0% were detected by physician exam. Detection method did not vary by stage (P=0.09). Conclusion: Distant metastatic recurrence risk is higher for all stages in this series compared to the literature, and 25% of recurrences were detected by imaging. Guidelines for surveillance imaging should reflect this increased risk of distant recurrence for stage IIB-IIC, and possibly IIA, particularly in the first 2-3 years. High metastatic failure risk demands further investigation of novel adjuvant strategies.



Recurrence-free Survival (A) and Yearly Risk of Recurrence (B) by Stage.

P274

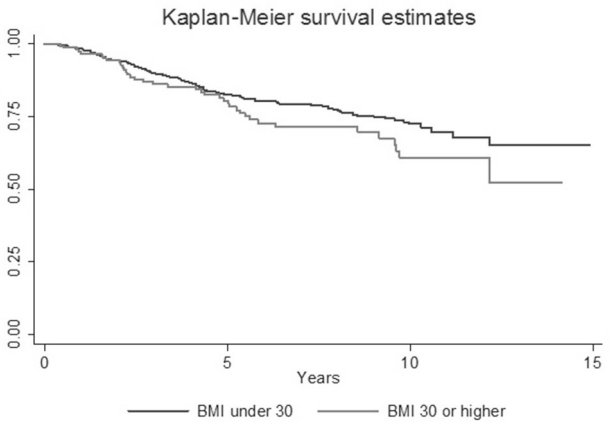
Relevance of the AJCC 8th Edition Staging System for Merkel Cell Carcinoma in the Canadian Setting B. Dingley,[1]* C. Nessim,[1] A.M. Ibrahim,[2] S. Rodriguez-Qizilbash,[3] D. Berger-Richardson,[4] G. Paull,[1] E. Sabri,[2] R. Younan,[5] J. Hetu,[6] F. Wright,[4] S. Johnson-Obaseki.[2] *1. General Surgical Oncology, University of Ottawa, Ottawa, ON, Canada; 2. Ottawa Hospital Research Institute, Ottawa, ON, Canada; 3. Université de Montréal and Université de Sherbrooke, Montreal, QC, Canada; 4. Sunnybrook Research Institute, Toronto, ON, Canada; 5. Université de Montréal, Montreal, QC, Canada; 6. Université de Sherbrooke, Sherbrooke, QC, Canada.*

Limited studies have reported on treatment outcomes in Merkel cell carcinoma (MCC). We describe treatment and survival outcomes of MCC in Canada and compare this to the American experience that formed the basis for the AJCC 8th edition for MCC. A Canadian multicenter retrospective review of early-stage MCC was conducted. Patient demographics, tumour characteristics, treatment and survival data were collected between June 2000-June 2015. Recurrence-free (RFS) and overall survival (OS) were calculated using the Kaplan-Meier method. Statistical comparisons (log-rank test and cox regression) were conducted. We identified 171 patients (36.4% Stage I, 12.4% Stage IIA, 17.3% Stage IIB, 12.4% Stage IIIA, 21.6% Stage IIIB). The majority of patients were male (64.3%), with a mean age of 73 and 12.1% having prior immunosuppression. The most common primary site of disease was head and neck (50.3%), followed by upper extremity (17.5%), lower extremity (17.0%), trunk (10.5%) and unknown primary (4.7%). Of all stages, 36.8% of patients were treated with surgery alone, 48.5% with surgery + neo- or adjuvant treatment and 14.7% with radiation alone. The median follow-up time was 2.22 years (IQR 0.97-4.17) for the whole cohort (3.01 years for patients still alive (IQR 1.28-4.74)) whereby 35.1% of patients recurred: 11.7% local, 25.7% regional, 19.9% distant. Five-year OS for Stage I, II and III was 72.3%, 57.3% and 52.9%, respectively. This contrasts to a large population based study that informed the AJCC 8th edition that reported Stage I, IIA, IIB, IIIA, and IIIB five-year OS of 62.8%, 54.6%, 34.8%, 40.3%, and 26.8% respectively. Patients treated with surgery + neo- or adjuvant treatment had better outcomes versus patients treated with radiation (HR 0.34 95% CI 0.15-0.75, p=0.008) or surgery (HR 0.50 95% CI 0.25-0.99; p=0.046) alone. In the first pan-Canadian cohort of MCC, across all stages, Canadian patients have a higher OS than those reported for the 8th edition of the AJCC. Further analysis is required to understand this difference. Benefit was found in the use of multimodality treatment approaches. This research will inform future Canadian guidelines on treatment for MCC.

P275

High Body Mass Index and Gender are Associated with Decreased Melanoma Specific Survival in Stage IB-II Melanoma: A Retrospective Single-Institution Analysis E. Deckers,[1]* B.L. van Leeuwen,[1] S. Kruijff,[1] L.B. Been,[1] E. Bastiaannet,[2] H. Hoekstra.[1] *1. Surgical oncology, UMCG, Groningen, Netherlands; 2. LUMC, Leiden, Netherlands.*

Introduction: Clinicopathologic characteristics, such as Breslow thickness, mitosis, the presence of ulceration and SLNB positivity are of prognostic value in melanoma patients. However, little is known about the prognostic value of patient-related characteristics in stage IB-II melanoma. Obesity has been associated with an increased risk for several types of cancer and worsened prognosis after cancer diagnosis. This study's aim was to examine the effects of obesity (BMI≥30) and gender on treatment outcome in Stage IB-II melanoma. METHODS: Data concerning melanoma patients who underwent SLNB between 1996-2017 at the UMCG were collected prospectively. Cox regression analyses were used to determine whether tumor and patient-related variables were associated with recurrences, melanoma-specific-, and overall survival. Variables included were: gender, obesity, Breslow thickness, localization, histology, ulceration, mitotic rate and SLNB status. RESULTS: SLNB was performed in 721 patients, 360 females and 361 males, median age 61 (range 18-92) years. Tumor location: 106 H&N (14.7%), 284 trunk (39.4%), 100 upper limb (13.9%) and 231 lower limb (32%). Median Breslow thickness 2.1 (range 0.2-20) mm. The SLNB positivity rate was 28%. There were 150 obese patients (21%), 79 females (52.7%) and 71 males (47.3%). Five-years Melanoma Specific Survival (MSS) was decreased in obese patients (p=0.04; HR=1.56 with 95% CI 1.02-2.37). Decreased Recurrence Free Survival (RFS, p=0.03; HR=1.46 with 95% CI 1.04-2.04) and MSS (p=0.05; HR=1.51 with 95% CI 1,00-2.28) were found in men. SLNB status was not related to BMI (p=0.56) or gender (p=0.29). CONCLUSIONS: Obesity was significantly associated with decreased 5-year melanoma specific survival in non-metastatic melanoma patients. Men were found to have a decreased melanoma-specific- and recurrence free survival. SLNB status was not related to BMI and gender.



Kaplan Meier - Melanoma Specific Survival

P276

Increase of Sentinel Lymph Node Melanoma Staging: A Population-based Study in the Netherlands E. Deckers,[1]* M. Louwman,[2] L.B. Been,[1] S. Kruijff,[1] H. Hoekstra,[1] B.L. van Leeuwen.[1] *1. Surgical oncology, UMCG, Groningen, Netherlands; 2. IKNL, Groningen, Netherlands.*

INTRODUCTION: The sentinel lymph node biopsy (SLNB) in Stage IB-II melanoma was introduced in the Netherlands in 1996. The Northeastern Comprehensive Cancer Center (since 2010 comprised in the Netherlands Comprehensive Cancer Organization) disseminated the SLNB concept in the region. A previous report in 2011 showed that SLNB was significantly less often performed in melanoma patients with a low social-economic status. Aim of this study was to describe current practice of SLNB and Completion Lymph Node dissection (CLND) in the Netherlands. METHODS: A total of 19.100 Stage IB-II melanoma patients were registered in the Netherlands Cancer Registry between 2010-2016. Multivariable logistic regression analysis was performed to estimate the odds for undergoing SLNB. RESULTS: SLNB was performed in 9.163 patients (48%). The proportion of melanoma patients who received SLNB in the Netherlands increased from 38% in 2010 to 59% in 2016. Median age was lower among those undergoing SLNB (58 vs 67 years, p<0.001) and melanomas were thicker (median Breslow thickness 1.7 vs 1.3 mm, p<0.001). After adjustment for gender, age and stage the odds for receiving SLNB were significantly lower among elderly (age>75 vs 15-29 (OR=0.11 with 95% CI 0.09-013), and among those with a melanoma in the head/neck area (head/neck vs limb: OR=0.23 with 95% CI 0.20-0.25). Socio-economic status was not related to SLNB (p=0.2). Sentinel positivity rate was 20% of which 54% consecutively received a CLND. CONCLUSION: Over the years, SLNB was increasingly performed up to almost 60% of the Dutch melanoma patients in 2016. Besides, SLNB was no longer related to socio-economic status, and is seldom performed in elderly, and in head/neck melanoma patients. With the expansion of potential treatment options, SLNB staging is of increasing importance for decision-making in overall melanoma treatment.

P277

The Association Between the Cumulative Metastatic Volume, the Total Metastatic Glycolysis and Levels of S-100B and LDH in Stage IV Melanoma Patients E. Deckers,* D. Vallez Garcia, S. Kruijff, S. Damude, L.B. Been, A.H. Brouwers, K.P. Wevers, H. Hoekstra.
Surgical oncology, UMCG, Groningen, Netherlands.

Standardized Uptake Values (SUV) of single lesions of ^{18}F-Fluorodeoxyglucose (FDG) in PET scans and serum S-100B concentrations in stage III melanoma patients are of prognostic value and have been shown to be inversely associated with disease-free survival (DFS). The aim of the present study was to assess the association between tumor markers (i.e. S-100B and LDH) and the PET-derived metrics (i.e. SUV, metabolic active tumor volume (MATV), and total lesion glycolysis (TLG)). In addition, we assessed their prognostic value in Stage IV melanoma patients. A total of 52 newly FDG PET/CT diagnosed stage IV melanoma patients were included between 2010 and 2015. S-100B/LDH samples were taken prior to FDG PET/CT scan. FDG images were analyzed with Accurate (in-house developed analysis software) to determine the PET metrics, corrected for lean body mass. The relationship between PET-derived metrics (i.e. SUV, MATV, and TLG(SUV_{mean}x-MATV)) and the S-100B/LDH was assessed using a linear regression model. Second, the predictive value of these markers on survival was analyzed by a Cox proportional hazard model. Of the 52 Stage IV melanoma patients, 30 were male (42.3%) and 22 female (57.7%), with a median age of 64 (range 29-88) years. A total of 36 patients with a S-100B >0.15µg/L showed higher values of TLG; median 186 (range 17-4306), compared to TLG in patients with a S-100B <0.15µg/L; median 33 (range 2-792). After log-transformation of TLG, this result was significantly different (p<0.001). Eleven patients with elevated LDH (>250U/L) had a significant higher TLG; median 831 (range 131-1673), compared to 41 patients with normal LDH (<250U/L); median 120 (range 2-4305). After log-transformation this result was significantly different (p<0.001). S-100B was associated with shorter melanoma specific survival (p=0.01; HR=1.08 with 95% CI 1.02-1.14), where TLG was not (p=0.916; HR=1.023 with 95% CI 0.67-1.57). Elevated S-100B is associated with higher TLG on FGD PET/CT scans. Besides, S-100B seems to be prognostic more valuable than TLG, as elevation of S-100B showed shorter melanoma specific survival in stage IV melanoma patients.

P278

Overall Survival Improved for Contemporary Patients with Melanoma N.E. Farrow,[1]* M.C. Turner,[1] A.K. Salama,[1] H.F. Seigler,[1] D.S. Tyler,[2] G. Beasley.[1] *1. Department of Surgery, Duke University Hospital, Durham, NC; 2. University of Texas Medical Branch, Galveston, TX.*

Introduction: Since 2011, multiple new therapies have become Federal Drug Administration approved for treatment of advanced melanoma. Access to these drugs, particularly immunotherapies, may be limited in part by cost. Impact on the population level is unknown. Methods: Stage I-IV melanoma patients were identified in the 2004-2015 National Cancer Data Base (NCDB). Patients were grouped into historic (2004-2010) and contemporary (2011-2015) cohorts. Chemotherapy, radiation, and immunotherapy are included, while BRAF/MEK therapies are not included in the NCDB. Overall survival (OS) was compared using Kaplan-Meier curves and Cox proportional hazard modeling adjusting for patient, tumor, and facility characteristics. Results: Of 268,668 included patients, 136,828 were identified from 2004-2010, and 131,840 from 2011-2015. Use of immunotherapy was significantly higher in the contemporary group (5.3% vs 5.1%, p=0.006). Both unadjusted and adjusted OS were improved in the contemporary cohort (Hazard Ratio (HR: 0.90 p<0.001). There was no difference in OS between stage I/II patients (54% of cohort) in the historic cohort compared to contemporary stage I/II (50% of cohort) (HR: 0.99, p=0.63). Significant improvement in OS was seen for stage III/IV in the contemporary vs historic cohort. (HR: 0.85, p<0.001) (Figure 1). Of patients who received immunotherapy, OS was improved for the contemporary compared to historic cohort (HR: 0.87, p=0.014). Conclusions: Contemporary OS rates for patients with melanoma are improved. The effect size is driven by improvements for those with advanced stage disease. Given the low reported use of immunotherapy, the survival benefit suggests that more rapid integration into standard practice may better serve patients with advanced melanoma.

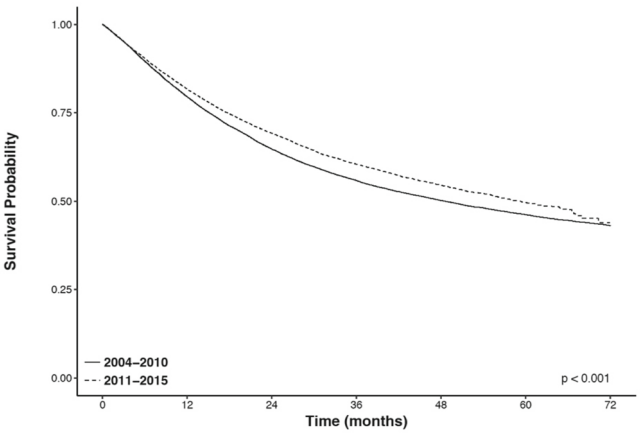


Figure 1: Unadjusted survival curves for Stage III/IV melanoma by contemporary (2011-2015) and historic (2004-2010) cohorts.

P279

Life After MSLT II: Adoption of Nodal Basin Observation for Melanoma Patients with Sentinel Lymph Node Metastases E. Parvez,[1]* J. Shaul,[2] T. Dumitra,[1] D. Morency,[1] A.N. Meguerditchian,[1] F. Tremblay,[1] S. Meterissian,[1] S. Dumitra.[1]
1. Department of Surgery and Oncology, McGill University, Montreal, QC, Canada; 2. McGill University Faculty of Medicine, Montreal, QC, Canada.

Background: The Multicenter Selective Lymphadenectomy Trial II (MSLT-II) demonstrated no survival benefit in patients with sentinel lymph node(SLN) metastases undergoing immediate completion lymphadenectomy(CL) compared to those undergoing nodal observation(NO). Following publication of the landmark trial, it is expected that practice patterns have changed. The objective of this study was to assess real world adoption of MSLT-II in the first year after publication. Methods: All patients undergoing SLN biopsy for melanoma between June 2007-July 2018 were identified from an operating room database. Demographic, clinical and pathological data was retrospectively abstracted from health records. Descriptive statistical analysis and multivariate regression were done. Results: Of the 704 patients undergoing SLN biopsy for melanoma, 89 (68 before and 21 after trial publication) were found to have a positive SLN. Mean age at diagnosis was 58.8 years and 63.3% of patients were male. The immediate CL rate was 77.9% vs. 19.0% before and after trial publication, respectively(p<0.001). For the entire cohort, characteristics of patients undergoing immediate CL vs. NO were comparable: 50.9% vs. 40.6% had primary tumours >3.5mm, 33.3% vs. 56.2% had ulcerated primary tumours, 7.0% vs.3.1% had ≥3 involved sentinel nodes, and 11.3% vs. 3.1% had extracapsular nodal extension. The mean diameter of the metastatic sentinel node deposit in those undergoing immediate CL vs. NO was 4.3mm vs. 3.8mm (p=0.760). On multivariate analysis, the only significant predictor of immediate CL was operation date before trial publication. Of the 4 patients undergoing CL after trial publication, 1 had residual nodal disease. Meaningful statistical comparisons between patients undergoing CL vs. NO after trial publication were not possible due to the low number of CL patients. Conclusion: A practice shift has occurred at our institution following publication of MSLT-II demonstrating rapid knowledge transfer. This study has important implications for the surgical oncologist and surgical oncology trainees, as achieving and maintaining competency to perform CL will become a challenge in the future.

P280

Identification of Immunotherapy Targets After IL-2 Treatment J.H. Terhune,[1]* D. Fisher,[1] N. Khushalani,[2] W. Ji,[1] K. Attwood,[1] J.J. Skitzki.[1] *1. Surgical Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY; 2. H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL.*

Interleukin-2 (IL-2) was the first effective immunotherapy, known to induce durable tumor regression in a subset of patients with melanoma. Today there are numerous immunotherapeutic options for advanced melanoma with vigorous development of new treatments and combinations of established therapies.

We sought to characterize the systemic immune phenotype after IL-2 treatment in patients that responded as compared to those that progressed, with the goal of identifying a therapeutic niche for IL-2, in combination or sequentially with current agents. We analyzed serum samples of patients with advanced melanoma treated at Roswell Park Comprehensive Cancer Center with high dose systemic IL-2 between 2008 & 2015. Flow cytometric analysis of T cell markers of differentiation and activation(CD3, CD4, CD8, CD62L, CD44, CD137/CD137L, CD40L, OX40), exhaustion(PD-1, CTLA-4, Tim3, Lag3), chemokines(CCR2, CXCR3, CCR5) was performed after patients received IL-2. Patients were categorized as responders if they had stable disease(SD), complete(CR) or partial responses(PR); all others had clinical and/or radiographic disease progression. In the subset of patients with serum samples available, the response rate was 43% (including CR, PR, SD). Five patients (12.5%) had a CR, all are alive with a median of 83.2 months of follow-up; only one required subsequent therapy. Patients with CRs had greater expression of CD137 (6.52 vs 1.4%,p=0.026), CD40L (13.99 vs 4.18%,p=0.047), CCR2 (11.97 vs 2.47%,p=0.008), and CXCR3 (11.60 vs 2.29,p=0.010) on their $CD4^+$ T cells. Patients with CRs had lower percentages of $CD8^+$ T cells (23.60 vs 42.85%,p=0.038), though the $CD8^+$ T cells had greater expression of CCR2 (6.64 vs 2.87%,p=0.037) and CXCR3 (13.52 vs 8.32,p=0.030). There was no correlation between checkpoint inhibitor expression and clinical response to IL-2 on $CD4^+$ or $CD8^+$ T cells. Patients with CRs had effective, coordinated immune responses, as evidenced by greater CCR2 and CXCR3 expression on $CD4^+$ and $CD8^+$ T cells and increased expression of CD137 and CD40L on $CD4^+$ T cells that led to destruction of their tumors and durable anti-tumor immunity. It remains unclear if responses to checkpoint inhibition are independent of IL-2 responses.

P281

Patterns of Gene Expression Profile Testing and Recurrence in Melanoma Patients at Two Tertiary Referral Centers

S. O'Brien,[1]* E.A. O'Halloran,[1] T. Sun,[1] C. Mayemura,[1] K. Liang,[1] A.C. Berger,[2] J. Farma.[1] *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Thomas Jefferson University Hospital, Philadelphia, PA.*

INTRODUCTION: Melanoma Gene Expression Profile (GEP) is a prognostic test that predicts metastasis risk in melanoma patients within 5 years of diagnosis through a Class 1 or 2 categorization. We examine the experience with testing and recurrence; evaluating two institutions' use of GEP. METHODS: Patients with melanoma who underwent GEP testing at two tertiary referral centers were included. We evaluated clinical and pathologic factors as well as timing and recurrence patterns. RESULTS: We collected specimens from 192 patients with stage I (n=43), II (n=124), and III (n=25) melanoma. Median age was 64 (range 21-93), and 46% were female. Median tumor thickness was 2.3mm, 42% were ulcerated, 77% had a mitotic rate >1; 87 patients were classified as Class 1, and 105 as Class 2. Sentinel lymphadenectomy was performed in 174 patients and 12% (n=21) had a positive node. Class 2 patients were older than Class 1 (63.8 vs 57.7 years, p=0.008). Class 2 patients had thicker tumors (3.7mm vs 2.3mm, p=0.001), had a higher mitotic rate (6.6 vs 2.7/mm2, p<0.001), and more frequently were ulcerated (61.9 vs 19.0%, p<0.001). Those with class 2 tumors were more likely to have a higher pathologic stage: Class 2 patients were 6.7% stage I, 78.1% stage II, and 15.2% stage III, while Class 1 patients were 41.4% stage I, 48.3% stage II, and 10.3% stage III (p<0.001). There was no difference in likelihood of node positivity. Median follow-up was 18 months (range 1-66). Overall, 29(12.5%) patients have recurred. Recurrence rate was 21.0% in Class 2 tumors and 8.0% in Class I tumors (p=0.013). Recurrence was distant in 40.9% of Class 2 patients and 42.9% of Class I patients (p=0.927). Time to recurrence was not different between groups (16.3 months in Class 2 vs 20.8 in Class I, p=0.472), nor was overall survival. CONCLUSIONS: Class 2 melanoma patients were older with thicker tumors and higher rates of ulceration and mitotic activity. Class 2 patients had a higher pathologic stage and recurrence rate. Further studies will correlate Class 1 and 2 subgroups with rates of first and distant metastatic recurrence.

P282

Glypican-2 Targeted Chimeric Antigen Receptor T-Cell Therapy for the Treatment of Neuroblastoma

M.B. Torres,[1]* N. Li,[1] L. Peng,[2] M. Ho.[1] *1. Laboratory of Molecular Biology, National Cancer Institute, Bethesda, MD; 2. Johns Hopkins University, Baltimore, MD.*

Background: Neuroblastoma is the most common extracranial solid tumor in children. Despite advances in systemic therapy, the 5-year survival for high risk neuroblastoma remains at 40%. Glypican-2 (GPC2) is a cell surface heparan sulfate proteoglycan highly expressed in neuroblastoma and minimally expressed in normal tissue making it a desirable target for chimeric antigen receptor (CAR) T cell therapy. We previously demonstrated the utility of targeting GPC2 with CAR T cells as a novel treatment for neuroblastoma using single domain antibodies. In this study, we sought to optimize GPC2 targeted CAR T cells by using CT3, a murine monoclonal antibody. Methods: We constructed CAR T cells using LH7 and CT3 antibodies that recognize two different epitopes on GPC2. The antigen binding domain was linked to a CD8α hinge and transmembrane region, a 4-1BB costimulatory domain, and a CD3ξ signaling molecule. A truncated version of human EGFR recognized by cetuximab was also introduced for CAR T cell expression determination. The cells were expanded for 12 days after activation and flow cytometry was used to assess transduction efficiency. A luminescent-based cytolytic assay was performed using luciferase expressing neuroblastoma cell lines: IMR5, SKNAS, SKNASH, GPC2 overexpression cells F8 and G10, and GPC2 non-expressing cell line A431. Results: The transduction efficiency of the CAR T cells ranged between 30-40%. In-vitro cytolytic assays demonstrated effective cytotoxicity of GPC2 specific CAR T cells against all neuroblastoma cell lines and GPC2 overexpressing cells. We found CT3 CARs demonstrated the highest level of cytotoxicity in F8 cells while humanized CT3 CARs demonstrated the highest cytotoxicity in G10 cells at the lowest effector to target ratio. Additionally, low cytotoxicity was observed in non-GPC2 expressing cells, A431, by all CAR T cells. Conclusions: In-vitro data demonstrated effective cytotoxicity of GPC2 targeted CAR T cells against neuroblastoma cells. Our study suggests that GPC2 targeted CAR T cells are a promising therapy option for the treatment of neuroblastoma. Ongoing animal testing will aid in the optimization of GPC2 targeted CAR T-cells.

P283

Cytoreductive Surgery with Adjuvant Systemic Therapy Followed by Interval Consolidation Hyperthermic Chemotherapy: A Novel Paradigm for Ovarian Cancer

J. Veerapong,[1]* J.M. Baumgartner,[1] B. Duggan,[2] A. Bahador,[2] R.N. Low,[2] A.M. Lowy,[1] R.M. Barone.[2] *1. University of California San Diego, La Jolla, CA; 2. Sharp Memorial Hospital, San Diego, CA.*

Introduction: Standard treatments for advanced stage ovarian cancer usually involve a combination of systemic therapy and cytoreductive surgery (CRS). Recent data have demonstrated that adding hyperthermic intraperitoneal chemotherapy (HIPEC) to CRS improves progression-free survival (PFS) and overall survival (OS). We present our experience with Stage III ovarian cancer patients who have undergone CRS, followed by chemotherapy and then interval consolidation HIPEC. Methods: This is a retrospective study of 28 patients at a single institution who underwent complete CRS (CC-0/CC-1) for Stage III gynecologic malignancies between 2001-2018. Twenty-two patients underwent HIPEC: 10 were for recurrent disease after initial CRS and adjuvant chemotherapy at an outlying facility, while 12 were done in a 2-staged fashion as interval consolidation HIPEC with CRS, following initial CRS and adjuvant chemotherapy. Six candidates for interval consolidation HIPEC declined. Median PFS and OS were calculated by the Kaplan-Meier method and compared with the log-rank test. Results: Mean age was 63.3 years. Histopathology subtypes were as follows: 21 epithelial ovarian, 3 fallopian tube, and 4 primary peritoneal carcinoma. Median PCI score was 20.5. Mean operative time was 9.7 hours. The CC-0 rate was 96.4%. Severe morbidity rate (Clavien-Dindo III/IV) was 46.4%, and 60-day mortality was 0%. Median PFS and OS for the whole group were 3.5 and 7.3 years. Median PFS and OS for those who declined HIPEC were 1.6 and 3.9 years, for the recurrent disease HIPEC group were 2.2 and 8.7 years, and for the consolidation HIPEC group were 5.1 and 9.7 years, respectively (Figure 1). Conclusion: Patients with advanced stage ovarian cancer benefit from multimodal therapy. Our data suggest that for patients who initially underwent upfront CRS, subsequent consolidation therapy with HIPEC should be strongly considered. A clinical trial should be considered comparing upfront CRS followed by consolidation HIPEC versus

neoadjuvant chemotherapy followed by CRS/HIPEC. Our results also suggest HIPEC with complete CRS may be beneficial in the recurrent setting.

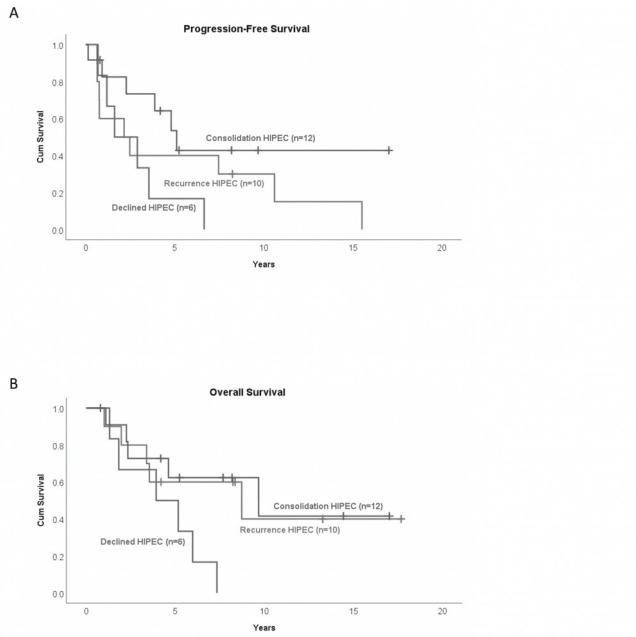


Figure 1. A) Progression-Free Survival and B) Overall Survival for patients who declined interval consolidation HIPEC (n=6), underwent HIPEC for recurrent disease (n=10), and underwent interval consolidation HIPEC (n=12).

P284

Perioperative Intestinal Integrity Compromise and its Association with Postoperative Complications in Older Cancer Patients
S. Stokmans,* M. Plas, J.J. de Haan, H. Van Der Wal - Huisman, E. Heineman, A.R. Absalom, G.H. de Bock, B.L. van Leeuwen. *Surgery, University Medical Center Groningen, Groningen, Netherlands.*

Introduction: The postoperative course in older cancer patients is frequently complicated. Disruption of the intestinal barrier due to perioperative stress facilitates an excessive inflammatory response, potentially contributing to postoperative morbidity. The aim of the current study was to investigate pre- and perioperative factors associated with the extent of intestinal integrity loss and identify its association with postoperative complications in older cancer patients. Method: Data were derived from the PICNIC trial, a prospective cohort study including patients ≥65 years undergoing surgery for a solid malignancy. A range of pre- and perioperative factors were registered. Urine Intestinal fatty acid protein (I-FABP) was used as a biomarker reflecting the intestinal integrity. Urine samples were collected preoperatively and at the end of surgery. Postoperative complications up to 30 days were classified as overall and severe (Clavien Dindo ≥grade 3a) complications. Results: A total of 204 patients with a mean age of 73 years were included. There was a significant peroperative I-FABP increase, from 101.1 ± 11.9 pg/ml to 179.2 ± 15.2 pg/ml ($p<0.001$), the meanΔI-FABP was 78pg/ml. Anesthesia duration, intracavitary surgery and total perioperative fluid transfusion were significantly associated with ΔI-FABP. One or more postoperative complications were present in 48% of patients; severe complications occurred in 12%. ΔI-FABP was significantly associated with the occurrence of overall ($p<0.001$) but not with severe post-operative complications. Multivariate logistic regression showed a significant association between overall postoperative complications and COPD, anesthesia duration and ΔI-FABP with an AUC of 0.764 (CI 0.699-0.828). Conclusion: This study indicates that, next to standard peri-operative factors, intestinal compromise may be a factor in the development of postoperative complications.

P285

Surgeon and Patient Perceptions of Cure: Are We on the Same Page? K.J. Lafaro,* A. Li, J. Rodriguez, K. Clark, M. Loscalzo, L. Wong, S. Warner. *Surgery, City of Hope, Pasadena, CA.*

Background: Effective communication is associated with improved recovery, pain control, and psychological wellbeing during cancer treatment. However, patients and physicians often have disparate expectations of treatment efficacy and perceptions of cure for advanced malignancies. There is a paucity of quantitative data examining surgeon-patient communication. This study measures correlation of patient and surgeon expectations and perceptions of cure. Methods: An electronic questionnaire was administered to patients with advanced GI malignancy and their surgeons before and after their first surgical consultation. The patient and surgeon pre- visit questionnaires were identical and asked questions related to surgical candidacy, chance of cure after surgery, and estimated life expectancy. A post-visit patient and surgeon questionnaire repeated the pre-visit questions in addition to rating surgeon and patient communication skills. Concordance between pre and post visit surveys was measured using McNemar's test and Generalized Estimating Equation approach. Results: There was no discordance between the pre and post visit patient surveys regarding whether or not they were a surgical candidate (Q1) ($p=0.82$), their chance of cure after successful surgery (Q2) ($p=0.81$), and estimated life expectancy (Q3) ($p=0.53$). There was also no discordance in the surgeon pre and post visit surveys for same questions (Q1: $p=0.17$, Q2: $p=0.32$, and Q3: $p=0.50$). There was discordance between patient and surgeon perception of likelihood of cure and prognosis during pre-visit (Q2: $p=0.005$, Q3: $p=0.006$), and post-visit (Q2: $p=0.006$, Q3: $p=0.03$). There was no change in concordance between the patients and surgeons from pre to post visit (Table 1). Conclusions: These data highlight the stark difference between patients and surgeon perceptions of cure and prognosis of GI cancers. It also suggests that these differences in perception are unchanged after their initial surgical visit. While this is a small cohort, it proves that a larger scale study using this electronic questionnaire is feasible and important to better understand these differences and intervene to enhance surgeon-patient communication.

Probability of concordance between patient and surgeon perceptions pre and post visit.

Questions	Probability of having concordance pre visit	Probability of having concordance post visit	p-value (GEE model)
Surgical candidacy	67.67% (44.69%-83.57%)	60.00% (36.41% - 80.02%)	0.63
Chance of cure	29.17% (13.44%-51.25%)	20.00% (6.61% - 44.27%)	0.42
Prognosis in years	25.00% (10.60% - 47.05%)	26.32% (10.12% - 51.42%)	0.97

P286

Diaphragmatic Peritoneal Stripping and Full Thickness Resection in CRS/HIPEC and Risk of Pleural Recurrence: Is Thoracic Perfusion Indicated? B.J. Sullivan,* E.Y. Bekhor, M. Carpiniello, N.L. DeNicola, E.R. Pletcher, D. Solomon, U. Sarpel, D.M. Labow, B.J. Golas, D.R. Magge. *Division of Surgical Oncology, Mount Sinai St. Luke's Roosevelt, New York, NY.*

Objective: Pleural-based recurrences following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) are poorly understood. Specifically, there is limited data investigating the effect of diaphragmatic peritoneal stripping versus full thickness resection on the nature of ipsilateral pleural recurrence. Thus, evidence regarding thoracic perfusion in these cases is lacking. Methods: Patients with peritoneal carcinomatosis (PC) who underwent CRS/HIPEC at our institution were included from a prospectively maintained database from 2007 to 2018. Patients were divided into three cohorts based on surgical management of the diaphragm: those who underwent diaphragm stripping (DS), full thickness resection (FTR), or no diaphragm manipulation (ND). We compared postoperative morbidity and incidence of ipsilateral pleural recurrence between the three cohorts. All diaphragmatic defects were closed prior to chemoperfusion and no patients underwent intended perfusion of the pleural cavity. Results: There were 419 patients that underwent a total of 409 CRS/HIPECs that met inclusion criteria: 66 in DS, 122 in FTR, and 238 in ND. Ipsilateral pleural recurrence rates were not significantly different between the three cohorts (DS 6%, FTR 3%, ND 3%, $p=0.470$). Postoperative respiratory complications (pleural effusion, respiratory distress, chest tubes) and overall morbidity were significantly greater in the patients undergoing diaphragmatic disruption (stripping and/or resection) versus without ($p<0.0001$). Conclusions: In our experience, neither

diaphragm stripping nor full thickness resection increases the incidence of ipsilateral pleural recurrences in CRS/HIPEC. However, patients undergoing manipulation of the diaphragm do experience significantly greater respiratory and non-respiratory morbidity. These data do not support the routine application of thoracic chemoperfusion undergoing CRS/HIPEC with concomitant diaphragmatic disruption.

P287

Combined Proctectomy and Hepatectomy for Metastatic Rectal Cancer Should be Undertaken with Caution: Results of a National Cohort Study S.J. Concors,* C. Vining, N. Saur, R.E. Roses, E.C. Paulson. *General Surgery, Perelman School of Medicine, Philadelphia, PA.*

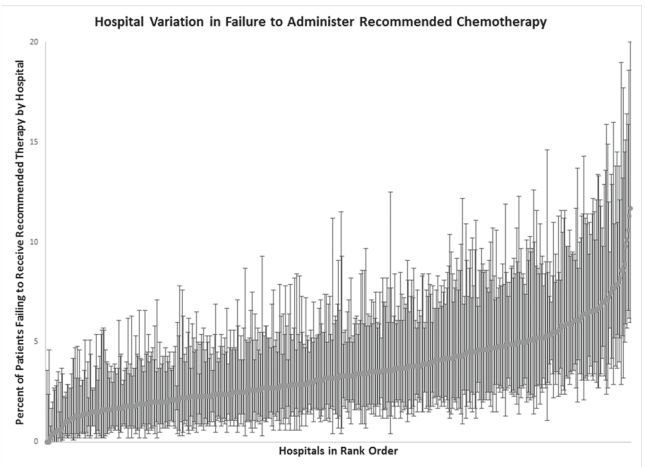
Background: Simultaneous proctectomy and hepatic resection for stage IV rectal cancer remains controversial due to concerns for increased morbidity and mortality. Objective: Associations between treatment selection, tumor and patient characteristics, 30- and 90-day mortality, as well as factors predictive of survival after surgery were examined. Design: This was a retrospective cohort study. Settings: This study was conducted utilizing a nationwide cohort. Patients: 9012 patients with stage IV rectal adenocarcinoma with hepatic metastases were identified in the National Cancer Data Base (2010-2015). Outcome Measures: Logistic regression analyses were used to evaluate associations between tumor/patient characteristics, and selection of combined proctectomy and hepatectomy (C-PH). Kaplan-Meier analysis was used to identify median survival stratified by age and other patient-specific factors. Results: Among patients included for analysis, 1331 (14.8%) underwent C-PH. The rate of C-PH decreased with age, 21% of patients <50 years old underwent C-PH, compared to 17% and 11% for patients 50-69 and >70 years old, respectively. Factors associated with lower rates of C-PH included increasing age, black/Hispanic race, increased Charleson co-morbidity score, Medicare/Medicaid/Uninsured status, and treatment at a community cancer program. 90- day mortality increased with increasing age, 0.63%, 1.62% and 7.38% for <50, 50-69 and >70 years old, respectively. Poorer survival after C-PH was associated with age>70, lymphovascular invasion, perineural invasion, kras mutation, positive circumferential margin, and omission of pre- and post-op chemotherapy (Table 1). Limitations: This study was limited by its retrospective design. Conclusions: Older, high-risk patients (stratified by tumor-specific characteristics), should undergo C-PH with caution. Such patients may be better served with a staged approach, or medical management, given poor perioperative outcomes and poor post-operative survival.

		Univariate		Multivariate	
		HR (95% CI)	*P*	HR (95% CI)	*P*
Age	< 50	ref		ref	
	50-69	1.1 (0.9-1.4)	0.4	1.1 (0.9-1.4)	0.4
	>70	2.0 (1.5-2.6)	<0.001	1.9 (1.4-2.5)	<0.001
Charlson-Dayo	0	ref			
	1	1.4 (1.1-1.8)	0.005		
	2+	1.3 (0.7-2.1)	0.3		
Insurance	Private	ref			
	Medicare	1.6 (1.3-1.9)	<0.001		
	Medicaid	1.1 (0.7-1.5)	0.8		
	Uninsured	1.7 (1.1-2.7)	0.02		
	Unknown	0.6 (0.3-1.4)	0.3		
LVI		1.3 (1.1-1.6)	0.007	1.3 (1.1-1.6)	0.02
PNI		1.6 (1.3-2.0)	<0.001	1.4 (1.1-1.8)	0.004
KRAS		1.5 (1.1-1.9)	0.01	1.5 (1.1-2.1)	0.006
Circumferential Resection Margin (Colon) Positive		2.1 (1.6-2.8)	<0.001	2.0 (1.5-2.7)	<0.001
Omission of neo-adjuvant chemotherapy		1.4 (1.1-1.7)	0.004	1.4 (1.1-1.8)	0.005
Omission of neo-adjuvant radiotherapy		1.3 (1.1-1.6)	0.004		
Omission of adjuvant chemotherapy		1.3 (1.1-1.6)	0.004	1.5 (1.2-1.8)	<0.001

P288

Failure to Administer Recommended Chemotherapy: Normal Hospital Variation or a Significant Quality Blind Spot? R.J. Ellis,* C.R. Schlick, A.D. Yang, K.Y. Bilimoria, R.P. Merkow. *Surgical Outcomes and Quality Improvement Center, Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL.*

INTRODUCTION: Hospitals are considered compliant with adjuvant chemotherapy quality measures when chemotherapy is recommended, even if it is not received. Instances in which recommended chemotherapy is not administered without a documented contraindication are poorly understood. Our objectives were (1) to assess hospital variation in failure to administer recommended chemotherapy in the absence of documented contraindications and (2) to characterize hospital factors associated with failure to administer recommended chemotherapy. METHODS: The National Cancer Database was used to identify patients from 2004-2015 with breast, colon, lung, and rectal cancers who failed to receive recommended chemotherapy without a documented contraindication. Hospital-level failure to administer recommended chemotherapy was calculated, and multivariable regression was used to identify hospital characteristics associated with failure to administer recommended chemotherapy. RESULTS: A total of 215,147 patients at 520 hospitals were included in the analysis. Overall, 3.3% of patients with breast cancer, 6.3% with colon cancer, 10.7% with lung cancer, and 2.2% with rectal cancer failed to receive recommended chemotherapy without a documented contraindication. Significant variation in overall hospital-level administration of recommended chemotherapy was observed (Figure). Variation was observed in all four diseases, with hospital-level rates as high as 19.5% in breast, 41.4% in colon, 80% in lung, and 31.4% in rectal cancers. Hospitals were more likely to not administer recommended chemotherapy if non-academic (OR 1.85 [95%CI 1.08-3.17]) or if the hospital patient population was the lowest income quartile (OR 2.55 [95%CI 1.16-5.63]). CONCLUSION: Hospital variation in failure to administer recommended chemotherapy may define a significant and unmeasured difference in hospital quality, as some hospitals may be considered compliant with chemotherapy measures despite many patients not actually receiving treatment. Mechanisms to cap the proportion of patients at a facility failing to receive recommended chemotherapy should be explored to more accurately define hospital quality.



Measured hospital-level rates of failure to administer recommended chemotherapy (blue dots) with 95% confidence intervals (bars) demonstrating both low and high outliers in administration of recommended chemotherapy.

P289

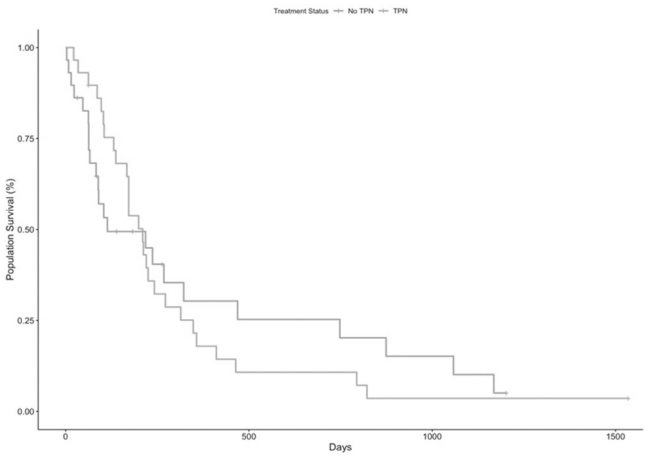
Improvement in Lymph Node Harvesting for Gastric and Esophageal Cancer K. Carman,* A. Gretschel, C. Medin, J. Dove, K.U. Chu, J. Oxenberg. *Surgical Oncology, Geisinger Wyoming Valley Medicial Center, Wilkes Barre, PA.*

Introduction: A minimum of 15 lymph nodes (LN) examined for gastric cancer is recommended for staging and prognostic purposes. Our Institution's LN counts were found to be low, and a pathologic process was instituted in 2015 that lead to improvements in LN examined for colorectal cancer. Although pathology process changes were not mandatory for gastroesophageal cancer (GEC), we hypothesized that LN counts for GEC also improved during this time period. Methods: Patients undergoing resection for GEC at our Institution from 2010-2015 and after 2015 were retrospectively reviewed. Patient, tumor variables, staging, surgery type, pathologist, LN sent separate from the main specimen and treatments were compared. Outcomes included total LN counts, final LN counts ≥15, specimens reexamined for LN and pathology reports addended. A multivariate analysis was used to identify factors associated with improvement in LN counts. Results: 70 patients underwent surgery between 2010-2015 and 24 patients after 2015. From 2010-2015, 53 gastrectomy (76%) and 17 esophagectomy (24%) specimens were examined vs. 18 gastrectomy (75%) and 6 esophagectomy (25%) specimens after 2015. Median age was higher in the 2010-2015 group (67 vs. 62 years, p= 0.04), but histology (p = 0.91), staging (p = 0.25) and neoadjuvant treatments (radiation p = 0.73; chemotherapy p = 0.50) were not significantly different. 55.7% from 2010-2015 vs. 62.5% after 2015 underwent neoadjuvant chemoradiation and 62.8% vs. 79.2% underwent neoadjuvant chemotherapy. 2.9% vs. 4.2% of pathology reports were addended for additional LN. Median number of positive LN were 0 for both groups (range 0-26). 70.0% of specimens had LN sent separately from 2010-2015 vs. 70.8% after 2015; a median of 2 separate nodal specimens were sent for each group. After 2015, median LN counts (13.0 vs. 17.5, p = 0.03) and percentage of specimens with ≥15 LN examined (47.1% vs 70.8%, p = 0.04) were increased. Pathologist and physician assistant performing LN harvests were associated with higher total LN (p= 0.03 and p < 0.0001 respectively). Conclusions: With education of staff in the LN harvesting process, a significant improvement in total LN counts was seen for GEC resections.

P290

Total Parenteral Nutrition (TPN) in the Setting of Malignant Bowel Obstruction Secondary to Ovarian Cancer A. Plana,* M. White, D. Schuitevoerder, P. Peters, K. Turaga, N. Lee, S. Yamada, C. Hoppenot. *University of Chicago, Chicago, IL.*

Use of TPN in the setting of malignant bowel obstruction (MBO) is controversial. There is currently little data available to support its efficacy. We sought to determine the impact of TPN on survival in patients with malignant bowel obstruction secondary to ovarian cancer. Patients with gynecological cancer admitted for MBO at academic medical centers over the duration of the study were included. Disease status was classified as no evidence of disease; undergoing treatment with chemotherapy and known disease but not receiving chemotherapy. Overall survival was determined from date of first malignant bowel obstruction presentation. Survival (OS) analysis was performed using Cox-proportional hazards models. Of the cohort of 130 patients with ovarian cancer, 44 (34%) patients received TPN. Ascites was more likely to be present in patients not receiving TPN (56.5% vs. 45.2%, p<0.001). Patients receiving TPN were more likely to be younger (58 vs. 65 yrs) and more likely to get chemotherapy (70% vs. 63%). Surgical management of the MBO was utilized in 11 patients (37.9%) in the no TPN group versus 19 (65.5%) in the TPN group (p = 0.066). Median overall survival from presentation was 211 days (IQR 132.5, 308.0) in patients who received TPN and had a surgical intervention; 296 days (IQR 165.0, 803.5 in patients with surgical intervention but no TPN; 193 days (IQR 81.25, 350.00) in patients who received TPN but no surgical intervention; and 82 days (IQR 45.0, 189.0) in patients who received neither TPN nor a surgical intervention (p.<0.001). Multivariate analysis adjusting for age, disease status, and stage of disease suggested benefit for TPN but did not reach statistical significant difference (HR 0.735; 95% CI = 0.335 – 1.135). TPN use in patients with ovarian cancer presenting with a MBO does not appear to clearly prolong life, although appears favorable. Utilization of TPN in this group of patients needs to be carefully guided by the patient's wishes and a multidisciplinary team until further data is accrued.



Kaplan-Meier analysis: TPN vs. no TPN in MBO

P291

Analysis of Patient Characteristics that are Associated with Urinary Prostaglandin E2 Metabolite Levels C.A. Isom,* M. Shrubsole, Q. Cai, W. Smalley, R. Ness, W. Zheng, H.J. Murff. *General Surgery, Vanderbilt University Medical Center, Nashville, TN.*

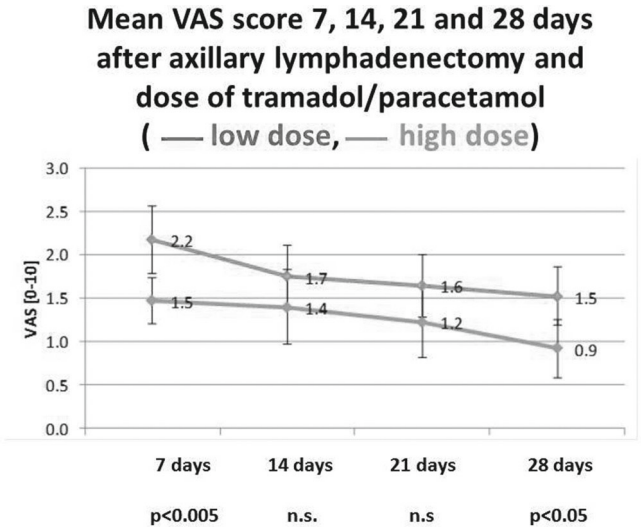
Background: There has been a surge in research into biomarkers that can predict disease or response to treatment. The inflammatory eicosanoid prostaglandin E_2 is over produced in multiple cancers and may be associated with poor prognosis. Urinary prostaglandin E_2 metabolite (PGE-M), a marker of systemic PGE_2 production, has been described as a marker of risk for developing cancer and as a possible indicator for patients more likely to respond to cancer treatment. To date, no large study has evaluated what patient characteristics may be associated with urinary PGE-M levels. Methods: The study cohort included a subset of patients from the Tennessee Colorectal Polyp (TCPS) study with urinary PGE-M levels measured. The TCPS study is a large, colonoscopy-based case-control study of colorectal adenomas. Participants included in the PGEM sub-study were matched on case status, race, age and time of colonoscopy. Demographic data, lifestyle data and dietary questionnaire and genotyped for SNPs in two genes associated with endogenous fatty acid synthesis (fatty acid desaturase and elongase) were obtained. PGEM levels were log transformed for analysis. Statistically significant variables from a univariate analysis were used to perform a multivariable analysis of factors associated with PGE-M levels. Results: Patients had a mean age of 58.2±7.2 year, were 30.7% female, 87% Caucasian and had a mean BMI of 28.7±5.8. On univariate analysis no correlation was seen between race or genotype and PGE-M. Male gender (p<.0001), older age (<.0001), higher BMI (<.0001), increase total caloric intake (<0.0001), alcohol use (0.0005), lack of regular exercise (0.0003) and smoking (<.0001) were all associated with higher PGE-M levels on univariate analysis. In the multivariable model age (.0004), sex (<.0001), smoking status (<.0001) and BMI (.004) was statistically significant. Case status, alcohol use, NSAID use, exercise and dietary factors were not significant. Conclusion: In a large case-control study we found that higher urinary PGE-M levels are associated with increased age, male gender, high BMI and smoking. These factors will need to be considered when measuring urinary PGE-M.

P292

Comparison of the Severity of Acute Pain and Side Effects After Weaker and Stronger Postoperative Analgesia with Tramadol After Axillary Lymphadenectomy in Breast Cancer Patients: Results of a Prospective Double-blind Randomized Study N. Besic,* B. Strazisar, J. Novak. *Surgical Oncology, Institute of Oncology, Ljubljana, Slovenia.*

Background: Tramadol is commonly used for pain treatment, but some patients experience insufficient pain relief or adverse events. The aim of this study was to evaluate the severity of acute pain after axillary lymphadenectomy in breast cancer patients treated with two regimens of tramadol. Methods: A prospective double-blind randomized study included 118 breast cancer patients

receiving tramadol for pain relief after axillary lymphadenectomy (Trial KCT 04/2015-DORETAonko/si) from 2015 to 2018. All patients used one of two analgesic regimens for 4 weeks. Patients with larger dose received 75/650 mg of tramadol with paracetamol every 8 hours and a group with lower dose received 37.5/325 mg of tramadol with paracetamol every 8 hours. All patients received for four weeks twice daily naproxen sodium 550 mg and once a day pantoprazole 20 mg. The association between tramadol and acute pain after surgery was evaluated using asymptotic z-test and chi-square test. Results: A visual analogue scale (VAS) value for pain was from 0 to 7 during the first four weeks after surgery. A mean VAS value for pain was 1.8, 1.6, 1.4 and 1.2 on the 7th, 14th, 21th and 28th day after surgery, respectively. Patients with higher dose of tramadol had less pain during the 1st and 4th week than patients with lower dose. Nausea was present in 26%, 12%, 17% and 12% of patients during 1st, 2nd, 3rd and 4th week, respectively. Constipation was present in 40%, 26%, 23% and 17% of patients during 1st, 2nd, 3rd and 4th week, respectively. Frequency of nausea, vomiting, lymphedema or range of shoulder movement was not significantly different in both groups of patients. Constipation was significantly more common in the group with stronger analgesia during the 2nd week in comparison to patients with weaker analgesia. Conclusions: The patients who received tramadol with paracetamol at a dose of 75/650 mg had less pain in comparison to patients who received tramadol with paracetamol at a dose of 37.5/325 mg. Side effects were common in both groups of patients.



P293

Disparate Palliative Care Utilization in Surgical Patients with Stage IV Colon Cancer D.R. Heller,[1] R.A. Jean,[1] H. Zhuo,[2] V. Kurbatov,[1]* J. Perez-Irizarry,[1] C. Cha,[1] Y. Zhang,[1] S. Khan.[1] *1. Surgery, Yale School of Medicine, New Haven, CT; 2. Yale School of Public Health, New Haven, CT.*

Background Palliative care (PC) for patients with advanced cancer is universally recommended by healthcare authorities, yet barriers to use persist. We explored national practice patterns and clinical outcomes of PC utilization in patients with Stage IV colon cancer undergoing surgical and non-surgical first-course therapies. Methods The National Cancer Data Base was queried for cases of de novo Stage IV colon adenocarcinoma from 2004–2015, stratified by receipt of PC. Demographic and clinical characteristics, including first-course colectomy, metastasectomy, radiation, and chemotherapy, were compared. Multivariable logistic regression identified factors predictive of PC. Propensity score matching compared overall survival (OS) with and without PC. Results Of 136,765 patients with Stage IV colon cancer, only 14,547 (10.6%) received PC. PC was more prevalent in non-Hispanic (10.8% vs 9.2%, p<0.01), uninsured (12.6% vs 10.5%, p<0.01), comorbid patients (11.8% vs 10.2%, p<0.01) from non-metropolitan regions (11.7% vs 10.4%, p<0.01) located in the Northeast (12.4%, other regions range 8.0%-11.5%, p<0.01). Strikingly, PC was preferentially used for patients receiving radiation (28.0%) or chemotherapy (11.0%) as first-course therapies, as opposed to colectomy (7.5%) and metastasectomy (7.3%) (p<0.01). On multivariable analysis, radiation (OR 3.40, 95% CI 3.16-3.65) and chemotherapy (OR 1.25, 95% CI 1.20-1.31) remained predictive of PC, while colectomy (OR 0.48, 95% CI 0.46-0.50) and metastasectomy (OR 0.81, 95% CI 0.76-0.86) were negatively associated. Median OS on unadjusted analysis was lower for PC than non-PC patients (8.9% vs 15.0%, log rank <0.01), but this difference narrowed after propensity matching (9.8% vs 13.0%, log rank <0.01). Conclusions Although PC is known to enhance satisfaction with care and quality of life, it is utilized in just a small subset of Stage IV colon cancer, a finding underscored in surgical patients. Practitioner biases against PC use, particularly among surgeons, may be contributing to disparities and must be further explored.

Multivariable logistic regression showing the strength of association between demographic/clinical characteristics and palliative care receipt.

Variable	Odds Ratio	95% CI (Low)	95% CI (High)	P-Value
Age (years)	*	*	*	
<50	Ref	Ref	Ref	0.45
≥50	0.97	0.91	1.04	
Race	*	*	*	
White	Ref	Ref	Ref	<0.01
Black	0.89	0.84	0.95	
Hispanic	*	*	*	
No	Ref	Ref	Ref	<0.01
Yes	0.83	0.76	0.91	
Location	*	*	*	
West	Ref	Ref	Ref	
Northeast	1.68	1.56	1.81	<0.01
South	1.31	1.20	1.40	
Midwest	1.47	1.37	1.58	
Urbanicity	*	*	*	
Metropolitan	Ref	Ref	Ref	<0.01
Urban	1.18	1.11	1.25	
Rural	1.19	1.09	1.31	
%No High School Degree	*	*	*	
>21%	Ref	Ref	Ref	
13 - 21%	1.08	1.00	1.14	<0.01
7 - 13%	1.10	1.02	1.18	
<7%	1.25	1.15	1.36	
Insurance	*	*	*	
None	Ref	Ref	Ref	<0.01
Private	0.75	0.68	0.82	
Medicare, Medicaid, Other Gov.	0.86	0.78	0.94	
Facility Type	*	*	*	
Community Program	Ref	Ref	Ref	
Comprehensive Community	1.00	0.94	1.06	<0.01
Academic	0.98	0.92	1.05	
Integrated Network	1.16	1.07	1.25	
Median Income Quartile	*	*	*	
<$38,000	Ref	Ref	Ref	
$38,000 - $47,999	0.99	0.93	1.06	<0.01
$48,000 - $62,999	0.91	0.85	0.98	
$63,000+	0.78	0.72	0.84	
Year of Diagnosis	*	*	*	
2004 – 2009	Ref	Ref	Ref	<0.01
2010 – 2015	1.45	1.39	1.51	
Charlson/Deyo Score	*	*	*	
0	Ref	Ref	Ref	<0.01
1	1.13	1.08	1.18	
2+	1.23	1.15	1.32	
Site of Metastasis	*	*	*	
Liver Only	Ref	Ref	Ref	<0.01
Multifocal	1.39	1.29	1.49	
Surgery of Primary Site	*	*	*	
No	Ref	Ref	Ref	<0.01
Yes	0.48	0.46	0.50	
Metastasectomy	*	*	*	
No	Ref	Ref	Ref	<0.01
Yes	0.81	0.76	0.86	
Radiation	*	*	*	
No	Ref	Ref	Ref	<0.01
Yes	3.40	3.16	3.65	

P294

National Trends in Access to Inclusive LGBT Patient-Centered Oncology Care B.M. Raber,[1]* K. Holmes,[2] S. Sun,[1] I. Bedrosian,[1] H. Kuerer,[1] M. Teshome.[1] *1. Breast Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; 2. Plaza Medical Center, Fort Worth, TX.*

Background: National cancer databases fail to capture sexual orientation, limiting health-care outcomes research and evaluation of disparities among LGBT patients. In 2007, The Human Rights Campaign established the Healthcare Equality Index (HEI), a voluntary self-reported annual survey, as a metric to evaluate LGBT patient-centered care. The HEI score is comprised of four components –nondiscrimination policies and staff training, patient services and support, employee benefits and policies, and patient and community engagement. The purpose of this analysis is to evaluate participation and performance in the HEI among NCI designated comprehensive cancer centers (NCI-CCCs).

Methods: Publicly available annual HEI reports were queried from 2010 to 2018 to identify participation and overall HEI scores among the 49 NCI-CCCs which were further sub-classified by geographic location. NCI-CCCs were then compared to regional hospitals by overall score and geographic location. Temporal trends in participation and performance among the NCI-CCCs were evaluated. Results: In 2018, 65% (n=32) of NCI-CCCs participated in the HEI with average score of 96.8 (range 40-100). Twenty-seven (55%) received a perfect score. NCI-CCC participation varied by geographic region and was highest in the pacific region (90%) and lowest in the mountain region (25%). When compared to participating regional hospitals, NCI-CCCs received significantly higher overall HEI scores (96.8 vs 89.7, p=0.024) which persisted by geographic location. NCI-CCC participation more than doubled from 29% in 2010 to 65% in 2018 and average HEI score increased by 58%. Eighty percent (n=39) of NCI-CCCs have participated in at least one HEI. Fourteen percent (n=7) participated in the past but not in 2018. Conclusion: The participation and performance of NCI-CCCs in HEI has increased over time although geographic variation persists. This trend indicates increased awareness in LGBT patient-centered care and changing policy. Furthermore, NCI-CCCs appear to perform better in the HEI compared to regional centers suggesting more inclusive oncologic care, although it is unclear if this translates into differences in patient outcomes.

2018 HEI score by NCI-CCC status and geographic region

Region	NCI-CCC Participants		Regional Hospital Participants	
	Average Score (Range)	n (%)	Average Score (Range)	n (%)
New England	97.5 (95-100)	2 (6)	90.3 (45-100)	33 (6)
Mid Atlantic	100 (100-100)	4 (13)	92.2 (5-100)	150 (25)
South Atlantic	87.5 (40-100)	6 (19)	83.8 (10-100)	110 (19)
East North Central	100 (75-100)	5 (16)	90 (15-100)	78 (13)
East South Central	100 (100-100)	2 (6)	88.9 (30-100)	22 (4)
West North Central	100 (100-100)	2 (6)	90.4 (20-100)	37 (6)
West South Central	75 (75-75)	1 (3)	85.1 (30-100)	36 (6)
Mountain	100 (100-100)	1 (3)	77.6 (40-100)	19 (3)
Pacific	100 (100-100)	9 (28)	95.7 (30-100)	107 (18)
Overall	95.9 (40-100)	32 (100)	89.7 (5-100)	592 (100)
				p=0.046

P295

Risk-Adjusted Nomogram Based on the National Cancer Data Base for Predicting Margin Positivity for Head of the Pancreas Adenocarcinoma K. Lam,[1]* B. Nuckles,[2] J. Dove,[2] M. Hunsinger,[2] M. Shabahang,[2] T. Arora,[2] J. Blansfield.[2] *1. Geisinger Commonwealth School of Medicine, Scranton, PA; 2. Geisinger, Danville, PA.*

INTRODUCTION: Pancreatic cancer is the 4th leading cause of cancer deaths and surgery is the only curative treatment. A significant portion of patients have inadequate resections with positive surgical margins which can affect survival. The purpose of this study is to develop a nomogram for head of the pancreas adenocarcinomas that predicts margin positivity. METHODS: This is a retrospective review of patients with head of the pancreas adenocarcinomas entered into the National Cancer Database (NCDB, 2004-2015). Logistic regression of associated factors was used to create a nomogram that predicts margin positivity following pancreatectomy. RESULTS: A total of 19,968 patients were included in the study. There were 24.3% of patients with positive margins. The mean age in the study population was 66 years old and 48.2% of patients were female. The majority of patients (65%) had a Charlson/Deyo Score of zero. Stage II tumors were present in 87% of patients and 62.5% of patients had tumors between 2-4cm in size. Multivariate analysis showed higher Charlson/Deyo comorbidity scores, higher tumor stage, larger tumor size, and worse tumor grade to be predictors of positive surgical margins. Stage III tumors were much more likely to have positive margins versus stage I (OR: 8.006, 95% CI: 6.414-9.993). Tumors between 2-4cm were more likely to be resected with positive margins compared to tumors that were less than 2 cm in size (OR: 1.52, 95% CI: 1.38-1.685). A nomogram was created using these criteria and then validated, yielding a bootstrap-corrected concordance index of 0.605. CONCLUSIONS: Our nomogram reliably predicted the number of margin positive resections based on unique patient and tumor characteristics that are known preoperatively. This nomogram could be useful to clinicians to steer preoperative discussions or encourage use of neoadjuvant therapy for more patients.

P296

Cancer-Associated Intestinal Obstruction at the End of Life S. Merchant,[1]* S. Brogly,[1] C. Goldie,[1] P. Peng,[1] C. Booth,[1] K. Lajkosz,[2] N. Baxter.[3] *1. Surgery, Queen's University, Kingston, ON, Canada; 2. Institute for Clinical Evaluative Sciences, Kingston, ON, Canada; 3. University of Toronto, Kingston, ON, Canada.*

Introduction: There is variation in the clinical management of intestinal obstruction (IO) in cancer patients with no clear guidance for best practice. We describe trends in management of cancer-associated IO near the end of life in a population-based cohort with universal health coverage. Methods: Patients who died of gastric, colorectal, ovarian and pancreatic cancers from 2002-2015 were identified from the Ontario Cancer Registry. Those with ≥1 hospital admission for IO in the final year of life were identified from administrative data. Factors associated with admission for IO were determined using log-binomial regression. Management of IO at first admission was categorized: surgery only, gastrostomy only and stent only. Trends in management over the study period were analyzed by the Cochrane-Armitage test. Results: The cohort included 66,372 deceased patients [gastric (n=8,538, 13%), colorectal (n=35,776, 54%), ovarian (n=7,284, 11%) and pancreatic (14,774, 22%) cancers]. Of those, 8,779 patients (13%) had ≥1 admission for IO in the final year of life, the majority (76%) of whom had only one admission. In adjusted analysis, factors associated with admission for IO were younger age (RR 2.60, 95% CI 2.41-2.80 for <50, ref=>81 years) and colorectal (RR 4.25, 95% CI 3.92-4.61, ref=pancreatic) and ovarian cancers (RR 5.65, 95% CI 5.17-6.17, ref=pancreatic). Of those with ≥1 admission for IO, 3,061 (35%) patients were managed with an intervention at first admission [surgery only (86%), gastrostomy only (8%) and stent only (6%)]. Surgical management consisted primarily of no bowel resection (37%), bowel resection (10%), bypass (11%) and ostomy (10%); the remainder (32%) underwent various combinations of surgical management. Over the study period, there was a statistically significant increase in use of stents (0% to 15%, p<0.0001) and decrease in use of surgery (96% to 77%, p=0.01) and gastrostomy tubes (6% to 3%, p=0.001) (Figure 1). Conclusions: Cancer-associated IO at the end of life occurs most commonly in patients with colorectal and ovarian cancers. Management of IO, while primarily surgical, has changed over time with increased use of stents and decreased use of surgery and gastrostomy tubes.

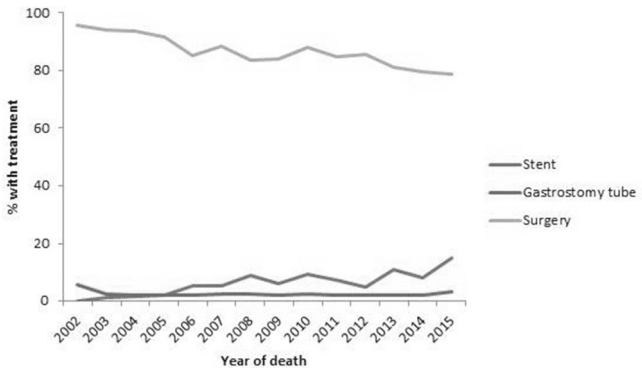


Figure 1: Trends in the management of cancer-associated intestinal obstruction over the study period (2002-2015) comparing stent, gastrostomy tube and surgery.

P297

Complex General Surgical Oncology Fellowship Applicants: Trends Over Time and the Impact of Board Certification Eligibility H.A. Lillemoe,* C.P. Scally, B.K. Bednarski, T. Aloia, C.M. Balch, J.E. Gershenwald, J.E. Lee, E.G. Grubbs. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: The Complex General Surgical Oncology (CGSO) fellowship recently obtained ACGME accreditation and board certification eligibility. Our aim was to assess time trends in the applicant pool and determine factors predictive of matching to our CGSO program. Methods: We conducted a retrospective review of CGSO fellowship applications to a major cancer center from 2008-2018. Data was analyzed for trends over time and factors were compared Pre- vs. Post-American Board of Surgery (ABS) certification eligibility in CGSO. Public reports were used to compare to national standards. Results: 846

applications were reviewed. A median of 88% of national CGSO applicants applied to our program annually. The median number of applicants increased over time: 67 (years 2008-11) vs. 73 (years 2012-14) vs. 85 (years 2015-18). The median applicant age was 33 years. Fewer applicants (35%) were female, which did not change over time despite a parallel increase in the proportion of female general surgery residents in the same period. 86% of applicants trained in a US residency program. Post-ABS applicants were more likely to complete ≥1 year between residency/fellowship (21% vs. 13%, p=0.003), more likely to be in practice at the time of application (12% vs. 7%, p=0.019), and more likely to reapply (6% vs. 1%, p<0.001; Table 1). Stable trends included that 58% of applicants performed ≥1 research year during residency and 30% had a dual degree. Post-ABS applicants listed more peer-reviewed publications, with a median of 8 (IQR 4,15) vs. 5 (IQR 2,10) among Pre-ABS applicants (p<0.001). On multivariable analysis, factors associated with matching at our institution included: allopathic medical school graduation (OR 4.4, p<0.001), Alpha Omega Alpha membership (OR 2.6, p<0.001), and performance of a clinical/research rotation at our institution (OR 4.7, p<0.001). Conclusion: A number of factors within the applicant pool changed over time, which may be due to recently established eligibility for CGSO board certification. The finding that the proportion of females applying to the program did not increase over the last decade warrants further investigation.

Table 1. Complex General Surgical Oncology fellowship applicant trends over time*

Factor	Pre-ABS CGSO Board Eligibility 2008-2014 (n=501)	Post-ABS CGSO Board Eligibility 2015-2018 (n=345)	P value
Age (years, median [IQR])	33 (31, 34)	33 (31, 34)	0.884
Gender, female	165 (33.1)	126 (36.6)	0.295
Foreign citizenship	166 (33.2)	118 (34.3)	0.481
Most recent training program, U.S.	441 (88.0)	288 (83.5)	0.060
≥1 year between residency completion and planned matriculation	66 (13.2)	72 (20.9)	0.003
Already fellowship trained	29 (5.8)	25 (7.3)	0.392
Currently in practice	33 (6.6)	42 (12.2)	0.005
Alpha Omega Alpha honor society membership	92 (18.4)	53 (15.4)	0.255
Dedicated research years during residency	282 (56.9)	209 (60.6)	0.281
NIH T32 research grant	51 (10.3)	50 (14.5)	0.065
Research/Clinical rotation at study's institution	32 (6.5)	16 (4.6)	0.265
Dual degree	140 (28.2)	106 (32.5)	0.183
Number of publications, any author (median [IQR])	5 (2, 10)	8 (4, 15)	<0.001
Number of publications, first author (median [IQR])	2 (1, 4)	3 (1, 7)	<0.001
Any failed USMLE?	6 (2.8)	30 (10.3)	0.001
Average ABSITE (median [IQR])	67 (52, 82)	68 (48, 82)	0.381
Applied more than once	5 (1.0)	19 (5.5)	<0.001

*Values presented as number (%) unless otherwise indicated; ABS, American Board of Surgery; CGSO, Complex General Surgical Oncology; IQR, interquartile range; NIH, National Institute of Health; USMLE, United States Medical Licensing Examination; ABSITE, American Board of Surgery In-Service Training Examination

P298

HIPEC Scoring System: A Preoperative Model Including Clinical and Radiographic Parameters to Improve Patient Selection

G. Gauvin,* M. Kilcoyne, K. Ang, L. Selesner, B. Egleston, J. Farma, E.R. Sigurdson, S. Reddy. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CS/HIPEC) is offered to some patients with metastatic disease limited to the abdominal cavity. Most studies looking at long-term outcomes in patients undergoing this procedure are based on scoring systems performed at the time of the operation. With a morbidity as high as 67%, it is of utmost importance to carefully choose the patients who will benefit from this procedure. In this study, we evaluated preoperative factors that could impact outcomes in order to create a preoperative scoring system for patients being considered for CS/HIPEC. Methods: Patients who underwent consideration for CS/HIPEC at our tertiary cancer center between January 2012 and December 2017 were considered for this study. Postoperative complications, recurrence free survival (RFS) and overall survival (OS) were used as endpoints, and multivariable analysis accounting for demographics, clinical, bloodwork, radiologic and pathologic findings was performed. Results: Sixty-eight patients were considered for CS/HIPEC. In our cohort, preoperative elements found to have an impact on OS were lymph node involvement (HR10.72, p=0.001) and high extent of carcinomatosis (HR14.07, p<0.001) on computed tomography (CT) scan. Findings that impacted RFS were lymphovascular invasion (HR3.48, p=0.042), as well as CT findings of lymph node involvement (HR2.91, p=0.061) and omental caking (HR4.21, p=0.010). Our preoperative predictive model is presented in table 1. An increased rate of complications was seen in smokers (p=0.031), obese patients (p=0.005) and carcinomatosis diagnosed ≤12 months from the primary diagnosis (p=0.069). In our experience, performing CS/HIPEC did improve overall survival (p=0.036) after adjustment for age, race, smoking, and body mass index. Conclusions: Preoperative findings could help practicing physicians in their discussions with patients prior to making the decision of pursuing CS/HIPEC, a highly morbid surgery. These interesting findings will be used to inform the next step of our study: a prospective clinical trial.

Table 1. HIPEC Preoperative Predictive Model

	Overall Survival		Recurrence Free Survival	
	Hazard Ratio	[95% CI*]	Hazard Ratio	[95% CI*]
Tumor Factors				
Lymphovascular Invasion				
Absent			Reference	
Present			3.48	1.04-11.58
Imaging Findings				
Carcinomatosis				
Absent or Missing	Reference			
Low	3.32	1.03-10.73		
High	14.07	3.36-58.90		
Lymph Node Involvement				
Absent	Reference		Reference	
Present	10.72	2.82-40.76	2.91	0.95-8.89
Omental Caking				
Absent			Reference	
Present			4.21	1.41-12.60

CI: confidence interval. The model also adjusted for race.

P299

Functional Impairment and Health-Related Quality of Life in Older Patients with Upper Gastrointestinal Cancers

E.C. Buckley,* H. Hu, L. Wong, J. Kim, Y. Woo, V. Jones, L.G. Melstrom, S. Warner, M. Raoof, G. Singh, Y. Fong, V. Sun. *City of Hope, Duarte, CA.*

Introduction: Functional impairments (as measured by inability to perform activities of daily living [ADL]) and poor health-related quality of life (HRQOL) may complicate outcomes in older patients with cancer. We characterized ADLs and HRQOL in adults over 65 years old with upper gastrointestinal (GI) cancers, and evaluated their association with surgery and cancer-specific survival. Methods: Patients with upper GI cancers (esophagogastric [EG; N=88] or hepatobiliary/pancreatic [HPB; N=68]), and 65 years or older were selected from the SEER-MHOS (Medicare Health Outcomes Survey) linked database. Demographics, co-morbidities, stage, ability to perform ADLs, and HRQOL physical component (PCS)/mental component (MCS) scores were summarized by patients managed with and without surgery. We compared PCS/MCS scores to previously reported means for non-cancer patients (PCS 40; MCS 50). Cancer-specific survival curves were modeled for changes to ADLs and HRQOL scores post-diagnosis. Risk factors for cancer-specific survival were assessed with hazard ratios and adjusted for demographics, stage and co-morbidities. Results: HRQOL scores were low, particularly in non-surgery cohorts. In HPB patients, both PCS and MCS score was significantly less in the non-surgery compared to surgery cohort (PCS 30 vs 37 p=0.005; MCS 45 vs 52 p=0.016). In EG group, the PCS score was significantly less in the non-surgery cohort (PCS 29 vs 37 p=0.004); MCS score was similar. On multivariate analysis of ADL scores (Figure 1), for HPB patients inability to eat was associated with worse survival for the non-surgery cohort only (HR 3.3 95%CI 1.7-6.5). For EG patients, inability to use the toilet was associated with worse survival for the entire cohort (HR 3.3 95%CI 1.5-7.9); whereas inability to dress or use the toilet were associated with worse survival in the non-surgery cohort (dress HR 14.1 95%CI 4.0-49.0; toilet HR 4.7 95%CI 1.8-12.3). Conclusions: Older adults with EG and HPB cancers report low HRQOL, especially those not undergoing surgery. The ability to perform ADLs may be linked to survival in this population.

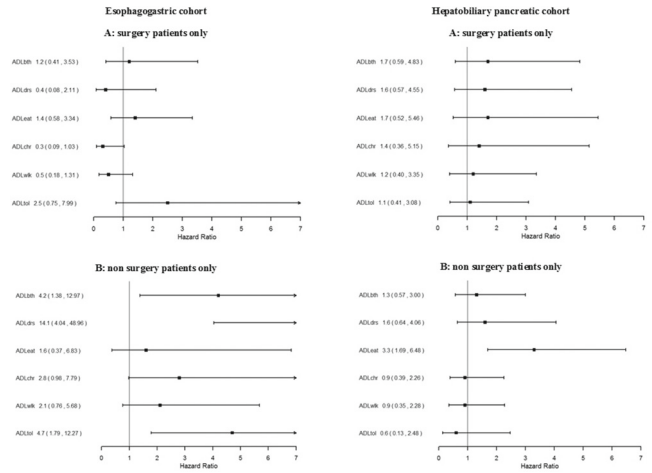


Figure 1: Adjusted hazard ratio for association between cancer specific death and activities of daily living impairment by cancer type and treatment with or without surgery. Reference group are cancer patients with ability to perform ADLs. Adjusted for demographic, stage and comorbidities. ADLs: bathing (ADLbth), dressing (ADLdrs), eating (ADLeat), getting in/out of chair (ADLchr), walking (ADLwlk), and using the toilet (ADLtol).

P300

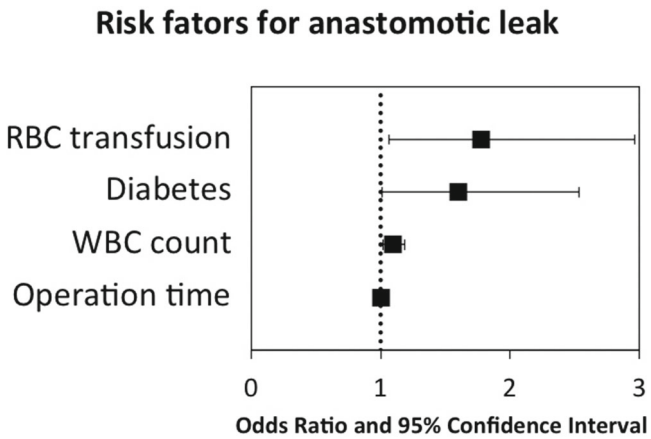
The Impact of Sarcopenia in Patients with Peritoneal Surface Disease A. Taylor Gehman, A. Juris, E. Schaefer, C. Pameijer.* *Surgery, Penn State College of Medicine, Hershey, PA.*

Introduction: Cytoreductive surgery and heated intraperitoneal chemotherapy (CRS/HIPEC) is increasingly used to treat patients with colorectal cancer and peritoneal metastasis. Better patient selection criteria and determinants of outcome are still needed. Sarcopenia has been shown to correlate with poor outcomes in patients with localized colorectal cancer, and women with ovarian cancer who undergo debulking surgery. We sought to assess the impact of sarcopenia in our patients who undergo CRS/HIPEC. Methods: A retrospective review of consecutive patients with peritoneal surface disease of any histology who were explored for CRS/HIPEC between 11/2013 and 4/2018 was conducted. The preoperative CT scan was used to determine skeletal muscle mass, measured at the L3 level. Demographic, pathologic, operative and outcome data were collected. Results: A total of 89 patients were included in this study. Sarcopenia was present in 25% of patients. Sarcopenic patients had a lower median BMI (24.5 vs 29, p=0.002), higher PCI (20 vs 15, p=0.057) and shorter post-HIPEC survival (1.5 years vs not reached, p=0.003) compared to non-sarcopenic patients. There was no difference in rates of preoperative chemotherapy, completeness of cytoreduction or postoperative complications. Sarcopenic patients had a 10 day median length of stay vs 8 days in non-sarcopenic patients, p=0.12. Only 5 of 22 sarcopenic patients had weight loss in the year prior to HIPEC. These results are the same when selecting for colorectal and appendiceal cancer only. Conclusion: Sarcopenia in patients with peritoneal surface disease correlates with a higher PCI and shorter overall survival, but does not predict lower rates of cytoreduction or an increase in complications. Sarcopenic patients had a BMI within normal range, and many did not demonstrate weight loss thus sarcopenia is often occult. Sarcopenia may be useful as a long term indicator of outcome, and may be helpful with decision-making in borderline candidates for CRS/HIPEC. More research into causes and possible interventions for sarcopenia is needed.

P301

Factors Associated with Anastomotic Leak After Esophagectomy for Cancer: An ACS-NSQIP Analysis Z.S. Parshall,[1]* B.R. Hall,[1] V.K. Shostrom,[2] C. Are.[1] *1. General Surgery, University of Nebraska Medical Center, Omaha, NE; 2. College of Public Health, University of Nebraska Medical Center, Omaha, NE.*

Introduction: Anastomotic leak remains the most common major complication after esophagectomy. We aim to identify factors predictive of anastomotic leak following esophagectomy for cancer using the newly created Procedure-Targeted National Surgical Quality Improvement Program (PT-NSQIP). Methods: The 2016 esophageal PT-NSQIP was queried for patients who underwent esophagectomy for cancer or Barrett's esophagus. Univariate analyses were performed and stratified by the presence or absence of anastomotic leak. Logistic regression models were created to identify factors predictive of anastomotic leak. Results: Of 915 patients included, 83% were male with a median age was 64 years. Patients with anastomotic leak were noted to be more frequently diabetic (25% vs. 18%, p=0.043), with higher preoperative predicted morbidity (27% vs. 26%, p=0.004) and preoperative WBC counts ($6.3x10^3$ μL vs. $5.7x10^3$ μL p=0.010). Patients with anastomotic leak less frequently underwent a planned open surgery (43% vs. 47%, p=0.007) and had longer median operative times (6.8 hours vs. 5.8 hours, p=0.001). Positive margin rates did not differ between patients who did or did not leak (9% vs. 7%, p=0.608), respectively. Patients with anastomotic leak were more likely to sustain ≥1 complication (87% vs. 36%, p<0.001), that included cardiovascular (6% vs. 2%, p=0.030), respiratory (44% vs. 15%, p<0.001), renal (5% vs. 1%, p= 0.003), infectious (77% vs. 21%, p<0.001), and thromboembolic complications (11% vs. 4%, p=0.001). In addition, these patients also experienced a higher rate of readmission (27% vs. 10%, p<0.001), reoperation (64% vs. 11%, p<0.001), perioperative mortality (8% vs. 2%, p<0.001) and longer median length of stay (17.5 days vs. 9 days, p<0.001). Regression analysis demonstrated that operative time (OR 1.002, p=0.003), WBC count (OR 1.098, p=0.019), diabetes (OR 1.601, p=0.045), and perioperative transfusion (OR 1.777, p=0.028) were predictive of the occurrence of anastomotic leak. Conclusion: Both patient and procedure-related factors contribute to a patient's risk of anastomotic leak. Optimal surgical technique and patient optimization may help to reduce the risk of anastomotic leak.



P302

Training Complex General Surgical Oncology Fellows (CGSO) to Competency: Rethinking Minimum Case Requirements and Training Assumptions S. Dineen,* V. Sondak, J. Fleming. *Moffitt Cancer Center, Tampa, FL.*

Intro: A basic goal of a CGSO program is to train fellows to competency within disparate oncologic disease sites. A standard assumption in curriculum design is that operative case numbers drive the education process and minimum case numbers approximate competency. Our hypothesis is that current minimum case requirements do not adequately capture the educational necessities of the disease sites comprising the CGSO curriculum. Methods: We reviewed self-reported ACGME case logs from 16 fellows graduating between 2015 and 2018 using the Residency Review Committee (RRC) Case Minimum Requirements as currently defined. Average case number per month of assigned service

(based on disease-site) was calculated to account for variations in schedule. The number of months required to complete RRC Minimum Requirement (RRC MR) was calculated. Results: The average number of cases performed was 458.6 ± 30.7 (range 219 – 719). Fellows spent a mean of 15.1 months on rotations aligned with CGSO Services. The wide variation in cases persisted when normalized to cases per month (table). The average time to complete RRC MR was 0.7, 0.8, 1.1, 2.6 and 3.5 months for Breast, Endocrine, Melanoma/Sarcoma, HPB and Non-HPB GI respectively. The average months needed to complete the RRC Case Requirements was 7.63 months (range 4.1 – 11.2) and the average time to complete the Total Case Requirement was 8.5 months (4.9 – 11.3). Conclusions: Our data demonstrate a wide range in the number of cases performed by each fellow per month, suggesting that calendar-based curricula are subject to significant variation. The time to reach RRC MR demonstrated wide variance between concentrations, which may not reflect competency. The combination of sarcoma and melanoma into a single minimum case requirement is particularly problematic, as the RRC MR was met in 1.1 months. These data question the assumed relation between case numbers, time on service and competency. Minimum Case requirements may give false representation of competency, particularly in certain disease sites. Development of true performance measures is needed for programs to better assess competency.

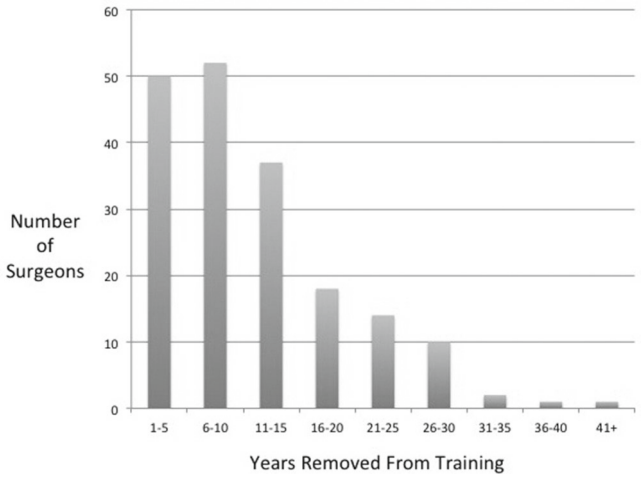
Case Numbers by Category

Category	RRC Minimum	Case Per Fellow (Mean ± SD)	Month on Rotation (Mean)	Cases/Rotation Month (Mean, Range)
Breast	40	126.7 ± 39.4	2	63.3 (32.5-105)
Endocrine	15	20 ± 10.5	0.9	24.3 (10 – 86)
Melanoma/Sarcoma	30	182.9 ± 65.6	5.4	33.7 (7.8 – 25.7)
HPB	35	47.8± 22.3	3.3	14.8 (8.4 – 25.7)
Non-HPB GI	50	81.2 ± 26.0	3.5	23.5 (11.4 – 37.7)
Total	240	458.6 ± 122.9	15.1	30.3 (15.6 – 48.6)

P303

Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy: Who is Performing these Procedures? D. Schuitevoerder,[1]* S. Sherman,[1] F. Izquierdo,[2] K. Turaga.[1] *1. University of Chicago, Chicago, IL; 2. Clinica Santa Maria, Santiago, Chile.*

Introduction: In response to recent data showing improved survival with cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC) in well-selected patients with certain stage IV cancers many institutions are establishing new HIPEC treatment programs. We hypothesized that more junior attendings are often tasked with performing CRS/HIPEC and sought to determine the experience and qualifications of surgeons performing HIPEC in the United States. Methods: We performed a systematic Internet search of AAMC affiliated medical schools, NCI designated cancer centers, hipectreatment.com, PMPpals.com, in addition to a general search to identify HIPEC surgeons, and recorded institution, specialty training, and years removed from residency/fellowship training. Results: Our search yielded 193 surgeons performing CRS/HIPEC procedures from 121 institutions (42 NCI cancer centers, 27 academic institutions, 18 academic affiliated centers, and 34 community programs). There were 12 states with no HIPEC surgeons. The vast majority of HIPEC surgeons were fellowship trained in surgical oncology (76%), followed by OB/GYN (11%), HPB (4%), and colorectal (3%). Eight surgeons had no fellowship training reported, eight had dual fellowship training, and all OB/GYNs had completed gynecologic oncology fellowships. The median length of time removed from training was 9 years. Fifty-three percent of surgeons were within 10 years of finishing training, 26% having < 5 years of independent clinical experience, and 18% < 3 years. Of those surgeons with 3 years or less of independent clinical practice, 51% had no senior partner that also performed CRS/HIPEC at their institution. Conclusion: The majority of surgeons performing CRS/HIPEC are <10 years removed from training with a substantial number in their first 3 years of practice. This likely reflects an exciting increased interest in this field and, given the complexity and steep learning curve associated with CRS/HIPEC, also highlights the need for formal training standards and minimum case number requirements in CRS/HIPEC.



P304

Pre-event Predictors for Unsuccessful Postoperative Transition of Care After Major Abdominal Oncologic Operations L.Y. Smucker,[1]* M.J. Minarich,[2] L. Henry,[2] U.W. von Holzen,[2] A.N. Hardy,[2] R.E. Schwarz.[1] *1. Indiana University School of Medicine, South Bend, IN; 2. Goshen Center for Cancer Care, Goshen, IN.*

Background: Visceral cancer resections can lead to complicated outcomes and prolonged hospitalization. Care transitions may be challenged by the failure to discharge to home, a need for intermediate care in a skilled nursing facility (SNF) or unexpected readmissions. Predictors for these care transition challenge events (CTCEs) are desirable to allow for early interventions. Methods: Clinicopathologic, therapeutic and early outcomes variables (n=36), 12 clinical risk scores (CRS) and 10 radiographic scan-based morphometrics (MM) of 240 consecutive patients in a tertiary care cancer center were compiled. Non-time-dependent associations with 3 CTCEs were tested via univariate and logistic regression analyses. Results: There were 107 women and 133 men, with a median age of 67 (range: 17-98) and a mean BMI of 27.7. Procedures included 28 upper GI (12%), 62 lower GI (26%), 69 pancreatic (29%), 54 hepatobiliary (22%), and 27 other resections (11%); eight percent of resections were multivisceral, and 4% emergent. LOS >14 d (in 16% of patients) had significant univariate associations with 12 clinical, 7 CRS and 2 MM variables; independent multivariate factors, however, were only sarcopenia index (SI), operation type, preoperative stay, functional status and albumin (all at $p<0.05$). Among 19 univariate variables associated with failure to discharge to home (seen in 16%), only age, functional status, weight loss, height, marital status and SI retained multivariate significance. Unplanned readmission within 90 days (in 26%) was linked to 6 clinical, 1 CRS and 1 MM parameters; independent variables were SSI or leak, SI, bilirubin, albumin, discharge to SNF and multivisceral resection. All CRS variables (NSQIP or POSSUM scores, frailty index) failed to retain significant associations in multivariate testing. Conclusions: Few preoperative risk scores correlate with specific CTCEs, but all lose significance when adjusted for other clinicopathologic variables. Targeted query of simple clinical parameters and a sarcopenia index would best inform potential early interventions in patients at risk for transition of care challenges.

P305

Impact of Clinical Versus Serologic Malnutrition in Patients with Gastrointestinal Cancers N. Villafane,[1]* L. Le,[1] L. Probstfeld,[2] N. Massarweh,[1] C. Chai,[1] A. Naik,[1] S. Awad,[1] H. Tran Cao.[1] *1. Surgery, Baylor College of Medicine, Houston, TX; 2. Michael E. DeBakey VA Medical Center, Houston, TX.*

Introduction: Malnutrition has been linked to an increased risk of postoperative complications and higher hospital costs. However, its recognition can be challenging due to lack of a standardized definition, with surgeons classically relying on serologic markers like serum albumin. In 2015, registered dietitians at our institution began screening surgical patients for malnutrition in the immediate postoperative period, using a set of clinical criteria proposed

by leading dietetic organizations. We sought to compare the performance of these criteria to that of traditional markers among surgical patients with gastrointestinal cancers, and to determine their impact on postoperative outcomes. Methods: We identified patients screened for malnutrition within 72 hours of elective oncologic surgery at a single academic institution (2015-2017). Patients with incomplete nutritional assessment and without preoperative albumin data were excluded. Preoperative serum prealbumin was missing for most patients. Patients were classified based on their clinical nutritional status (malnourished versus not) and albumin level (low (< 3.5 g/dL) versus normal (≥3.5 g/dL)). The primary outcome of interest was the incidence of Grade 3+ Clavien-Dindo complications. Results: 151 patients received nutritional assessment in the postoperative period. Of these, 75 had complete clinical assessment and preoperative albumin data. 35 (46.7%) met clinical criteria for malnutrition. Of these, 21 (60%) had low and 14 (40%) had normal albumin levels. Of the 40 patients who did not meet clinical criteria for malnutrition, 6 (15%) had a low albumin. Major complication rates were 28.6% for patients who were clinically malnourished with normal albumin versus 5.9% for those who were not malnourished and had normal albumin. None of the 6 patients who had low albumin but did not meet clinical criteria for malnutrition suffered a major complication (Table). Conclusion: Serum albumin is insufficient in identifying patients with malnutrition. Patients with clinical malnutrition but "normal" albumin experienced a rate of complications not different from that of patients with clinical malnutrition and low albumin.

Characteristics	Clinically malnourished, LOW albumin (< 3.5 g/dL) (n=21)	Clinically malnourished, normal albumin (≥ 3.5 g/dL) (n=14)	NOT clinically malnourished, LOW albumin (< 3.5 g/dL) (n=6)	NOT clinically malnourished, normal albumin (≥ 3.5 g/dL) (n=34)
Age	64 (60-69)	63 (60-71)	67 (61-70)	67 (61-69)
Female	2 (9.5%)	1 (7.1%)	2 (33.3%)	1 (2.9%)
BMI*	22 (20-24)	21 (19-23)	32 (27-34)	30 (25-34)
MIS** (%)	2 (9.5%)	4 (28.6%)	3 (50.0%)	15 (44.1%)
HPB Non-HPB foregut SB/CR*** Other	1 (4.8%) 4 (19.0%) 8 (38.1%) 8 (38.1%)	7 (50.0%) 0 (0%) 6 (42.9%) 1 (7.1%)	0 (0%) 0 (0%) 5 (83.3%) 1 (16.7%)	9 (26.5%) 6 (17.6%) 17 (50.0%) 2 (5.9%)
Grade 3 complications	5 (23.8%)	4 (28.6%)	0 (0%)	2 (5.9%)
LOS****	8 (5-12)	8 (6-12)	6 (4-9)	6 (4-9)

*Body mass index
**Minimally invasive surgery
***Small bowel/colorectal
****Length of stay

P306

Disparities in Radiation-Dose Compliance and Esophageal Cancer Overall Survival S. Naessig,* M. Fluck, K. Young, M. Hunsinger, A. Mahadevan, T. Arora, J. Blansfield. *General Surgery, Geisinger Medical Center, Bronx, NY.*

Introduction Management of esophageal cancer is complex. National Comprehensive Cancer Network (NCCN) guidelines recommend neoadjuvant chemoradiation with a standard radiation dose of greater than 41.4 Gray (GY). The present study aims to analyze disparities in compliance with radiation dosing, assess factors affecting compliance, and evaluate whether compliance improves overall survival (OS). Materials and methods This is a retrospective review of esophageal cancer patients entered into the National Cancer Data Base (NCDB). Patients were selected based on the inclusion criteria set by the CROSS trial (75>age<18, clinically T2/4 or clinically N1). Compliant patients received a total radiation >41.4Gy and noncompliant patients received <41.4GY. Results A total of 24,543 patients met study criteria. Among them, 11,564 (47%) patients did not undergo esophagectomy. Another 3,275 patients (13%) did not undergo any radiation therapy. This left 9,704 patients included in the dose compliance analysis. Of these, 8,440 (87%) patients were compliant with radiation dosing (34% compliance from the entire cohort). Compliance improved complete resection rates (p<0.001). Compliant patients had improvement in OS (HR: 0.91 [95% CI: 0.85–0.98]) compared to noncompliant patients. On multivariate analysis, age, facility type, and facility volume affected compliance. Compliance increased with 10-year age increases (OR: 1.30 [95% CI: 1.040–1.210]). Compliance was better at high-volume centers (OR: 1.26 [95% CI: 1.06–1.50]) and the worst at community programs. 81% were compliant with radiation dosing at community centers versus 88% at academic or integrated network programs (p=0.006). Lower income patients also exhibited worse compliance (p=0.036). Conclusion In this large national cohort, dose compliant >41.4Gy resulted in improved OS among patients that received radiation and surgery. There is a disparity in care with low volume and community cancer centers having lower compliance with guidelines. Future studies are needed to learn reasons for non-compliance to improve survival for esophageal cancer.

P307

PET-MRI as a Highly Sensitive Diagnostic Tool for Peritoneal Carcinomatosis: Early Results from a Single Center Prospective Study E.Y. Bekhor,[1]* B. Sullivan,[1] a. law,[2] N. Violi,[2] S. Gavane,[3] D. Solomon,[1] m. hofstedt,[1] b. golas,[1] u. sarpel,[1] D.R. Magge,[1] b. taouli,[4] D.M. Labow.[1] *1. Division of Surgical Oncology, Icahn School of Medicine at Mount Sinai, New york, NY; 2. Department of Radiology, Icahn School of Medicine at Mount Sinai, New york, NY; 3. Department of Radiology, Division of Nuclear Medicine, Icahn School of Medicine at Mount Sinai, New york, NY; 4. Department of Radiology, Translational and Molecular Imaging Institute, Icahn School of Medicine at Mount Sinai, New york, NY.*

Introduction: Peritoneal carcinomatosis (PC) carries a poor prognosis, but that can be treated with Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy (CRS/HIPEC) if detected at an early stage, in appropriate patients. Current imaging methods however, are limited in their ability to detect PC. PET-MRI may provide a new modality to identify PC. Methods: Patients with PC who were eligible for CRS/HIPEC underwent PET-MRI prior to surgery. Preoperative PET and MRI were reviewed separately by 2 blinded obserevs from the nuclear medicine and abdominal imaging departments. De-identified PET, MRI diffusion weighted (DWI), and MRI contrast enhanced (CE) images were evaluated independently based on Sugarbaker's Peritoneal Cancer Index (PCI). Hybrid PET/MRI radiological PCI was created by combining the study data. The abdominal cavity exploration was performed by an experienced team, and intraoperative PCI was documented at the time of surgery. Results: Overall, 12 patients were enrolled to this prospective study during 2 yers 2016-2018 in a single high volume center. Age (mean 57 years, SD =12), gender (female, 75%), BMI (mean 28, SD=4), primary disease (colon= 6, appendiceal =3, ovarian =1, mesothelioma = 1, gallbladder = 1), PCI (mean 10, SD=9), number of resected organs (mean 2, SD=2), and cytoreduction score (CC=0-1, 83%) were collected. The mean PCI determined by PET-MRI and in surgery were similar at 9.8 (SD=9) and 9.6 (SD=9), respectively. The abdomen was divided into 4 discrete locations, right and left flank, central abdomen, and small bowel. The sensitivity of PET-MRI in determining the location of disease was 89.5% and specificity was 20% and the positive predictive value (PPV) was 81.0% and negative predictive value (NPV) was 33.3%. Conclusions: PET-MRI was able to accurately score PCI, and is a valid non-invasive method to determine the amount of disease in the peritoneal cavity of patients with PC. However, PET-MRI was limited in its ability to determine the precise location of PC.

P308

Second Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis as Affective and as Safe as the First E.Y. Bekhor,* B. Sullivan, D. Solomon, n. DeNicola, m. hofstedt, b. golas, u. sarpel, n. bolton, D.M. Labow, D.R. Magge. *Division of Surgical Oncology, Icahn School of Medicine at Mount Sinai, New york, NY.*

Introduction: Recurrence of peritoneal carcinomatosis (PC) post-cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) poses a real dilemma. Repeat CRS/HIPEC represents a viable treatment option for selected patients. Methods: Patients with PC who underwent CRS/HIPEC between 2007 and 2018 at our institution were included from a prospectively maintained database. Perioperative outcomes of patients that underwent a second CRS/HIPEC were compared to those of patients that had undergone a singular CRS/HIPEC procedure. Results: Overall, from 2007 to 2018, 411 CRS/HIPEC procedures were recorded at our institution; among these, 355 patients underwent their first CRS/HIPEC and 56 patients had their second. Gender (female, 62% vs. 61%, 1st vs 2nd respectively), ASA class (%)(II- 16 vs. 21, III- 75 vs. 70, IV, 9 vs. 9), and tumor origin (colorectal-32% vs 27%, appendiceal- 22% vs 27%, gastric- 10% vs. 10% other- 36% vs. 36%) were comparable (p=NS). The patients receiving their second CRS/HIPEC were significantly younger (median 56 vs. 48 years, p<0.001) and fewer patients received neoadjuvant chemotherapy (55% vs. 39%, p=0.02). Intraoperatively, optimal cytoreduction (CC=0-1, 88% vs. 86 %), mean operative time

(330 vs. 300min), median length of stay (10 vs. 8days), ICU admissions (30% vs 29%), 30-day major morbidity (Clavien-Dindo III-V, 19% vs.18 %), and 90-day mortality (5% vs 0%) were all comparable. Median PCI (13 vs. 8 p= 0.001) and median number of resected organs (4 vs.2 p<0.001) were lower for patients receiving their second CRS/HIPEC. At median follow-up of 32 months, there was no significant difference between recurrence rate (61% vs. 63% p=0.47), disease-free survival mean months, (18 vs. 13, p=0.27), and overall survival mean months, (30 vs. 25, p= 0.24). Conclusions:Repeat CRS/HIPEC for PC in selected patients is as safe as a singular CRS/HIPEC, with comparable overall survival (OS) and disease free survival (DFS).

P309

To Do or Not to Do – Palliative Surgery for Disseminated Malignancy S. Lek,* G. Tan, C. Chia, J.C. Ong, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: There is an increasing emphasis on the appropriateness of palliative surgery for patients with disseminated malignancies. However, predictive factors of surgical outcomes to guide therapeutic decisions are not well established. We aim to ascertain the outcomes of palliative surgery for intestinal obstruction (IO) in patientswith disseminated malignancies. We also sought to validate the use of UC Davis Comprehensive Cancer Centre (UCDCCC) nomogram to predict 30-day mortality risks for patients with disseminated malignancy undergoing surgical intervention in our population. Methods: A retrospective analysis of patients with disseminated malignancies who underwent palliative surgery for IO between January 2000 and August 2018 was performed. Patient demographics, comorbidities and pre- and post-operative variables were examined. Continuous and categorical variables were analysed using independent t-test and Fisher's exact test respectively. Stepwise logistic regressionwas performed. Validation of the nomogram was analysed using concordance index and Hosmer-Lemeshow test. Results: 256 palliative operations for IO were studied. Median overall survival (OS) was 3.9 months (0.03-147.7 months). The presence of ascites (p=0.016), ECOG status 2/3 (p=0.008) and low pre-operative albumin levels (p<0.0001) were significantly associated with a higher 30-day mortality. On multivariate analysis, high ECOG status and low pre-operative albumin levels remained statistically significant. Post-operative respiratory (p<0.0001) and cardiac (p=0.0008) complications, ventilator use for >48 hours (p=0.020) and longer duration of in-hospitalization (p=0.0001) were significantly associated with mortality. Validation of UCDCCC nomogram had a concordance index of 0.71 and Hosmer-Lemeshow test of 0.969(p>0.05), indicating good model fit. Conclusion: Palliative surgery for IO may be considered in patients with good ECOG status and high pre-operative albumin levels. The UCDCCC nomogram may be useful for pre- operative prediction of early mortality and can be used to guide treatment options.

P310

Undertreatment of Non-Curative Pancreatic Adenocarcinoma? A Population-based Analysis M. Mavros,[1]* L. Davis,[2] A. Mahar,[3] K. Beyfuss,[2] C. Earle,[1] Y. Liu,[4] N. Coburn,[1] J. Hallet.[1] *1. Surgery, University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Research Institute, Toronto, ON, Canada; 3. University of Manitoba, Winnipeg, MB, Canada; 4. ICES, Toronto, ON, Canada.*

Background: Non-curative pancreatic adenocarcinoma (PA) portends a guarded prognosis. Advancements in systemic therapy have improved this outlook. It is unknown whether patients get access to these therapies. We sought to define patterns of access to care and therapy for non-curative PA. Methods: We conducted a population-based analysis of non-resected PA over 2005-2016 by linking administrative healthcare datasets. Primary outcome was non-receipt of cancer-directed therapy (radiation/chemotherapy; NRCDT). First contact and overall consultations with specialized care (surgery, medical, or radiation oncology) were examined. Multivariate models examined factors associated with NRCDT. Results: Of 10,881 patients surviving a mean of 3.3 months (IQR: 1.2-8.5), 62% had NRCDT. More of patients of older age (65% of 71-80 years old, 89% of >81 years old), high comorbidity burden (68%), and lower socio-economic status (69%), had NRCDT. Distance from residence to nearest cancer centre did not differ based on NRCDT. 35% of all patients did not see medical oncology, including 56% of NRCDT patients; 17% had no consultation with specialists. First contact with specialized care was surgery for 55% of all patients, and 50% with NRCDT. Most patients saw palliative care (81%) at median 27 days (IQR: 9-75) after diagnosis. Older age (OR 0.42 [0.37-0.48], and OR 0.14 [0.12-0.16] for 71-80 and >81 years old respectively), lowest income quintile (OR 0.62 [0.54-0.71]) and rurality (OR 0.63 [0.56-0.71]) were independently associated with lower odds of seeing medical oncology. First contact with oncology was independently associated with higher odds of receiving therapy (OR 1.48 [1.34-1.62]), compared to surgery. Conclusions: The majority of patients with non-curative PA did not receive cancer-directed therapy. Of those, more than half did not see medical oncology. While some patients may not be eligible to therapy, we identified disparities in receipt of cancer-directed therapy that indicate potential gaps in assessment for therapy and undertreatment, especially for vulnerable populations. This information is important to optimize access to and delivery of evidence-based care, and improve PA outcomes.

P311

Addressing Racial and Socioeconomic Disparities in Comprehensive Cancer Care by Improving Access to Ambulatory Clinics A. Ferguson Bryan,* J. Tseng. *Department of Surgery, The University of Chicago, Chicago, IL.*

Background: Healthcare disparities are magnified in cancer care by the number of unique steps patients must navigate: adequate screening and access to preventative medicine; timely and thorough diagnostic work-up; consistent and ready access to a multidisciplinary team; access to resources aimed to improve quality of life during treatment; and access to years of post-treatment surveillance and support. Methods: This qualitative study sought knowledge and concerns of the University of Chicago Medicine (UCM) Comprehensive Cancer Center first-line providers of specific mechanisms of cancer care disenfranchisement among oncology patients. Semi-structured interviews were conducted with UCM surgical oncology clinic nurses, schedulers, intake coordinators and social workers. Interview questions captured responses related to the existing pathway of care for cancer patients, problems with accessing health services, and proposed solutions for helping patients make and keep appointments. Results: We conducted semi-structured interviews with nine subjects. Major themes included 1) barriers to care, 2) origin of barriers to care, and 3) proposed interventions. Subthemes identified related to barriers to care: availability of staff, communication difficulties/health literacy, insurance, patient factors, patient volume, medical records, scheduling and transportation. These issues were encountered at multiple points of care: at the patient and provider-level, in the clinics and at the intake center, and originating from the referring institution or in multidisciplinary efforts. Potential interventions encompass holistic elements of individual provider practice changes to reimagining the use of clinic space and administrative coordination of staff expertise. Conclusions: The best cancer care can only be delivered to those who can attend their appointments. This unique qualitative study of interprofessional team members identified key issues busy major cancer centers should be aware of in screening and caring for surgical oncology patients to minimize issues in healthcare disparities and to improve survivorship tracking, education, and outcomes.

Table 1. Themes and subthemes

Theme	Subtheme	Frequency
Barriers to care (total = 46)	Availability of Staff	3 (6.5%)
	Communication Difficulties/Health Literacy	1 (2.2%)
	Insurance	6 (13.0%)
	Patient Factors	9 (19.6%)
	Patient Volume	5 (10.9%)
	Records	7 (15.2%)
	Scheduling	7 (15.2%)
	Transportation	8 (17.4%)
Origin of barriers (total = 40)	Clinic-level	5 (12.5%)
	Multidisciplinary Coordination	7 (17.5%)
	Patient-level	9 (22.5%)
	Provider-level	7 (17.5%)
	Referring Institution	5 (12.5%)
	UCM Intake Center	7 (17.5%)
Proposed interventions (total = 31)	Administration	6 (19.4%)
	Solutions from prior systems	5 (16.1%)
	Patient	7 (22.6%)
	Providers	8 (25.8%)
	Space	1 (3.2%)
	System-level	4 (12.9%)

P312

Perioperative Fluids in Cytoreductive Surgery with HIPEC: The Art of Resuscitation and Its Impact on Morbidity B.J. Sullivan,* E.Y. Bekhor, M. Carpiniello, N.L. DeNicola, E.R. Pletcher, D. Solomon, U. Sarpel, D.M. Labow, B.J. Golas, D.R. Magge. *Division of Surgical Oncology, Mount Sinai St. Luke's Roosevelt, New York, NY.*

Objective: Complications are common after cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC). Despite a trend to reduce volume in patients with abdominal surgery, the CRS/HIPEC patient population undergo complex hemodynamic changes and often receive high volumes of fluid in the perioperative period. We sought to determine which patients receive more volume and the association of intraoperative/perioperative fluids with morbidity. Methods: We analyzed all patients with peritoneal carcinomatosis (PC) undergoing CRS/HIPEC at our institution from a prospectively maintained database from 2007-2018. Patients were divided into cohorts based upon PCI (0-7=A, 8-15=B, >15=C) and volume of fluid received over \72 hours (less than median=LM, greater than median=GM). Results: 163 patients completed CRS/HIPEC for PC that met inclusion criteria. 68 patients were in cohort A, 56 in B, and 39 in C. The median fluid volume given intraoperatively through 72 hours postoperatively was 10.9, 11.4, and 14.0L for A-C respectively. Those in the higher volume groups had higher EBL (p=0.0001) and longer OR time (p<0.0001). There were no significant differences in CC score or PCI. Respiratory distress requiring intervention and use of diuretics were more common in the GM groups (p=0.006). LOS was slightly longer (8 vs 6d, p=0.009), and ICU admission was more prevalent for the groups that received more volume (33% vs 13%, p=0.02). Those receiving less volume did not have higher rates of AKI. There was no significant difference in ileus rates or wound infection between the LM and GM cohorts. Post-operative complications (Clavien I-IV) were significantly higher in GM groups A and B (p=0.008, p=0.035), but no difference was seen in OS or PFS. Conclusions: At our center, those patients undergoing CRS/HIPEC for PC who received more intraoperative/perioperative volume had higher overall morbidity and significantly higher rates of respiratory complications in particular. In this high risk patient population, judicious use of fluids and careful respiratory monitoring is crucial to avoid over-resuscitation.

P313

Variability in Mastectomy Cost Across Five Hospitals in a Single Health System A. Dombrowska,* V. Prasath, J. Canner, E. Hoang, R. Gilmore, K. Broderick, A. Azizi, M. Habibi. *Johns Hophins Hospital, Baltimore, MD.*

INTRODUCTION: The fast growing cost of healthcare in the United States requires our medical community to optimize spending. In 2016, the healthcare expenditure was $3.3 trillion and is projected to exceed $5.7 trillion by 2026. Breast cancer, the most common cancer in women, consumes a substantial amount of the limited financial resources. Our study examines the variability of mastectomy costs and factors that may influence price. METHODS: Data was collected using QlikView Perioperative Dashboard, a business intelligence software, which provides the cost of every procedure. Women who underwent a mastectomy between 7/2017 and 9/2018 were included in the study. All forms of mastectomy including reconstruction with tissue expander were included in analysis, while partial mastectomy was excluded. The data from the five hospitals in our health system, three of which have associated outpatient surgery centers, was compared. The cost of supplies (disposable and reusable), patient demographics, and length of procedure were recorded. RESULTS: There were 1300 mastectomies performed in the specified time period. The most expensive was a community hospital A. The least expensive was a hospital E, an academic center. The cost difference between the hospitals A and E was 60%. The majority of cases were done in hospitals B and C, both major academic centers, at an intermediate cost. The longest operating times were associated with the academic centers as well. Further analysis between the hospitals and associated surgical centers showed additional variability of cost. The patients' demographics were similar between hospitals. CONCLUSION: We identified significant cost differences for disposable and reusable mastectomy supplies between the five hospitals in our health system. Closer evaluation of these cost discrepancies between the hospitals will allow for greater optimization across the health enterprise.

P314

Prospective Comparative Analysis of Total Parietal Peritonectomy Versus Involved Field Peritonectomy with CRS + HIPEC in Peritoneal Surface Malignancy-Indian Society of Peritoneal Surface Malignancy (ISPSM) Collaborative Group Study R. C,* S. SP, A. KR, S.S. Zaveri, V. Ahuja, A. Rauthan, R. Y. *Surgical Oncology, Manipal Comphrensive Cancer Centre, Bangalore, India.*

Background: Inspite of doing selective disease directed peritonectomy, fluoroscopic imaging & microscopy of remaining peritoneum has shown presence of disease that is not visible to naked eyes. The aim of this study was to assess the recurrence pattern, oncological outcomes (DFS & OS), morbidity & mortality of extent of parietal peritonectomy with CRS & HIPEC. Material & Methods: Patients diagnosed with peritoneal surface malignancy from various diseases underwent total parietal peritonectomy (TPP) or involved field parietal peritonectomy (IPP) with CRS & HIPEC. All data prospectively entered in the HIPEC registry was analyzed. Results: Of the 163 cases, primary organ of origin were ovary, colorectal, stomach, mesothelioma (67.4%, 16.5%, 4.9%, 11%) respectively. Prior surgical score was 0,1,2,3 (101, 18, 38, 6 patient) respectively. 20 upfront, 94 interval and 49 recurrent cases. 70 & 93 patients underwent TPP & IPP respectively. TPP group had higher PCI (18.5vs8), longer duration of surgery (11 vs 9), more blood loss (1050 vs 600 ml) and increased hospital stay (14 vs 11) when compared to IPP group. The number of diaphragmatic resections, bowel resections, anastomosis and stoma were comparable in both group but TPP group had more multivisceral resections. Overall G3-G5 morbidity was comparable in both groups 39% v/s 32%. TPP group had increased intra-pleural & intra-abdominal collections. With a median follow up of 45 months, TPP group had a DFS & OS of 29 & 48 months respectively whereas IPP group had 20 & 43months respectively. Most of the recurrences in TPP group were in lymph nodes 55%, liver 18% & extra abdominal (27%) Whereas in IPP most common site of recurrence were peritoneal (45%), nodal (30%) & extra-abdominal (25%). Conclusion: Complete parietal peritonectomy lead to change in pattern of recurrence moving from peritoneal to systemic recurrence. TPP group had better DFS and ther was trend towards improved OS. A prospective randomized multi-institutional study needs to be designed for more evidence.

P316

Comparison of Hepatocellular Carcinoma Outcome Disparities Between the Mountain Region and the Nation D. Cheng,* G. Calfee, C.R. St. Hill, S. Williams, J.L. Baynosa, D.M. Kirgan. *Surgery, UNLV School of Medicine, Las Vegas, NV.*

Background: Treatment patterns for hepatocellular carcinoma (HCC) vary across the nation, and there is currently no literature on outcomes in the Mountain Region (MR). Our objective is to explore whether these regional differences result in outcome disparities. Methods: Using the National Cancer Database, we identified 149,849 HCC cases from 2004 to 2015, and divided them into two groups based on region, MR (AZ, CO, ID, MT, NM, NV, UT, WY; n=6500) and National (all other states; n=143,349). We compared these groups across several demographic and outcome strata. Overall and subgroup analysis were performed with Cox proportional hazards regression. Results: There were significant differences in age, race, ethnicity, Charlson/Deyo Score, NCDB Analytic Stage Group, Facility Type, Primary Payer, Median Income, education, and urban/rural status between the MR and National regions (p<0.001). To control for these differences, Cox proportional hazards regression analysis was performed. On overall analysis, hazard ratio (HR) for female gender (0.91; p<0.01), Asian race (0.77; p<0.01), Hispanic ethnicity (0.87; p<0.01), Mountain Region (0.96; p=0.03), treatment at an Academic Program (0.63; p<0.01), having any insurance (0.64, 0.85, 0.74 for Private, Medicaid, Medicare; p<0.01), and higher income quartiles (0.94, 0.90, 0.85; p<0.01) were protective. Black race (1.02; p=0.05) and living outside of populated urban areas increased risk. On subgroup analysis of MR, treatment at an Academic Program (0.60; p<0.01), any insurance (0.46, 0.61, 0.53 for Private, Medicaid, and Medicare; p<0.01), and the two highest income quartiles (0.87, p=0.01 and 0.78, p<0.01) were protective. Living in less populated rural areas increased risk. Conclusion: Although MR and National HCC populations are different, when controlling for the differences, living in the MR was found to be slightly protective. Treatment at an academic program, having any insurance, higher income, and living in populated metro areas were protective. These trends persisted in the subgroup analysis. Given these findings, increased access to insurance and academic centers are crucial to improving HCC outcomes in our region.

Cox Proportional Hazard Regression Analysis for Hepatocellular Carcinoma

	Hazard Ratio Overall	p-value	Hazard Ratio MR Subgroup	p-value
Age	1.01	<0.01	1.01	<0.01
Gender: Male	--	--	--	--
Female	0.91	<0.01	0.94	0.08
Race: White	--	--	--	--
Black	1.02	0.05	0.94	0.43
American Indian/Native American	0.96	0.28	1.07	0.49
Asian	0.77	<0.01	0.92	0.30
National Hawaii/Pacific Islander	1.02	0.80	1.48	0.09
Other	0.84	<0.01	0.84	0.43
Unknown	0.95	0.07	0.76	0.06
Ethnicity: Non-Hispanic	--	--	--	--
Hispanic	0.87	<0.01	0.94	0.15
Unknown	1.08	<0.01	1.31	0.02
Region: National	--	--	--	--
Mountain Region	0.96	0.03	--	--
Facility Type: Community Cancer Program	--	--	--	--
Comprehensive Community Cancer Program	0.88	<0.01	0.94	0.54
Academic/Research Program	0.63	<0.01	0.60	<0.01
Integrated Network Cancer Program	0.80	<0.01	0.88	0.22
Primary Payer: Not Insured	--	--	--	--
Private Insurance	0.64	<0.01	0.46	<0.01
Medicaid	0.85	<0.01	0.61	<0.01
Medicare	0.74	<0.01	0.53	<0.01
Other Government	0.70	<0.01	0.58	<0.01
Unknown	0.79	<0.01	0.52	<0.01
Median Income Quartile: <$38,000	--	--	--	--
$38,000-$47,999	0.94	<0.01	0.92	0.11
$48,000-$62,999	0.90	<0.01	0.87	0.01
$63,000+	0.85	<0.01	0.78	<0.01

Other variables included in regression analysis, but not displayed: NCDB Analytic Stage Group, Charlson/Deyo Score, Urban/Rural status, Percent No High School Degree, Great Circle Distance

P317

Academic Productivity of Surgical Oncologists: Comparison of Oncological Fellowship-Trained Residency Faculty Across General Surgery, Neurosurgery, Otaryngology and Orthopedic Surgery M.A. Hoof,* D. Weinert, T. Nguyen, T. Yusin, M. Razavi, H. Adib, M. Killackey, E. Kandil. *General Surgery, Tulane School of Medicine, New Orleans, LA.*

Background: General surgery, neurosurgery, otaryngology and orthopaedic surgery have focused accredited oncology fellowships. The Hirsch Index (H-index) considers both the quality and quantity of a contribution. The aim of this study is to compare academic productivity of accredited residency faculty who have completed a surgical oncology fellowship in their respective field. Methods: Demographic and leadership information of accredited residency faculty members who have completed a surgical oncology fellowship in general surgery, neurosurgery, otaryngology and orthopedic surgery was collected from program websites. H-index and publication data was collected from the Web of Science Database. Results: 1,454 surgical faculty that have completed an oncology fellowship are included. Surgical oncologists in general surgery have a higher H index(17.2+/-SD) compared to Orthopaedic surgery faculty (12.3+/- SD) and Otaryngology (12.3+/-SD) (but lower than neurosurgery faculty (21.3+/-SD) (P<0.05 for all). The majority of faculty are males (79.8%), 10.5% of full professors were females. Male faculty mean H-index is higher than female counterparts: orthopaedic (13.3v7.0+/-SD), neurosurgery (21.9v16.3+/-SD), otaryngology (13.4v7.9+/-SD) and general surgery (18.4v13.9+/-SD). There is a significant gender proportion difference within leadership positions, less than 10% of chairs were women (p<0.05). Conclusion: Male faculty hold a significantly greater proportion of leadership positions. This may indicate a disparity in opportunity to start or complete fellowship training and obtain leadership positions. Surgical oncologists in general surgery has a higher academic productivity compared to orthopaedic and otaryngology surgeons. This data is helpful in promotion of surgical oncologists within the respective specialties.

P318

1000-Day Survival Following Palliative Intent Operations: An Analysis of Advanced Cancer Patients that Do Better than Anticipated J.T. Cohen,* E.A. Fallon, K.P. Charpentier, W.G. Cioffi, T.J. Miner. *Rhode Island Hospital, Providence, RI.*

Introduction: Palliative surgery (PS) can offer significant symptom relief in carefully selected patients with advanced cancers. Potential benefits are minimized by postoperative complications and the development of new or recurrent symptoms. We sought to evaluate those patients that experienced longer than expected survival in order to better characterize outcomes following PS. Methods: All procedures performed from 2003 to 2015 to palliate symptoms of advanced cancer were identified from a comprehensive palliative surgery database. Patients were observed for >90 days or until death. Results: 188 patients were included in the analysis. The median overall survival was 221 days following an initial palliative operation. Sixteen of the patients (8.5%) were alive at 1000 days. There was no significant difference in the cohorts' age, gender, comorbidities, length of stay, or type of primary cancer. There were equivalent rates of systemic therapy (92% (11/12) vs. 69% (72/113), p=0.19) and symptom control following the initial PS (94% (15/16) vs. 77% (133/172), p=0.2239). Survival to >1000 days was independently associated with only the need for repeat PS (HR 27.20 (1.47-1221.92), p=0.04). Time to re-operation was significantly longer in the 1000-day survivors (943 vs. 169 days, p<0.0001) with new symptoms accounting for the operative indication 71% (5/7) of the time. There was no association of survival with pre-operative CRP, albumin, hemoglobin, weight loss, rate of major complications, NCI fatigue score, or ECOG score. Conclusions: Although not the primary goal, long-term survival can be achieved following PS. Many long-term survivors go on to require additional PS to manage new or recurrent symptoms, reflecting not only the success of the index operation but also the influence of favorable tumor biology and the contributions of systemic therapy. Taken together, this highlights the need for sustained surgical care in these patients with the understanding that the need for additional PS may represent palliative surgical success rather than failure.

P319

Prehabilitation Programs Improve Exercise Capacity Before and After Surgery in Gastrointestinal Cancer Surgery Patients: A Meta-Analysis C. Lau,[1]* R. Chamberlain.[2] *1. Oncology, Abrazo Central Campus, Phoenix, AZ; 2. Abrazo Central Campus, Valley Surgical Clinics, Phoenix, AZ.*

Introduction: Prehabilitation programs or interventions are employed prior to surgery and are aimed at optimizing or improving a patient physiological capacity to recover from surgery. Examples of these interventions include both nutritional supplements and exercise programs. This meta-analysis examines the impact of prehabilitation programs on surgical outcomes in patients undergoing gastrointestinal (GI) cancer surgery. Methods: A comprehensive literature search of all published randomized control trials (RCT) assessing the use of prehabilitation programs (unimodal or multimodal) in GI cancer surgery patients was conducted using PubMed, Cochrane Central Registries of Controlled Trials, and Google Scholar. Primary outcome analyzed was postoperative complications. Secondary outcomes analyzed included 6-minute walk test (6MWD), length of stay (LOS), surgical site infections (SSI), 30-day readmission, and mortality. Results: Eleven RCTs including 951 patients (489 prehabilitation program and 462 controls) were analyzed. Patients receiving prehabilitation programs noticed an improvement in 6MWD while those who did not noticed a deterioration in 6MWD. Prehabilitation programs were associated with significantly improved 6MWD immediately before surgery (MD 42.040m; 95% CI, 26.824-57.256; p<0.001) and 4-8 weeks following surgery (MD 69.135m; 95% CI, 18.337-119.933; p=0.008) compared to those who did not. There was no significant difference in the risk of postoperative complications (RR 0.956; p=0.592), SSI (RR 0.896; p=0.564), 30-day readmission (RR 0.933; p=0.866), mortality (RR 0.630; p=0.573), or length of stay (MD 0.054 days; p=0.784). Conclusions: Prehabilitation programs improve exercise capacity, with no significant difference in LOS, or rates of postoperative complications, readmission, and mortality. Further studies are required to assess the most beneficial components of prehabilitation programs.

P320

Sarcopenia is Predictive of Negative Outcomes in Gastrointestinal Cancer Patients Undergoing Surgery C. Lau,[1]* R. Chamberlain.[2]
1. Oncology, Abrazo Central Campus, Phoenix, AZ; 2. Abrazo Central Campus, Valley Surgical Clinics, Phoenix, AZ.

Introduction: Sarcopenia is the progressive loss of skeletal muscle mass and strength and has long been accepted as an age related process. Sarcopenia is also frequently observed among cancer patients and has been reported to affect as many as 57.7% of gastrointestinal (GI) cancer patients. This meta-analysis examines the impact of sarcopenia on surgical outcomes in GI cancer patients. Methods: A comprehensive literature search of all published studies evaluating the impact of sarcopenia on GI cancer patients undergoing surgery was conducted using PubMed, Cochrane Central Registries of Controlled Trials, and Google Scholar. Keywords searched included combinations of 'sarcopenia', 'gastrointestinal', 'gastric', 'colorectal', 'hepatic', 'pancreatic', 'cancer', 'surgery', and 'outcomes'. Outcomes analyzed included total complications, major complications (Clavien-Dindo grade ≥3), in-hospital/30-day mortality, 30-day readmission rates, length of stay, and hospital costs. Results: Fifty studies including 14,531 patients (4,774 sarcopenia and 9,757 no sarcopenia) were analyzed. Patients with sarcopenia were 1.619 times more likely to develop complications (OR 1.619; p<0.001), and 1.536 times more likely to develop major complications (Clavien-Dindo grade ≥3) (OR 1.536; p<0.001) compared to those without sarcopenia. Sarcopenia was also associated with higher rates of mortality (OR 1.558; p=0.005), 30-day readmissions (OR 1.425; p=0.019) and longer lengths of stay (MD 1.450 days; p<0.001). Total hospital costs were significantly higher among those with sarcopenia (MD = $1,478.85 USD; p=0.035). Although poorer outcomes were seen among all types of cancers (gastric, colorectal, hepato-pancreatic), differences between sarcopenic and non-sarcopenic groups were greatest among those with gastric cancer. Conclusion: Sarcopenia is associated with a significant increase in total complications, major complications, mortality, 30-day readmissions, length of stay, and hospital costs. Sarcopenia is a poor prognostic factor in GI cancer patients undergoing surgery, and preoperative muscle mass assessments may have significant value in predicting and improving patient outcomes.

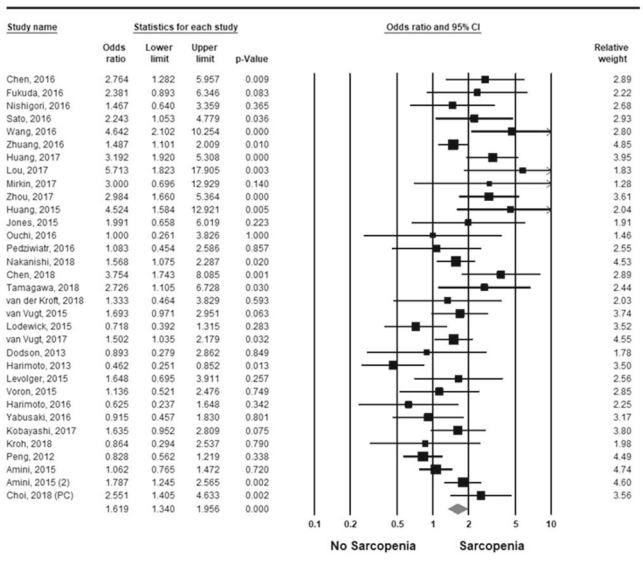


Figure 1: Forest plot evaluating the odds ratio of total complications among surgical cancer patients with sarcopenia

P321

Interventional Management for Malignant Bowel Obstruction: The Importance of a Multidisciplinary Approach G. Gauvin,* C. Do-Nguyen, E.A. O'Halloran, L. Selesner, J. Lou, M.E. Collins, J. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Malignant bowel obstruction (MBO) is a common consequence of advanced malignancy. It can lead to poor prognosis, frequent hospitalization, and impaired quality of life. The aim of this study is to explore the current multidisciplinary consultation pattern and the decompressive gastrostomy practices to improve patient care in the setting of MBO. Methods: Patients who underwent gastrostomy tube (g-tube) placement at our tertiary cancer care center between 2013 and 2017 were included in this study. Patients' demographics, diagnosis, procedures, postoperative course, and clinical data were collected. Complications and overall survival (OS) were used as endpoints. Results: Fifty-five patients were considered for decompressive g-tube placement. Average age at MBO requiring g-tube was 59.5 years (range 35-88). Only 45.5% of patients had a palliative care consult, 56.4% were seen by social work, and 25.5% had both consults, while 23.6% had neither. In the group that had a palliative care consult, a social work consult, or both (n=42), placement was achieved in interventional radiology (IR) for 78.6%, the endoscopy suite (ES) in 2.4%, and in the operating room (OR) in 19.0%. This was similar to the group without a consult: 92.3% in IR, 7.7% in ES, and 0% in OR (p=0.176). Complications occurred in 24.1% of the cohort, with a rate of 22.0% in those with a consult versus 30.8% in those without (p=0.517). Overall, 47.3% of the patients were discharged to hospice. The frequency of hospice discharge in patients who had consults was higher than in those who did not (52.8 vs 23.1%, p=0.008). There was no difference in survival between the two groups: 30-day, 6 month, and 1-year survivals were 50%, 15%, and 8.1%, respectively, in patients with a consult compared to 69.2%, 15.4%, and 0%, respectively, in patients without a consult. Conclusions: In our experience, a large proportion of patients who undergo gastrostomy tube insertion for malignant bowel obstruction have a life expectancy of less than a month. These findings will help us create a tool to create a better multidisciplinary approach and help decision making at every malignant bowel obstruction admission.

P322

Lancet Commission in Global Surgery Indicator-Use to Understand Access to Surgical Gastric Cancer Care in Colombia G. Herrera,[1]* M.F. Moreno,[2] C. Chamorro,[1] D. Londono,[1] M. Pinilla,[2] C. Paez,[2] L. Gomez,[2] M. Pena,[2] C. Hamilton,[3] S. Rehman,[3] L. Hernandez,[2] G. Peck,[3] J. Hanna.[3] *1. Surgery, Fundacion Santa Fe de Bogotá, Bogota, Colombia; 2. Universidad de los Andes, Bogota, Colombia; 3. Robert Wood Johnson Medical School, New Brunswick, NJ.*

Introduction Five billion people lack access to safe, timely and affordable surgical care. The Lancet Commission in Global Surgery proposed 6 indicators in preparedness, delivery and cost of surgical systems to inform national surgical planning and facilitate transnational conversations regarding surgical capacity. In Colombia little is known regarding reproducible methodologies to evaluate surgical oncology capacity or access to surgical gastric cancer care which is a leading cause of cancer related mortality. Methods The goal of this study was to query data in national public databases to inform indicators 1 and 2 of the lancet commission in global surgery applied to surgical gastric cancer care. A governmental registry of physicians was queried for general surgeons and surgical oncologists in Colombia. International Classification of Disease - 10 codes describing gastric cancer codes were used and cross-referenced with procedure codes used for billing to identify hospitals that had performed gastrectomies for gastric cancer during last verified year (2016). Results Results indicate that during 2016 there was an estimate of 1843 general surgeons and 22 surgical oncologists registered in the database. 103 institutions were registered for surgical oncology practice. A total of 603 gastrectomies (partial or total gastrectomy and endoscopic resections) were performed in 152 institutions countrywide. Only 16 institutions (10.5%) reported performing more than 10 gastrectomies in one year. 64 institutions (42.1%) reported 1 gastrectomy procedure in 2016. 42.2% of gastrectomies were performed in the 3 largest urban centers (Bogotá, Medellin and Cali). Conclusion Data for indicator 1 and 2 in Colombia show concentration of capacity in urban centers with the majority of procedures being performed by general surgeons in institutions that take care of less than 10 patients in a year. Understanding surgical oncology access through the Lancet Commission indicators is a key step and novel approach to describe capacity and build a common methodology that will allow opportunities for national surgical planning and a reproducible global surgical oncology language.

P323

The Role of Nutritional Support Using Gastrostomy Tubes in Patients with Advanced Malignancies G. Gauvin,* L. Selesner, E.A. O'Halloran, C. Do-Nguyen, J. Lou, M.E. Collins, J. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Malnutrition is a common consequence of advanced malignancy. Enteral nutrition through gastrostomy tubes (g-tubes) is often used in malnourished patients to improve clinical outcomes. The aim of this study is to compare the outcomes between patients undergoing active treatment and those who are not, in order to better understand the role of g-tubes in palliation at the end of life in patients with advanced malignancies. Methods: Patients who had g-tube placement for nutritional support at our tertiary cancer center between 2013 and 2017 were included in this study. Demographics, diagnoses, procedures, postoperative course, and clinical data were collected. Complications and overall survival (OS) were used as endpoints. Results: One hundred eighty-five patients underwent g-tube placement for nutritional support. Average age at placement was 65 years (range 36-94). Only 37.8% of patients received active chemotherapy treatment within 3 months of the g-tube insertion, and 8.1% of patients required intravenous nutrition despite g-tube placement. There was no difference between the two groups in terms of tumor stage at placement, placement technique, or patient ASA score. There was no difference in post-procedure mortality between the two groups. Patients undergoing active treatment had a complication rate of 51.3%, while those not undergoing treatment had a rate of 57.1% (p=0.426). One month after placement, the mean weight of both groups had decreased from their pre-procedure weights (6.4 lbs in treatment group vs 4.2 lbs in non-treatment group, p=0.189). Serum prealbumin and albumin were recorded prior to g-tube insertion and one month post-procedure, and no significant difference between the groups was noted. The 30-days, 1-year and 3-year survival rate was similar between those undergoing active treatment and those not undergoing active treatment. Conclusions: These findings provide a better understanding of the benefits and risks associated with g-tubes in advanced malignancies. The next step of our study is to create a discussion tool to help coordinate better care and decision making for every patient considered for gastrostomy tube placement.

P324

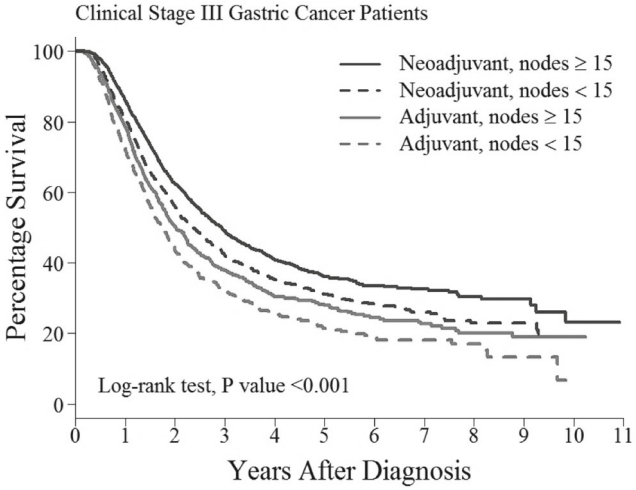
Clinicopathologic and Short-term Outcomes of Robotic Proctectomy in Rectal Cancer: Experience at a Single Institution B. Nasri,[1]* M. Calin,[2] K. Singh,[1] N. Patel,[1] p. Park,[1] N. Gupta,[1] T. Glass.[1] *1. Surgery, St Vincent Indianapolis, Carmel, IN; 2. Montclair Hospital, Montclair, NJ.*

Introduction: Minimally invasive proctectomy is technically challenging. The number of institutions introducing robotic surgeries has increased steadily nationwide. However, there is ongoing debate regarding benefits of robotic surgery for rectal cancer surgery. Aim: We retrospectively analyze all robotic and laparoscopic proctectomy for rectal cancer performed by a team of skilled laparoscopic surgeons who aimed to transition to robotic approach. The purpose of this study is to clarify that robotic proctectomy can be a safe, feasible option. Methods: All patients between January 2010 till June 2018 who underwent elective proctectomy for rectal cancer were identified. After the exclusion of high anterior resection, simultaneous colectomy, open proctectomy, Stage IV or incomplete data, 111 robotic, 95 laparoscopic proctectomy were identified. Clinicopathologic and 30-day clinical outcomes were analyzed. Results: Robotic proctectomy was associated with higher rate of neoadjuvant chemoradiation (60.4% vs 22.1%, p<0.0001), increased operative time (308.55 min vs 244.76 min, p<0.0001), decreased blood loss (140.68 ml vs 251.37 ml, p<0.0001), and decreased length of stay (4.49 vs 5.51 days, p=0.021). There was no significant difference with respect to number of harvested lymph nodes (19.67 vs 18.93, p=0.5), rate of positive circumferential margin (3.6% vs 3.2%, p=0.86), conversion rate (2.7% vs 1.1%, p=0.39), mortality (0.9% vs 1%, p=0.91), anastomotic leak (2.7% vs 1.1%, p=0.39). At a mean follow up of 36.9 months, there was no significant difference with respect to recurrence rate (14.4% vs 10.8%, p=0.44), local recurrence (3.6% vs 1.1%, p=0.39). Robotic proctectomy was more likely to preserve for patient with early stage (65.2% vs 36.5%, p=0.002). Conclusion: Our study suggests that robotic proctectomy surgery is safe, feasible and oncologically sound with short-term outcomes comparable to conventional laparoscopic proctectomy. In the hand of experienced laparoscopic surgeons, robotic platform enables comparable clinical and oncologic outcomes even at early learning stage.

P325

Effect of Number of Lymph Nodes Harvested on Overall Survival in Gastric Cancer After Neoadjuvant Therapy: Analysis of the National Cancer Data Base A. Khader,[1]* S. Chang,[2] M. Garland-Kledzik,[1] A.J. Scholar,[1] J. Santamaria-Barria,[1] A. Teng,[1] A. Uppal,[1] L. Foshag,[1] M. Goldfarb.[1] *1. John Wayne Cancer Institute, Santa Monica, CA; 2. Providence Health and Services Center, Portland, OR.*

Background: Neoadjuvant therapy (NT) and extent of lymph node (LN) dissection have both been correlated with improved survival in gastric adenocarcinoma (GA), but there is little data on the optimal number of LN harvest or its impact on survival after NT. Methods: Adult patients diagnosed with clinical stage II/III GA that had a therapeutic operation between 2006 and 2014 were identified in the NCDB. Patients were divided into two groups based on whether or not they received NT [chemotherapy (NC) +/- radiation (NR)]. Cox regression analysis evaluated the independent impact of NT on overall survival (OS). Results: Of 12,450 patients, 63.8% received NT (99.1% NC, 56.3% NR), which was most common for proximal (69.7% vs 24.0%, p<0.001) compared to distal GAs (30.7% vs 9.8%, p<0.001). Patients that received NT were more commonly younger, male, White non-Hispanic, and treated at an academic center (all p<0.001). After controlling for demographic and clinico-pathologic factors, receipt of NT was associated with a 22% decreased risk of death for clinical stage III disease (HR 0.78; CI:0.71–0.85); NT did not impact OS for stage II. By correlating OS with number of LNs harvested, 15 LNs was determined as the optimal cutoff by the maximally selected rank statistics. In stage III disease, patients who had >=15 LNs examined had significantly improved OS compared to those with <15 nodes examined, regardless of NT (p-values < 0.001), even after adjustment for all other factors. (Figure 1) Moreover, there was a positive correlation between number of LNs harvested and OS in both stage II and III disease, with a decreased risk of death as more LNs were removed (p<0.001). Conclusions: Patients with stage III GA that receive both NT and increased lymph node harvest have the greatest survival advantage. However, a greater lymph node yield also confers a survival benefit in both clinical stage II and III patients regardless of NT. To maximize survival, surgical techniques to increase LN harvest should be advocated along with management by multidiscipplinary teams that can provide NT.



P326

Impact of Lymph Node Evaluation on Survival in GI Malignancies A. Dann,[1]* P.R. Varley,[2] S.S. Kim,[1] A. Moore,[1] M. Girgis,[1] A. Tsung,[2] T.R. Donahue.[1] *1. General Surgery, UCLA, Los Angeles, CA; 2. UPMC, Pittsburgh, PA.*

Background Adequate lymph node (LN) evaluation is important to stage and treat GI malignancies. More lymph nodes evaluated has been associated with better survival within individual malignancies. The mechanism(s) underlying this improved survival and how the strength of this association compares across GI cancers is not well known. Methods The National Cancer Database was used to identify 670,818 patients with surgically resected GI adenocarcinomas (22,392 esophageal, 39,992 gastric, 46,007 pancreatic, 562,427 colorectal)

from 2004-2014. Within each cancer type, patients were grouped into quintiles based on number of LNs evaluated. Stratified, multivariable Cox proportional hazards modeling were then developed to estimate the impact of total number of lymph nodes harvested on overall survival. Results A higher number of LNs evaluated was associated with lower hazard of death in all investigated cancers (HR for 5th vs 1st quintile: esophageal: 0.646, 95% CI: 0.605-0.689, p<0.0001; gastric: 0.471, 95% CI: 0.446-0.498, p<0.0001; pancreatic: 0.689, 95% CI: 0.658-0.723, p<0.0001; colorectal: 0.700, 95% CI: 0.690-0.711, p<0.0001). The same relationship was observed when stratifying by node negative and node positive disease. Gastric cancer exhibited the largest reduction in hazard of death with increasing LN evaluation (Table 1). Conclusions Increasing lymph node evaluation is associated with improved survival across GI malignancies, and most strongly in gastric cancer. This is seen in both node positive and node negative disease, suggesting stage migration alone is insufficient to explain this association. These results support extended lymphadenectomy in resection of GI malignancy and suggest number of nodes harvested is an prognostic factor.

Relative Hazard if Death: 5-year Cumulative Survival																
	Number of LN harvested															
	Q1: 0-4			Q2: 5-9			Q3: 10-13			Q4: 14-19			Q5: 20+			
Esophageal	HR	CI	p	HR	CI	p	HR	CI	p	HR	CI	p	HR	CI	p	
All (n=22,392)	1 (referent)			.911	.856-.969	<.0001	.813	.763-.867	<.0001	.763	.717-.812	<.0001	.646	.605-.689	<.0001	
Node-Negative (n=14,170)	1 (referent)			.881	.817-.950	<.0001	.792	.736-.866	<.0001	.750	.691-.815	<.0001	.646	.591-.705	<.0001	
Node-Positive (n=8,222)	1 (referent)			.963	.863-1.076	.509	.843	.756-.941	.002	.792	.713-.880	<.0001	.661	.595-.734	<.0001	
	Number of LN harvested															
	Q1: 0-5			Q2: 6-10			Q3: 11-15			Q4: 16-22			Q5: 23+			
Gastric	HR	CI	p	HR	CI	p	HR	CI	p	HR	CI	p	HR	CI	p	
All (n=39,922)	1 (referent)			.833	.795-.874	<.0001	.727	.694-.760	<.0001	.648	.617-.680	<.0001	.471	.446-.498	<.0001	
Node-Negative (n=18,457)	1 (referent)			.803	.752-.857	<.0001	.686	.642-.732	<.0001	.631	.586-.680	<.0001	.520	.478-.565	<.0001	
Node-Positive (n=21,465)	1 (referent)			.865	.807-.927	<.0001	.756	.707-.809	<.0001	.664	.618-.712	<.0001	.464	.430-.501	<.0001	
	Number of LN harvested															
	Q1: 0-6			Q2: 7-11			Q3: 12-15			Q4: 16-21			Q5: 22+			
Pancreatic	HR	CI	p	HR	CI	p	HR	CI	p	HR	CI	p	HR	CI	p	
All (n=46,007)	1 (referent)			.885	.852-.920	<.0001	.829	.796-.863	<.0001	.750	.718-.783	<.0001	.689	.658-.723	<.0001	
Node-Negative (n=17,428)	1 (referent)			.866	.819-.914	<.0001	.816	.767-.868	<.0001	.749	.705-.796	<.0001	.691	.641-.744	<.0001	
Node-Positive (n=28,579)	1 (referent)			.903	.856-.951	<.0001	.842	.798-.890	<.0001	.757	.715-.802	<.0001	.696	.655-.738	<.0001	
	Number of LN harvested															
	Q1: 0-9			Q2: 10-13			Q3: 14-17			Q4: 18-23			Q5: 24+			
Colorectal	HR	CI	p	HR	CI	p	HR	CI	p	HR	CI	p	HR	CI	p	
All (n=562,427)	1 (referent)			.848	.836-.859	<.0001	.782	.772-.793	<.0001	.739	.728-.749	<.0001	.701	.690-.711	<.0001	
Node-Negative (n=365,984)	1 (referent)			.838	.824-.852	<.0001	.776	.762-.789	<.0001	.729	.715-.742	<.0001	.684	.671-.697	<.0001	
Node-Positive (n=196,443)	1 (referent)			.874	.854-.894	<.0001	.802	.785-.820	<.0001	.760	.743-.777	<.0001	.725	.709-0.742	<.0001	

P327

The Volume-Outcome Relationship in Gastrectomies: A Population-Based Study of Texas Inpatient Data N. Ikoma,* L. Elting, T. Shih, B. Kim, P. Mansfield. *Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX.*

Background We previously reported a significant volume-outcome relationship in mortality rates after gastrectomies for gastric cancer patients in Texas (1999-2001). We used Texas Inpatient Data to investigate changes in the volume distribution of gastrectomies, whether volume-outcome relationships persist, and potential changes in the factors influencing a volume-outcome relationship. Methods We performed a population-based study using Texas Hospital Discharge Public Use Data File. We identified of 2733 gastric cancer patients who underwent gastrectomy at 193 hospitals, between July 1, 2010 and June 30 2015. Hospitals were stratified as high-volume centers (HVC) (>15 cases/y), intermediate- (IVC) (3-15 case/y), and low-volume centers (LVC) (<3 cases/y). Multivariate analyses were conducted to evaluate factors associated with inpatient mortality and adverse events. Results The proportion of patients with comorbidities increased from 32.3% (602/1864) to 52.5% (1435/2733) over this 15 year period. Fewer hospitals performed gastrectomy than before (193 vs 214). There were more HVC (5 vs 2) and LVC (142 vs 134) but fewer IVC (46 vs 78). The proportion of patients who underwent gastrectomy at HVC increased from 12 to 29% while the proportion at IVC decreased from 67 to 48% and LVC increased from 21 to 23%. HVC maintained lower in-hospital mortality rates (0.9% in no comorbidity and 2.6% in comorbidity patients) than IVC- (2.0% and 5.0%) or LVC (2.0% and 5.3%), though mortality rates decreased in both LVC and IVC. In multivariable analyses, after adjustment for other factors, treatment at high-volume centers remained a strong predictor for lower mortality (OR 0.39, p=0.019) and adverse events (OR 0.56, p=0.013). Conclusion Despite improvements in patient morbidity and mortality at LVC and IVC, they remain higher than at HVC demonstrating that volume-outcome relationships still exist for gastrectomy. The proportion of patients undergoing gastrectomy at HVC has increased significantly, but despite a well reported volume-outcome relationship, the majority of patients still undergo gastrectomy at low or intermediate volume centers.

P328

Frailty Influences Respiratory Capacity and Quality of Life in a Prospective Cohort of Patients Undergoing Hepatobiliary Resection P.R. Varley,* P. Bou-samra, J. McDonnell, D. Geller, A. Tsung. *University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Though retrospective application of frailty metrics has identified a negative impact on standard surgical outcomes such as mortality and surgical complications, less is understood about the underlying physiology and baseline quality of life in frail patients undergoing surgery for malignancy. Methods: A prospective cohort of patients undergoing surgery for hepatobiliary malignancy at a high-volume were assessed for functional measures of frailty including extended timed up-and-go (eTUG), walking speed, grip strength, and Mini-Cog. Bedside spirometry was performed to estimate FEV1 and FVC. Health-related quality of life (HRQoL) was measured using the Focused Assessment of Chronic Therapy- Hepatobiliary (FACT-Hep) instrument. Fried Frailty Phenotype (FF), Edmonton Frail Scale (EFS), and Risk Analysis Index (RAI) were calculated from collected data.. Results: As part of a pilot project, 81 patients were evaluated. 42 (51.9%) of the patients were male. The cohort had a mean age of 62.7±14 years, and mean BMI of 30.6±7.7. Median scores for the RAI were 9 [IQR 5-15], 3 [IQR 2-5] for the EFS, and 1 [IQR 0-2] for FF. With respect to frailty, 14 (17.3%) of the patients were frail by at least one measure. Median FEV1/FVC for the cohort was 0.78 [IQR 0.73-0.81], and decreased for frail compared to non-frail patients (0.75 [IQR 0.70-0.77] vs. 0.78 [IQR 0.74 – 0.82], p = 0.062). Frail patients also had a trend toward higher scores on the FACT-Hep indicating lower health-related quality of life when (90.5 [IQR 71-94] vs. 76 [IQR 71-82], p = 0.052). Conclusions: The results of this pilot project suggest that it is feasible to implement a routine frailty screening process in a busy surgical clinic. This study also reveals that frailty is associated with both impaired physiologic parameters such as FEV1/FVC as well as baseline reduction in HRQoL in patients being prepared for hepatobiliary surgery. Future work should focus on the utility of routine frailty screening as a mechanism for identifying potentially correctable physiologic impairment, as well as identifying outcomes particularly important to frail patients such as impairment in HRQoL.

P329

Exploring the Safety and Utility of Intraoperatively Placed Central Lines Maintained During Postoperative Recovery in Complex Gastrointestinal Surgery A.D. Patel,* M. Betha, K. Brown, G. Malhotra, U. Yanala, J.M. Foster. *Surgery, University of Nebraska Medical Center, Omaha, NE.*

INTRODUCTION Intraoperative central lines (IOCL) placed for complex gastrointestinal surgery are performed with the same antimicrobial protocols as ports and dialysis catheters., The current health care climate promotes immediate removal of OR placed and has become a more standard practice in an effort to reduce hospital CLABSI without any evidence of IOCL safety. Currently there is no data defining IOCL safety, complication rates, or postoperative utility. This study retrospectively explores the safety and utility of prolonged postoperative central line use in patients undergoing CRS/HIPEC. METHODS Between 2010-2017, 200 patients with IOCL and comprehensive medical data were identified. IOCL safety was determined based rates of CLABSI, catheter related DVT, and any other reported central related adverse events. Utility was determine based on rates of vasopressor use, fluid restrictive electrolyte replacement, and avoidance of peripheral IV insertion and complications. RESULT The median duration of IOCL placement was 8 days (7-20 days). The CLABSI rate and CR-VTE were both 0.5% (1) with an overall complication rate of 1% (2). No patients required any additional peripheral access for the duration of IOCL. Post-op vasopressors were used in 12% of patients and central lined fluid restrictive potassium and/or phosphorus replacement in 65% of patients. CONCLUSION Maintaining IOCL for post-operative care was safe with an observed low rate of complication 2% with only 1 case of staph epidermis CLABSI. IOCL was integral in rapid fluid restrictive electrolyte correction and safe and rapid delivery of vasopressors. This data demonstrates that IOCL have low complication and in high risk, surgical procedures can be safely maintained.

P330

Prospective Evaluation of Morbidity and Quality of Life (QoL) in Multivisceral Resection (MVR) for Retroperitoneal Sarcoma (RPS) M. Fiore,* R. Miceli, C. Brunelli, D. Callegaro, M. Manara, S. Lenna, N.N. Rampello, A. Caraceni, A. Gronchi. *Dept. of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy.*

Background MVR (median 2 organs, IQR 1-3) retrospectively showed a Clavien-Dindo (CD) ≥ 3 morbidity of 18%, reoperation rate of 12% and 3% mortality (2002-2011). Methods A prospective study enrolled primary RPS undergoing MVR (NCT03480399). Morbidity was recorded. Renal function by 2002 National Kidney Foundation (NKF) stages was studied. QoL was measured (EORTC QLQ-C30, Lower Extremity Function, Pain, Neuropathic Pain). Results From 2014 to 2016, 62/111 pts were enrolled. Median resected organs were 4.3 (CI95%, 3.9 – 4.7). Most frequent were colon (87%), kidney (84%), psoas (73%), pancreas/spleen (37%), diaphragm (27%), duodenum (16%), major vessels (16%). After a median follow up of 30 mos, 55 (89%) pts were alive (8 AWD, 47 NED). CD ≥ 3 morbidity occurred in 16 (25.8%), reoperation in 10 (16.1%), 1 pt (1.6%) died for complications. Preoperative renal function was stage 1-2-3 in 62.5%, 33.9%, and 3.6% of pts. After 12 mos, stage 1-2-3-4 in 9.3%, 50%, 37% and 3.7%. Median EGFR change was -34.8 and -7.6 mL/min with nephrectomy or not, respectively (p=.01). According to preoperative stage, after nephrectomy median EGFR reduction was: stage 1 = 35.2%; stage 2 = 32.2%; stage 3 = 16.7%. Mean global QoL did not change after surgery (4.6 to 5.0 in a 0-7 scale, p=0.063, Figure 1A) and it was not affected by organs resected (p=0.52), perioperative treatments (p=0.46), age (p=0.13). Significant neuropathic pain was referred by 48% and 43% of pts at 4 and 12 mos. Pts with neuropathic pain reported higher average pain (p=.004) (Figure 1B). Lower extremity function was lower after surgery (p<0.001). Psoas muscle resection correlated to worse neuropathic pain (p=0.003) but not to lower limb function (p=0.9). Conclusions In this prospective series of primary RPS treated by MVR, postoperative morbidity, reoperation rate and mortality were 25.8%, 16.1% and 1.6%, consistent to the ones in retrospective series. Enbloc nephrectomy reduced EGFR, depending on preoperative values. EGFR stage 4 occurred in <5% of pts. Global QoL in surviving patients is not inferior to baseline. Psoas resection may cause significant chronic neuropathic pain in 43% of cases.

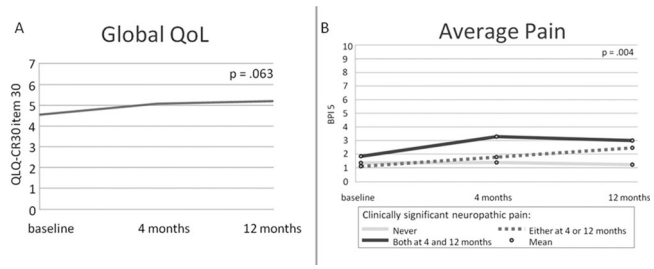


Figure 1. Panel A, Global Quality of Life (EORTC QLQ-CR30 item 30). Panel B, Average pain in last 24 hours (Brief Pain Inventory item 5), according to the presence/absence of significant neuropathic pain after surgery (DN4 score ≥4).

P331

The Association Between Hospital Type and Survival Among Patients with Soft-Tissue Sarcoma of the Extremity A.S. Moten,[1]* S. Movva,[2] M. von Mehren,[2] S. Reddy,[2] K. Howell,[2] E. Handorf,[2] J. Farma.[2] *1. Surgery, Temple University Hospital, Philadelphia, PA; 2. Fox Chase Cancer Center, Philadelphia, PA.*

Background: Prior research has suggested that the type of hospital in which a patient receives treatment may affect patient outcomes. The goal of this study was to investigate the association between facility type and outcomes among patients with soft tissue sarcoma (STS) of the extremity. Methods: Information on patients diagnosed with STS of the extremity between 2006 and 2015 was obtained from the National Cancer Database. The study sample was stratified by type of facility at which treatment was received (academic/research, community, comprehensive community, and integrated network). Demographic and clinical characteristics were compared using chi-square tests. Kaplan-Meier analysis was used to estimate survival by facility type. Cox regression was used to calculate hazard ratios. Results: The study sample included 18,491 patients. Mean age was 64.5 years, 54.5% were male and 84.6% were white. The greatest proportions of patients were treated at academic/research facilities (56.7%) and comprehensive cancer facilities (27.1%). The proportion of patients who underwent limb-sparing resection was greatest at academic/research facilities compared to community, comprehensive community and integrated network facilities (55.7% versus 32.8%, 43.1% and 54.1%, respectively; p < 0.001). A lower proportion of patients treated at academic/research facilities had residual tumor after surgery compared to those treated at community, comprehensive community and integrated network facilities (14.8% versus 20.8%, 18.1%, 18.0%, respectively; p < 0.001). In addition, a greater proportion of patients treated at academic/research facilities received chemotherapy compared to those treated at community, comprehensive community and integrated network facilities (19.2% versus 13.8%, 14.7% and 16.0%, respectively; p < 0.001). Survival analysis revealed that the risk of death was greater at both community (HR = 1.20; 95% CI: 1.06 – 1.37) and integrated network (HR = 1.18; 95% CI: 1.07 – 1.30) facilities compared to academic/research facilities. Conclusion: Further investigation into the reasons why patients treated at academic/research facilities have better outcomes is warranted.

P332

Postoperative Pancreatic Fistula and Morbidity After Distal Pancreatectomy for Non-Pancreas Retroperitoneal Tumor Resection E.Z. Keung,* E. Asare, Y. Chiang, L.R. Prakash, N.F. Rajkot, C.L. Roland, K.E. Torres, J. Cormier, K. Hunt, B. Feig, J.E. Lee, M.H.G. Katz, C.D. Tzeng. *The University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Patients requiring retroperitoneal (RP) tumor resection with en bloc distal pancreatectomy (DP) are at significant risk for postoperative pancreatic fistula (POPF) and associated morbidity. While outcomes after DP alone are widely published, short-term outcomes after DP for RP tumor resection are relatively unknown. Our primary aim was to analyze rates of POPF and morbidity in this rare population. Methods: A retrospective cohort study of consecutive patients who underwent open DP during en bloc RP tumor resection at a single institution (1/2011–12/2017) was performed. Clinicopathologic and perioperative factors associated with POPF and surgical outcomes were summarized and compared. Results: 43 patients underwent DP with RP tumor resection. Median age was 60 (range 22-81) years; 59% were male. 17 (40%) pts had RP sarcoma, 12 (28%) renal cell carcinoma, 11 (26%) gastrointestinal stromal tumor, and 3 (7%) adrenocortical carcinoma. Grade III-IV complications occurred in 7 (16%) patients, with 1 death. Stapled pancreatic transection was performed in 26 (60%) patients vs. suture ligation in 17 (40%). Clinically significant grade B POPF occurred in 14 (33%) patients, grade C POPF in 0, and biochemical leak in 6 (14%). The grade B leak rate was 38% (n=10/26) for stapled transection and 24% (n=4/17) for suture ligation. Median length of stay (LOS) was 9 (range 3-38) days (8 days for stapled, 12 days for sutured). Of 22 (51%) patients who developed a radiographically evident peri-pancreatic fluid collection, 7 required percutaneous drainage for symptomatic collections. The 90-day readmission rate was 33% (n=14), with grade B POPF being the reason in 8 patients. Conclusions: Patients undergoing DP with RP tumor resection experienced higher rates of clinically relevant POPF, longer LOS, and greater readmission rates, compared to historical results reported for standard DP alone for pancreatic tumors. Due to the limited population of these patients, future analyses will likely require multi-center studies to identify targetable predictors and risk mitigation strategies for POPF in this surgically high-risk population.

P333

Management and Outcomes of Patients with Fistulized Mesenchymal Tumors C.H. Davis,* E. Asare, S.H. Sabir, C. Roland, K.E. Torres, K. Hunt, J. Cormier, B. Feig. *University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction Fistulized intraabdominal/retroperitoneal sarcomas pose a significant clinical challenge with little information available on which to base treatment algorithms or determine prognosis. Historically, mesenchymal tumors that have fistulized to the bowel are believed to have a poor prognosis due to the loss of local control. Additionally, the combination of sepsis and malnutrition can make them unsuitable for urgent oncologic resection. We have reviewed our experience with this group of patients to address those two concerns. Methods A retrospective review of patients seen by the sarcoma surgical oncology section was performed. Clinicopathologic factors, preoperative and operative interventions as well as outcomes were reviewed. Results From 1998-2018, 13 patients treated for perforated mesenchymal tumors were identified. Median age was

45 years and 11 were males. The most common histologic diagnosis was GIST (n=6); other histologies included desmoid, liposarcoma, pleomorphic spindle cell sarcoma, and nonseminomatous germ cell tumor. Five patients presented with sepsis; 8 were treated with preoperative antimicrobial therapy (average 14 days); 4 underwent percutaneous drainage (0/4 developed drain tract seeding). The average time from presentation to oncologic resection was 75 days and the average preoperative days in hospital were 21. Primary tumor locations were small bowel (n=7) and retroperitoneal (n=6). All cases required concomitant resection of adjacent structures (average 3 structures). Margin status was R0=6, R1=4, R2=2. One patient is currently undergoing medical optimization before oncologic resection. At 90 days, there was no mortality, and there was only one Clavien-Dindo 3 complication. At last follow up, one patient is deceased after 286 days while all others are alive. Conclusion Patients with perforated mesenchymal tumors have significant preoperative morbidity that can be mitigated with preoperative antibiotics and nutritional support. Percutaneous drainage, traditionally felt to be contraindicated, can be helpful in controlling symptoms without compromising oncologic outcome. Oncologic resection with good outcomes can be achieved once patients are medically optimized.

P334

GISTs and Bariatric Surgery: A Tale of Observation J. Tisch,[1]* Z. Rogers,[2] C. Wilson,[3] C.M. Schammel,[4] S.D. Trocha.[5] *1. University of South Carolina Greenville, Greenville, SC; 2. Wake Forest, Winston-Salem, NC; 3. Moffitt Cancer Center, Tampa, FL; 4. Pathology, Pathology Associates, Greenville, SC; 5. Greenville Health System, Greenville, SC.*

Background: Gastrointestinal stromal tumors (GIST) are rare GI tumors comprising 1% of all GI tumors and affecting approximately 4,000-6000 people per year. With the rise in obesity, bariatric surgery is becoming an increasingly common procedure and the incidence of GISTs in the bariatric population has been shown to be greater than that of the general population. We evaluated and characterized the incidental GISTs in this unique population. Methods: All GIST tumors identified during laparoscopic sleeve gastrectomy (LSG) and Roux-en-Y gastric bypass (RYGB) between 1/1/2005 and 12/31/2016 were retrospectively evaluated. Typical demographic, clinicopathologic, treatment, follow-up and outcome data were recorded. Fisher's t-tests were completed to determine significance (alpha=0.05). Results: Within the 2677 bariatric surgeries, 17 GISTs were identified (0.64%). Mean age was 54.4 years. All lesions were not identified pre-operatively. GISTs were in the fundus (5, 29.4%) or body (12, 70.6%) of the stomach; 16/17 (94%) were identified intra-operatively. All lesions were unifocal and <1 cm in size, with 12/17 (70.6%) of the lesions < 0.5 cm. Surgical margins were clear on 16/17 (94.1%) resection specimens; 15 tumors had spindle cell (88.2%) and two (11.8%) were mixed histology. All tumors had less than 5 mitoses/50 fields portending a low malignancy rate. While all patients had typical post-operative follow up with their bariatric surgeon, only three patients (17.6%) were followed by oncology with CT scans; all were negative for recurrence or metastasis. The patient with the positive surgical margin was followed by EGD for four years (all negative). Upon completion of this study, there were no reports of recurrences or GIST-related deaths for any patient in our cohort. Conclusion: We present the largest cohort to date of incidental GISTs in a bariatric population. As pre-operative examination was unable to identify these lesions, which could be catastrophic for this subset of patients, a diligent examination of the mucosa is paramount for identification of these tumors. Of course, early identification of low risk tumors is the advantage to acknowledging this correctable blind spot.

P335

Effect of Chemotherapy on Overall and Recurrence-free Survival in Resectable Soft Tissue Sarcoma: A Meta-analysis A.C. Istl,[1]* J.M. Ruck,[3] C.D. Morris,[2] A.S. Levin,[2] C.F. Meyer,[4] F.M. Johnston.[5] *1. Division of General Surgery, Western University, London, ON, Canada; 2. Division of Orthopaedic Oncology, Johns Hopkins Hospital, Baltimore, MD; 3. Department of Surgery, Johns Hopkins Hospital, Baltimore, MD; 4. Department of Medical Oncology, Johns Hopkins Hospita, Baltimore, MD; 5. Division of Surgical Oncology, Johns Hopkins Hospital, Baltimore, MD.*

Background: The heterogeneity of soft tissue sarcomas (STS) and patient reluctance to accept therapy of uncertain benefit has limited the development of chemotherapy trials for STS. Changes in chemotherapeutic regimens for STS demand an updated analysis of the efficacy of chemotherapy as an adjunct to surgery. Methods: We searched Embase, MEDLINE, CENTRAL, and clinicaltrials.gov. We included studies since 1997 assessing adult patients with resectable STS who received systemic therapy and met histologic inclusion criteria. Data abstraction was completed in duplicate. Quality of studies was assessed using Cochrane risk of bias tool and Newcastle Ottawa Scale. Data from separate studies were combined for meta-analysis where appropriate. Pooled hazard and risk ratios were calculated for OS, PFS, and local and distant recurrence (LRFS and DRFS). Results: 10 studies totaling 3157 patients were included. Five studies assessed only adjuvant chemotherapy, 2 assessed retroperitoneal sarcoma (RPS), and 3 assessed extremity STS. Most assessed mixed histologies. Only one study reported survival outcomes at 1 year, and standard reporting of survival outcomes at 5 years was inconsistent. Pooled analysis for 5-year OS, PFS, LRFS, and DRFS showed no significant benefit of chemotherapy over locoregional therapy alone. Hazard of death, progression, and recurrence were not improved with chemotherapy on pooled analysis. Subgroup analyses of 800 extremity STS patients also showed no survival benefit with chemotherapy. Median survival was only reported in two studies, which showed an improved OS of 33 months with chemotherapy over locoregional therapy alone ($p<0.01$). Quality indices were poorly reported across randomized trials and variably reported in observational literature. Conclusions: This updated meta-analysis demonstrated no improvement in OS, PFS, or local or distant RFS after receipt of chemotherapy in all-comer or site-specific STS. Standard outcomes and quality indices were poorly reported. RCTs for STS are challenging, and higher-quality observational studies are needed; recommendations have been provided to this end.

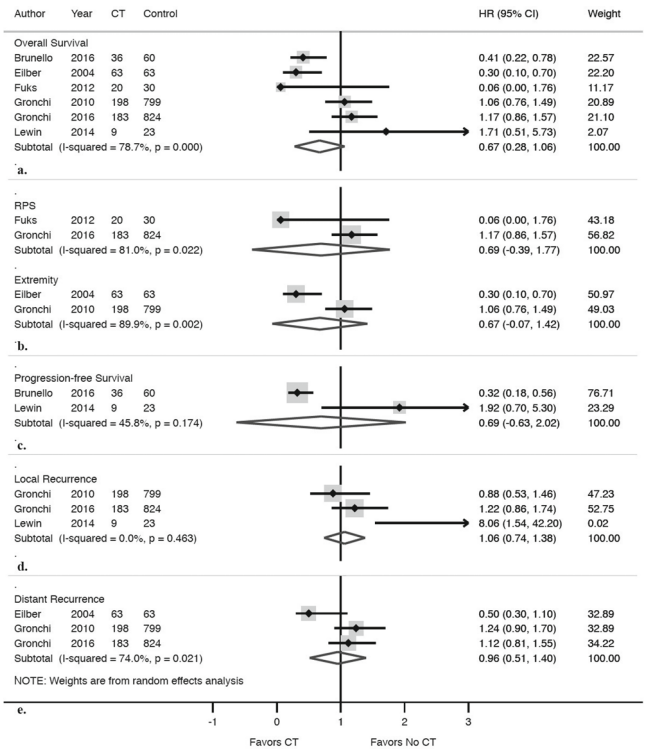


Figure. Combined hazard ratios associated with receipt of chemotherapy for a. overall survival from all reporting studies, b. subgroup analysis of overall survival by tumor site (RPS and extremity), c. progression or any recurrence, d. local recurrence, and e. distant recurrence.

P336

The Role of FDG - PET in Retroperitoneal Sarcomas - A Multicenter Retrospective Study S. Subramaniam,[3]* J. Callahan,[1] M. Bressel,[2] M. Hofman,[1] C. Mitchell,[4] S. Hendry,[5] F.L. Vissers,[6] B. van der Hiel,[7] D. Patel,[8] W.J. van Houdt,[6] W. Tseng,[9] D.E. Gyorki.[3] *1. Cancer Imaging, Peter Maccallum Cancer centre, Melbourne, VIC, Australia; 2. Centre for Biostatistics and Clinical trials, Peter MacCallum cancer centre, Melbourne, VIC, Australia; 3. Division of surgical oncology, Peter MacCallum cancer centre, Melbourne, VIC, Australia; 4. Department of Pathology, Peter MacCallum Cancer centre, Melbourne, VIC, Australia; 5. Department of pathology, St Vincents hospital, Melbourne, VIC, Australia; 6. Department of surgical oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; 7. Depatment of nuclear medicine, Netherlands Cancer Institute, Amsterdam, Netherlands; 8. Department of Radiology, Keck school of Medicine of USC, Los Angeles, CA; 9. Department of surgery, Surgical oncology section, Keck school of Medicine, Los Angeles, CA.*

Introduction: The role of F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) in the evaluation of retroperitoneal sarcomas (RPS) is undefined. Clinical studies of bone and soft tissue sarcomas have demonstrated a correlation between SUVmax and mitotic rate and Ki 67 expression. Tumor grade is the most important prognostic factor in patients with primary RPS and forms an essential component of staging. We sought to evaluate the correlation between SUV max measured by FDG-PET with pathologic tumor grade in the surgical resection specimen of primary retroperitoneal dedifferentiated liposarcoma (DDLPS) and leiomyosarcoma (LMS). Description: Patients with the above two histological subtypes of RPS were identified from the database of sarcoma units at Peter MacCallum Cancer Centre (Australia), The Netherlands Cancer Institute (Netherlands), and the University of Southern California (USA) from July 2013 till June 2018. All patients who underwent preoperative PET scan and definitive surgical resection with histopathological specimen available for review were included in the study. Experienced sarcoma pathologists reported pathology. The resected tumor was graded using French Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading. The association between SUVmax and pathological grade was assessed using Spearman correlation. Results: Fifty-eight patients were included in the study, with a median age of 63.5 years. The final pathological subtype was DD LPS in 44(75.9%) patients and LMS in 14 (24.1%). 27 (46.6%) patients had neoadjuvant radiotherapy; 7 had neoadjuvant chemotherapy; none received both modalities. The mean SUVmax was 8.7 with median 7.1 (range 2.2 to 33.9). The median tumor size in the resected specimen was 18.4cms. The tumors were graded I, II and III in 6(10.3%), 35(60.3%) and 17(29.3%) patients respectively. There was a moderate association of higher histological grade with higher SUVmax (r_s=0.40, p=0.002). Conclusion There is a correlation between SUVmax and pathologic grade in patients with DDLPS and LMS. Larger studies are required to evaluate whether this imaging modality has a role in patients receiving neoadjuvant therapy.

P337

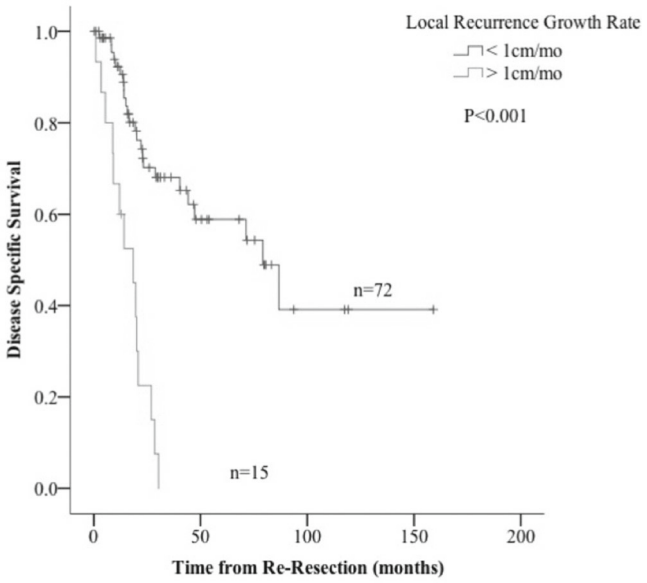
Hyperbaric Oxygen Therapy for Radiation-Induced Tissue Injury Following Sarcoma Treatment: A Retrospective Analysis of a Dutch Cohort. J.D. Generaal,[1]* C.A. Lansdorp,[2] O. Boonstra,[2] B.L. van Leeuwen,[1] H.A.M. Vanhauten,[3] M.G. Stevenson,[1] L.B. Been.[1] *1. University of Groningen, University Medical Center Groningen, Department of Surgery, Groningen, Netherlands; 2. Institute for Hyperbaric Oxygen, Rotterdam, Netherlands; 3. University of Groningen, University Medical Center Groningen, Department of Radiation Oncology, Groningen, Netherlands.*

Introduction. Localized sarcomas are commonly managed by surgical resection and external-beam radiotherapy (EBRT), administered pre- or postoperatively. Frequent complications include postoperative wound complications, chronic wounds and late radiation tissue injury (LRTI). Hyperbaric oxygen therapy (HBOT) is hypothesized to have positive effects on these complications by improving tissue oxygenation, mobilizing stem cells and reducing fibrosis. This study aims to gain insight in the use and results of HBOT for radiation-induced tissue injury following sarcoma treatment. Methods. All sarcoma patients treated between January 2006 and October 2017 in one of the five centers of the Institute of Hyperbaric Oxygen in the Netherlands were included for retrospective analysis. Results. Thirty patients were included. Treatment indications were either chronic wounds or LRTI, 18 (60.0%) patients were treated for chronic wounds and 12 (40.0%) for LRTI. Twenty-two (73.3%) patients reported no HBOT-induced adverse events, the others temporary ear/eye problems and fatigue. Two patients with chronic wounds were excluded from further analysis as HBOT was discontinued within five sessions. In 11 of 16 (68.8%) patients treated for chronic wounds, improved wound healing was seen. Nine of 12 (75.0%) patients treated for LRTI reported a decline in pain. Reduction of fibrosis was seen in five of eight (62.5%) patients treated for LRTI. Conclusion. In this cohort, HBOT has shown to be a safe and beneficial treatment option for sarcoma patients experiencing chronic wounds or LRTI following multimodality sarcoma treatment. Research is needed to determine the effects of HBOT in prospective trials.

P338

Local Recurrence Growth-Rate Predicts Survival Following Repeat Resection for Recurrent Retroperitoneal Liposarcoma: Validation of the One-Centimeter Per Month Rule T. Tran,[1]* C. Ethun,[2] V. Grignol,[3] J.H. Howard,[3] T. Gamblin,[4] M. Bedi,[4] J. Tseng,[5] K. Roggin,[5] K. Chouliaras,[6] K.I. Votanopoulos,[6] D. Cullinan,[7] R. Fields,[7] K. Cardona,[2] G. Poultsides.[1] *1. Stanford University, Stanford, CA; 2. Emory University, Atlanta, GA; 3. The Ohio State University, Columbus, OH; 4. Medical College of Wisconsin, Milwaukee, WI; 5. University of Chicago, Chicago, IL; 6. Wake Forest University, Winston Salem, NC; 7. Washington University in St. Louis, St. Louis, MO.*

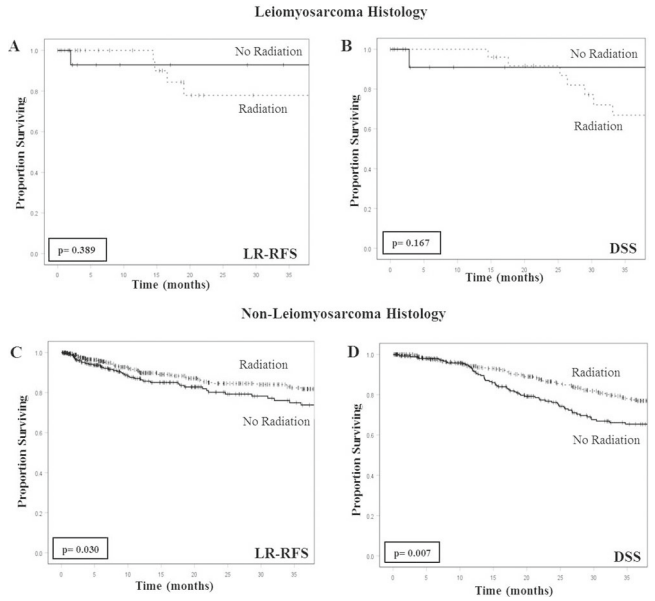
Objective:Local recurrence is a common problem following resection for retroperitoneal liposarcoma (RPLPS). Complete surgical resection for recurrent RPLPS remains the primary treatment modality, if safe and feasible. This study aims to validate the results of a prior single-institution study, which has shown that local recurrence growth rate (LRGR) of <1 cm/month is associated with favorable survival after re-resection. Method:Patients who underwent curative-intent resection for locally recurrent RPLPS were identified from the U.S. Sarcoma database. LRGR was defined as the cumulative radiographic size of the local recurrence divided by the time from initial resection to the detection of local recurrence. Endpoints included local recurrence free survival (LRFS), and disease-specific survival(DSS). Results:From 2000-2016, 87 patients underwent re-resection for recurrent RPLPS. The median age was 61 yrs and 35.8% were female. Histologic subtypes included 35.7% dedifferentiated, 28.7% well-differentiated, 16.1% myxoid, and 11.5% pleomorphic LPS. R0 resections were achieved in 48% of cases while 31% underwent multi-organ resection for RPLPS. LRGR>1cm/mo was associated with worse DSS compared to LRGR <1cm/mo (median 16.1 vs 87.4 mo,P<0.001). LRGR >1cm/mo after initial recurrence was also associated with worse second LRFS (median LRFS 8.8 vs. 64 mo,P=0.042). On multivariate analysis, independent predictors of poor DSS among those with locally recurrent RLPS include FNCLCC grade 3 (HR4.1, P=0.048) and LRGR>1cm/mo (HR7.4, P=0.001), while R1 margins were associated with worse second LRFS (HR2.7,P=0.02). Conclusions:This multi-institutional study validates previously published data showing that local recurrence growth rate is strongly associated with local recurrence free and disease-specific survival following resection of recurrent RPLPS. Given the worse survival associated with re-resection of local recurrences growing >1cm per month, these patients should be offered clinical trials of systemic chemotherapy with or without radiotherapy, and not surgery, unless the latter can facilitate palliation of symptoms.



P339

A Closer Look at the Natural History and Recurrence Patterns of High-Grade Truncal/Extremity Leiomyosarcomas: An Analysis from the U.S. Sarcoma Collaborative R.M. Lee,[1]* C. Ethun,[1] M.Y. Zaidi,[1] T. Tran,[2] G. Poultsides,[2] V. Grignol,[3] J.H. Howard,[3] M. Bedi,[4] T. Gamblin,[5] J. Tseng,[6] K. Roggin,[6] K. Chouliaras,[7] K.I. Votanopoulos,[7] B.A. Krasnick,[8] R. Fields,[8] S. Oskouei,[1] D. Monson,[1] N.B. Reimer,[1] S. Maithel,[1] K. Cardona.[1] *1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Surgery, Stanford University Medical Center, Palo Alto, CA; 3. Division of Surgical Oncology, Department of Surgery, The Ohio State University, Columbus, OH; 4. Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI; 5. Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI; 6. Department of Surgery, University of Chicago Medicine, Chicago, IL; 7. Department of Surgery, Wake Forest University, Winston-Salem, NC; 8. Department of Surgery, Washington University School of Medicine, St Louis, MO.*

Background: The natural history and treatment data for truncal/extremity (TE) soft tissue sarcoma (STS) is derived primarily from studies investigating all histiotypes as one homogenous cohort. The aim of this study was to define the recurrence rate (RR), recurrence patterns, and response to radiation of TE leiomyosarcomas (LMS). Methods: All pts from the US Sarcoma Collaborative (2000-16) database with primary, high-grade TE STS who underwent curative-intent resection were identified. Pts were grouped into LMS or other high-grade histology (non-LMS). Primary endpoints were locoregional recurrence-free survival (LR-RFS), distant-RFS (D-RFS), and disease specific survival (DSS). Results: 93 pts had LMS and 1122 had non-LMS. In pts with LMS, median age was 63yrs and median tumor size was 6cm. In pts with non-LMS, median age was 58yrs and median tumor size was 8cm. In pts with LMS, overall RR was 42% with 15% LR-RR and 29% D-RR. The 3yr LR-RFS, D-RFS, and DSS were 84%, 65%, and 76%, respectively. When considering LMS pts with high-risk of recurrence (>5cm and high-grade, n=49), the overall RR was 45% with 12% LR-RR and 35% D-RR. In this group, 61% received radiation. There were no pathologic differences in those who did and did not receive radiation. The 3yr LR-RFS (78vs93%,p=0.39,FigA), D-RFS (53vs63%,p=0.27), and DSS (67vs91%,p=0.17,FigB) were similar in those who did and did not receive radiation. High-risk non-LMS pts had a similar overall RR of 42% with 15% LR-RR and 30% D-RR. 60% of pts in this cohort received radiation and there were no pathologic differences in those who did and did not receive radiation. However, there was an improved 3yr LR-RFS (82vs75%,p=.030,FigC) and DSS (77vs65%,p=0.007,FigD) in non-LMS pts who received radiation. Conclusion: In our multi-center cohort, pts with high-grade TE LMS have a low LR-RR (12-15%) and a modest D-RR (29-35%), which are comparable to other high-grade STS in our database. However, radiation was not associated with improvement in local control in LMS. Thus, in pts with high-risk TE LMS, the value of radiation merits further investigation.



P340

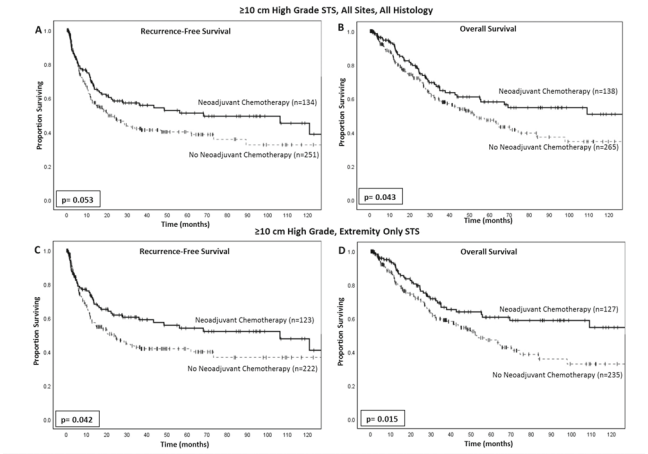
Novel Therapy with ^{103}Pd-Directional Brachytherapy Device for Recurrent Soft Tissue Sarcomas: Safety and Early Postoperative Outcomes F. Macedo,* M. Studenski, R. Yechieli, B. Wilky, J. Trent, D. Franceschi, N. Merchant, A.S. Livingstone. *Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL.*

Background: Recurrent soft tissue sarcomas (STS) are frequently associated with poor regional control and high relapse rates despite aggressive treatment. Conventional external beam radiation (EBRT) and boost dosing remain controversial due to concerns regarding toxicity. The CivaSheet® (CivaTech Oncology Inc., Durham, NC) is a novel radiotherapy device that may facilitate highly localized radiation while limiting toxicity. However, evidence reporting its safety and postoperative outcomes are lacking. Methods: From March to June 2018, three patients with recurrent STS underwent resection with intraoperative brachytherapy and were prospectively reviewed at our Institution. CivaSheet®, an implantable unidirectional palladium-103 (^{103}Pd) planar low-dose brachytherapy device, was used. Postoperative imaging of the implanted membrane were obtained for dosimetric analysis and surveillance. Results: Mean age was 42 years (19-63 years) and there were 2 females. Mean tumor size was 7.6 cm. All patients underwent preoperative radiation with mean dosimetry of 56.1 Gy. Pathology included recurrent high-grade pleomorphic liposarcoma involving the vertebral body, recurrent dedifferentiated liposarcoma involving the left psoas muscle and recurrent phyllodes tumor of the right breast and chest wall. Surgical resection included right lower pneumonectomy, left colectomy, and radical mastectomy with partial chest wall resection. Mean intraoperative brachytherapy dose was 40.7 Gy. Surgical margins were negative in all cases. Mean follow-up was 5.4 (4.4-7.0) months and there is no evidence of recurrence to date. Conclusion: The device was well tolerated in all patients and allowed irradiation of potential microscopic disease within the tissue immediately overlying the tumor cavity. The device may be of value especially in cases in which local control is suboptimal in patients with prior history of EBRT. Despite relatively small number of patients, this is the largest series assessing the clinical utilization of ^{103}Pd device in patients with recurrent STS to date. Further experience with larger series and longer follow-up is warranted for widespread use.

P341

Assessing the Role of Neoadjuvant Chemotherapy in High-Risk Truncal/Extremity Soft Tissue Sarcomas: An Analysis of the Multi-Institutional U.S. Sarcoma Collaborative M.Y. Zaidi,[1]* C. Ethun,[1] T. Tran,[2] G. Poultsides,[2] V. Grignol,[7] J.H. Howard,[7] M. Bedi,[6] H. Mogal,[6] J. Tseng,[5] K. Roggin,[5] K. Chouliaras,[4] K.I. Votanopoulos,[4] B.A. Krasnick,[3] R. Fields,[3] S. Oskouei,[1] N. Reimer,[1] D. Monson,[1] S. Maithel,[1] K. Cardona.[1] *1. Surgery, Emory University, Atlanta, GA; 2. Stanford University, Palo Alto, CA; 3. Washington University School of Medicine, St. Louis, MO; 4. Wake Forest University, Winston-Salem, NC; 5. University of Chicago SOM, Chicago, IL; 6. Medical College of Wisconsin, Milwaukee, WI; 7. The Ohio State University, Columbus, OH.*

Background: A lack of consensus remains on the role of neoadjuvant chemotherapy (NCT) in treating high-risk soft tissue sarcomas (STS). Given heterogeneous selection criteria of tumor size, location, and histology, clinical trials have yet to demonstrate a clear benefit. Thus, the aim of our study was to define which patients may experience a survival advantage with NCT. Methods: All pts from the US Sarcoma Collaborative database (2000-16) who underwent curative-intent resection of high-grade, primary truncal/extremity STS ≥5cm were included. Primary endpoints were recurrence-free survival (RFS) and overall survival (OS). Results: Of 4153pts, 770 were included. Median age was 62yrs; 56% were male. Median tumor size was 10cm, 87% (n=669) had extremity tumors, and most common histologies were undifferentiated pleomorphic sarcoma (UPS) 42%, synovial sarcoma 8%, and myxofibrosarcoma 8%. 28% (n=216) of pts received NCT. Pts who received NCT were younger (p<0.001), more likely to be male (p=0.049), functionally independent (p=0.043), and had deep, larger tumors (p<0.001). When considering tumor sizes ≥5 and ≥8cm, NCT was not associated with improved RFS or OS. However in tumor sizes ≥10cm, pts with NCT had improved 5-yr RFS (51vs40%,p=0.053) and 5-yr OS (58vs47%,p=0.043) compared to pts without NCT(Fig A-B). When stratifying tumors ≥10cm by location, pts with extremity tumors, but not truncal, had improved 5-yr RFS (54vs42%, p=0.042) and 5-yr OS (61vs47%,p=0.015) with NCT (Fig C-D). On histology-specific analysis, no subtype regardless of size (≥5, ≥8, or ≥10cm), had improved RFS or OS with NCT, though pts with UPS histology had a trend towards improved 5-yr RFS (56vs42%,p=0.092) and 5-yr OS (66vs52%,p=0.103) with NCT. Conclusion: In our multi-institutional cohort, patients with high-grade STS had an improved RFS and OS with NCT when tumors were ≥10cm and located in the extremity; however, no histiotype-specific advantage was identified. Future studies assessing the efficacy of NCT may consider amending selection criteria to focus on these patients, with added focus on histology-specific strategies.

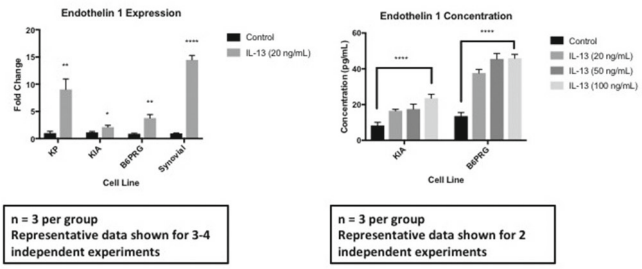


P342

An Interleukin-13-Endothelin 1-Axis in Soft Tissue Sarcoma Pulmonary Metastasis I.W. Folkert,[1]* S. Devalaraja,[2] R. Norgard,[2] T. To,[2] Z. Alam,[2] R.E. Roses,[1] M. Haldar.[2] *1. Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA; 2. Perelman School of Medicine, Philadelphia, PA.*

Introduction: Soft tissue sarcomas (STS) comprise a heterogeneous group of solid tumors arising from mesenchymal tissues. Nearly 60% of patients with high-grade tumors will develop metastasis, which is almost uniformly fatal. Lung is the most common site of metastasis, but pathways controlling pulmonary metastasis are poorly understood. Methods: Multiple murine sarcoma cell lines and mouse models of sarcoma were utilized in the present study: (1) a genetically engineered mouse model of synovial sarcoma (SS) driven by the SYT-SSX fusion gene, (2) a genetically engineered mouse model of undifferentiated pleomorphic sarcoma (KP-UPS) driven by concomitant loss of P53 and activation of oncogenic KRAS, (3) a subcutaneous transplant model of a pro-metastatic murine UPS cell line driven by concomitant loss of Ink4a/Arf and activation of oncogenic KRAS (KIA-UPS), and (4) a carcinogen induced (MCA) mouse model of fibrosarcoma (B6PRG). Endothelin 1 levels were quantified by RT-qPCR and ELISA. Lung metastasis was modeled by subcutaneous transplant or tail vein injection of KIA-UPS cells in Nude mice, and quantified using flow cytometry. Results: Using murine sarcoma cell lines derived from our mouse models, we discovered that the Th2 cytokine interleukin 13 (IL-13) significantly increases the expression of the small vasogenic peptide Endothelin 1 (Edn1) in sarcoma cells in vitro (Figure 1). We next generated sarcoma cell lines expressing shRNAs targeting Edn1, and preliminary data demonstrate that Edn1 knockdown leads to a decrease in the frequency of lung metastasis in vivo (p<0.05). Furthermore, Edn1 knockdown led to a significant enrichment in pro-inflammatory gene sets by Gene Set Enrichment Analysis (GSEA), suggesting reductions in Edn1 may promote anti-tumor immunity. Finally, we also found that Edn1 promotes disruption of lung microvascular endothelial tight junctions in vitro, suggesting a possible mechanism through which Edn1 promotes sarcoma pulmonary metastasis. Conclusions: Our findings suggest the existence of a previously unknown pathway wherein Th2 cytokines from tumor-infiltrating leukocytes promote lung metastasis by upregulating Endothelin 1 expression in sarcoma cells.

Figure 1: IL-13 Upregulates Endothelin 1 in Sarcoma Cells



P343

Outcomes of Plastic Surgical Reconstruction in Extremity and Truncal Soft Tissue Sarcoma: Results from the U.S. Sarcoma Collaborative S. Thalji,[1]* S. Tsai,[1] T. Gamblin,[1] C.N. Clarke,[1] M. Hembrook,[1] M. Bedi,[2] J. LoGiudice,[3] C. Ethun,[4] T. Tran,[5] G. Poultsides,[5] V. Grignol,[6] J.H. Howard,[6] J. Tseng,[7] K. Roggin,[7] K. Chouliaras,[8] K.I. Votanopoulos,[8] D. Cullinan,[9] R. Fields,[9] K. Cardona,[4] H. Mogal.[1] *1. Department of Surgery, Medical College of Wisconsin, Milwaukee, WI; 2. Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI; 3. Department of Plastic Surgery, Medical College of Wisconsin, Milwaukee, WI; 4. Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; 5. Department of Surgery, Stanford University Medical Center, Palo Alto, CA; 6. Division of Surgical Oncology, Department of Surgery, The Ohio State University, Columbus, OH; 7. Department of Surgery, University of Chicago Medicine, Chicago, IL; 8. Department of Surgery, Wake Forest University, Winston-Salem, NC; 9. Department of Surgery, Washington University School of Medicine, St. Louis, MO.*

Objective: Patients with extremity and truncal soft tissue sarcoma (ETSTS) often require plastic surgical reconstruction (PSR) after radical resection. However, the effect of PSR on short- and long-term outcomes is not well defined. The primary aim of this study is to define the effect of PSR on post-operative wound-related complications, locoregional recurrence free survival (LRRFS) and overall survival (OS). The secondary aim is to identify factors associated with PSR. Methods: Patients who underwent resection of ETSTS between 2000 and 2016 were identified from a retrospective 7-institution United States Sarcoma Collaborative database. PSR was defined as any complex primary closure, skin graft or tissue flap reconstruction requiring a plastic surgeon. Multivariable analysis (MVA) was performed to determine factors associated with PSR and wound-related complications. LRRFS and OS were estimated by the Kaplan-Meier method. Cox-proportional hazards models of patient- and treatment-related factors were constructed to determine their effect on LRRFS and OS. Results: Of a total 2750 distinct operations, 1060 (38.6%) involved PSR. Tissue flap (n=854, 80.6%) was the most commonly used PSR. Larger tumor size (OR 1.99, CI 1.11-3.55, p=0.02), neoadjuvant radiation (OR 2.12, CI 01.33-3.39, p=0.002), higher BMI (OR 1.05, CI 1.02-1.08, p=0.002) and tissue flap PSR (OR 1.72, CI 1.1-2.7, p=0.017) were independently associated with the development of wound-related complications. LRRFS (16.8 vs 20.9 months; p=0.096) and OS (41.9 v. 39.6 months; p=0.588) were comparable for PSR and non-PSR patients. PSR was not independently associated with OS or LRRFS (Table 1). High tumor grade (OR 1.73, CI 1.18-2.55, p=0.005) and neoadjuvant radiation (OR 1.55, CI 1.08-2.20, p=0.016) independently predicted need for PSR on MVA. Conclusions: While there is a higher incidence of postoperative wound-related complications in patients receiving tissue flap PSR, there is no effect on LRRFS or OS as long as patients undergo radical resection. High tumor grade and receipt of neoadjuvant radiation predict requirement of PSR in patients undergoing radical resection of ETSTS.

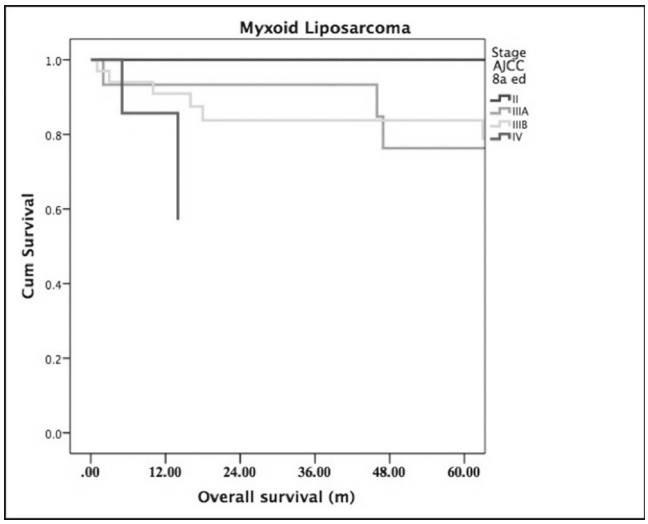
Table 1: Cox Proportional Hazards Model of Factors Associated with Locoregional Recurrence Free Survival (LRRFS) and Overall Survival (OS).

	Locoregional Recurrence Free Survival			*Overall Survival*		
	Hazard Ratio	95% Confidence Interval	*P* value	Hazard Ratio	95% Confidence Interval	*P* value
Age	0.98	0.97 – 0.99	**0.019**	1.02	1.01 – 1.03	**<0.001**
ECOG Functional Status						
Partially Dependent	-	-	-	1.92	0.69 – 5.35	0.215
Totally Dependent	1.12	0.44 – 2.83	0.807	1.09	0.63 – 1.89	0.745
Pre-operative Albumin	1.23	0.74 – 2.04	0.415	0.75	0.64 – 0.89	**0.001**
Smoking History	0.64	0.30 – 1.36	0.244	1.35	0.98 – 1.86	0.068
Number of Comorbidities						
1-2	0.88	0.57 – 1.36	0.564	1.07	0.85 – 1.36	0.556
>2	7.83	1.86 – 32.99	0.005	1.79	0.95 – 3.34	0.070
Tumor Size						
5-10 cm	1.00	0.61 – 1.62	0.989	1.29	0.95 – 1.76	0.104
>10 cm	0.47	0.29 – 0.77	**0.003**	1.36	1.01 – 1.78	**0.048**
High Grade Tumor	2.65	1.40 – 5.03	**0.003**	3.43	2.26 – 5.20	**<0.001**
Neoadjuvant Chemotherapy	1.43	0.87 – 2.35	0.154	1.11	0.86 – 1.43	0.425
Neoadjuvant Radiation	0.49	0.28 – 0.84	**0.010**	0.66	0.50 – 0.87	**0.003**
Plastics Closure						
Complex Primary	0.98	0.34 – 2.82	0.973	1.24	0.62 – 2.47	0.540
Skin Graft	1.18	0.58 – 2.38	0.643	1.00	0.62 – 1.61	0.991
Tissue Flap	0.97	0.65 – 1.46	0.888	0.89	0.71 – 1.13	0.347
Vascular Resection	1.19	0.53 – 2.65	0.670	1.27	0.87 – 1.83	0.211
Resection Status						
R1	1.51	0.97 – 2.35	0.068	1.70	1.29 – 2.26	**<0.001**
R2	13.35	3.20 – 55.71	**<0.001**	4.23	2.72 – 6.59	**<0.001**
Severity of Complications						
Clavien-Dindo I-II	1.14	0.58 – 2.23	0.702	1.12	0.79 – 1.59	0.525
Clavien-Dindo III-IV	0.65	0.34 – 1.25	0.195	1.05	0.78 – 1.41	0.742
Adjuvant Chemotherapy	0.85	0.47 – 1.56	0.608	1.33	1.02 – 1.74	**0.037**
Adjuvant Radiation	0.87	0.54 – 1.40	0.564	0.78	0.59 – 1.03	0.083

P344

Recurrence Pattern in Extremity Myxoid Liposarcoma: A Cohort Study of 58 Cases from a Sarcoma Unit in Mexico D. Garcia-Ortega,[1]* A. Alvarez-Cano,[2] H. Martinez-Said,[1] J.F. Corona-Cruz,[1] M. Clara-Altamirano,[1] C. Caro-Sanchez,[1] D. Prada-Ortega,[1] M. Cuellar-Hubbe.[1] *1. Skin and soft tissue tumors, Instituto Nacional de Cancerologia (Mexico), Tlalpan, Mexico; 2. Hospital Universitario UANL, Monterrey, Mexico.*

Background. Myxoid liposarcoma (mLPS) is a liposarcoma subtype with a predominant myxoid component. 90% of the cases harbor a FUS-DDIT3 t(12;16)(q13;p11) mutation, in the remaining cases, mutations EWSR1-DDIT3 t(12;22)(q13;p11) and ins(12;16)(q13;p11.2p13) are found. Prognosis factors are size, resection margin, grade and the presence of round cells. More than 5% round cells is associated with recurrence, distant metastases and poor OS. mLPS has a higher frequency of extrapulmonary metastases. We aimed to analyze recurrence patterns in a cohort of mLPS. Material and methods. We performed a retrospective review of a prospectively maintained database. Cases from January 2005 to December 2016 were analyzed. We included 58 with histologically and/or molecular diagnosis of mLPS. Univariate and multivariate analysis was performed. Survival and recurrence-free survival were estimated using the Kaplan-Meier method. A p-value <0.05 was considered significant. Results 58 patients were included. 27(56.6%) women and 31 (53.4%) men with a mean age of 43 (17-69). 2 (3.4%) were in stage II, 49 (84.5%) had a locally advanced disease (IIIA 25.9%, IIIB 58.6%) and 7 (12.1%) stage IV. The thigh was the site affected in 31(53.4%) cases, followed by the leg in 12 (20.7%), gluteal in 8(13.8%). Median follow up was 50.8 months (1 – 140 months). 41 (71%) cases were treated with wide resection and radiation, 4 (6.9%) with isolated limb perfusion and resection, and 4 (6.9%) with amputation. Resection status was R0 in 40(69%), R1 in 14 (24.1%). Any recurrence was recorded in 25(43.1%) cases. Lung only metastasis developed in 4(6.9%); local recurrence in 5(8.6%). Most recurrences were extrapulmonary, according to other series. Bone and retroperitoneal recurrences happened in 4(6.9%) cases each. Round cell >5% was associated with retroperitoneal recurrence. 5-year OS was 86%, 100% in early stages, 67% in locally advanced and 28% in advanced disease. Conclusion. Recurrence pattern is different to other sarcomas. We found a relation between percentage of round cells and retroperitoneal recurrence. Management in a high volume sarcoma center should be encouraged



P345

Frequent Rectal GIST Recurrences in the Imatinib Era: Retrospective Analysis of an International Registry E. Stuart,[1]* S. Banerjee,[1] N. Scherzer,[2] J. Call,[2] J. de la Torre,[1] A.M. Burgoyne,[1] P.T. Fanta,[1] L. Parry,[1] S. Ramamoorthy,[1] J. Sicklick.[1] *1. University of California, San Diego, San Diego, CA; 2. Life Raft Group, Wayne, NJ.*

Introduction: Rectal gastrointestinal stromal tumor is rare and comprises about 3% of GIST. Few studies have examined these patients and none have studied an international cohort. Methods: Registry data was collected by the Life Raft Group, an international advocacy foundation, from 06-1976 to 12-2015. All patients were histologically confirmed to have GIST at the time of diagnosis or retrospectively. Recurrence-free survival (RFS) was analyzed using the Kaplan-Meier method and Cox regression analysis. Results: Of 1798 patients in the database, 48 had localized rectal GIST (2.7%). Patients were frequently male (58.3%) and non-Hispanic whites (58.3%). The median age at diagnosis was 52 yo. A majority of patients (77%) were diagnosed in the imatinib (IM) era (after 2000). Over half (54.2%) of the cohort had mutation profiling and all tumors possessed KIT mutations (exon 9: 7.7%; exon 11: 88.5%; exon 13: 3.8%). Most evaluable patients (26/28; 92.9%) had high risk disease (modified NIH criteria) and 95.8% of all patients received IM at some time during treatment. The median follow-up and RFS of the cohort were 8.8-y (range 0.3-30.7) and 8-y (95% CI 2.9-13.1), respectively. Univariate analysis demonstrated that adjuvant IM (HR=0.39, 95% CI 0.15-1.01; P=0.046) was associated with improved RFS. Although all patients (11/11, 100%) diagnosed in the pre-IM era developed recurrent GIST, 32% of patients (12/37) also developed recurrent disease in the IM era (P<0.001). Despite the high rate of recurrences in both periods, a diagnosis in the IM era was associated with improved RFS (HR=0.22, 95% CI 0.08-0.62; P=0.004) in the multivariate model. Conclusion: Herein, we report the largest international series of rectal GIST patients. In contrast to a recent single institution study (Cavnar et al., Ann Surg Onc, 2017) that reported 30 patients without rectal GIST recurrences in the IM era, we find that disease recurrence remains prevalent in one-third of patients treated during the same period. Despite improved patient outcomes in the IM era, further studies are warranted to investigate additional prognostic factors and treatment strategies for rectal GIST.

P346

Visceral Angiosarcoma: A Nationwide Analysis of Treatment Factors and Outcome B.R. Zambetti,* L. Hendrick, P.V. Dickson, E. Glazer, D. Shibata, S.W. Behrman, M.D. Fleming, J.L. Deneve. *Department of Surgery, University of Tennessee Health Science Center, Memphis, TN.*

Background: Visceral angiosarcoma arises within the vasculature and lymphatic system and accounts for 2% of soft tissue sarcomas. We examined treatment factors and determinants of outcome for patients who present with this rare disease using a national dataset. Methods: The 2004-2015 National Cancer Database (NCDB) was queried for patients with angiosarcoma. Trends in treatment and outcomes for visceral angiosarcoma were examined. Factors affecting overall survival (OS) were assessed with log rank test and Cox regression. Results: 893 patients with visceral angiosarcoma were identified [median age 65 years, male (63%), Charlson comorbidity index <1 (86%)]. The tumor size was < 5 cm in 20.7%, 5-10 cm in 21.1% and >10 cm in 21.8% while 34.2% were moderate/high grade. The most common location of origin was liver/biliary (N=488, 54.6%), urinary tract (N=126, 14.1%), peritoneal/retroperitoneal (N=81, 9.1%), adrenal (N=59, 6.6%), small bowel (N=53, 5.9%), colon (N=40, 4.5%) and other (N=46, 5.1%). Treatment consisted of surgery (N=288, 32%), radiation (N=77, 8.6%) or systemic chemotherapy (N=323, 36.7%). The median survival for all patients was 3.8 months (95% CI 3.4-4.4) while the median OS was 12.3 months (95% CI 7.9-21.8) for peritoneal/retroperitoneal tumors, 10.6 months (95% CI 4.7-18.6) for colon tumors and 2.0 months (95% CI 1.8-2.4) for liver/biliary tumors. On univariate analysis, female gender, higher tumor grade, larger tumor size, liver/biliary origin and urinary tract origin were associated with a worse survival while surgery, radiation and systemic chemotherapy use were associated with improved OS (all p<0.01). On multivariate analysis, higher tumor grade, larger tumor size, liver/biliary and urinary tract origin were associated with a worse outcome while surgery, radiation and systemic chemotherapy use were associated with improved OS (all p<0.001). Conclusions: Visceral angiosarcoma are rare tumors with a poor outcome. Liver/biliary origin, higher tumor grade and larger tumor size are associated with a worse outcome while peritoneal/retroperitoneal tumors have a better outcome. Consideration for multimodality therapy for this aggressive pathology should be considered.

P347

How to Obtain Adequate Surgical Margins for Dermatofibrosarcoma Protuberans: A Multicenter Analysis E. Huis in 't Veld,[1]* F. van Coevorden,[1] D. Grunhagen,[2] m. smith,[3] A. van Akkooi,[1] M. Wouters,[1] A. Hayes,[3] C. Verhoef,[2] D. Strauss,[3] W.J. van Houdt.[1] *1. Netherlands Cancer Institute, Amsterdam, Netherlands; 2. Erasmus MC, Rotterdam, Netherlands; 3. Royal Marsden NHS, London, United Kingdom.*

Background: Dermatofibrosarcoma protuberans (DFSP) is a rare locally aggressive soft tissue sarcoma. Pathological tumor free margins are associated with lower recurrence rates in patients with DFSP. The objective of this study is to evaluate the most optimal strategy for obtaining tumor free margins. Material & Methods: Patients with DFSP treated between 1991 and 2016 at three tertiary centers were included. Patient- and tumour characteristics were obtained from a prospectively held database and patient files. Patient with missing data regarding margins were excluded. Results: A total of 279 patients with a median age of 39 (range, 5-87) years and a median follow-up of 48 (Interquartile range, 17-93) months were included. Of these, 79 patients (28.3%) underwent primary excision at the tertiary center, in which complete resection within the first procedure was achieved in 86.1% of the cases. A total of 149 patients presented for re-excision of primary DFSP (53.4%) of which 79.9% achieved clear pathological margins after a re-excision. Furthermore, 51 patients (18.3%) were referred for recurrent disease or follow-up. From all patients with primary DFSP, radical resection was not obtained in 6.3% even after multiple resections. Subdividing surgical margins in the following three groups; 1-2cm, 2-3cm and >3cm, the percentages of radical resection were 17.7%, 67.7%, and 95% respectively. A total of 60 patients needed a flap reconstruction (21.5%). The need for a reconstruction did not differ between the various surgical resection margins (p=0.182). A substantial discrepancy in surgical intra-operative macroscopic- and pathological margins was found with a median difference of 20 (range, -10 – 50) mm (figure 1). Of all patients with R1 resections, 39.5% developed a recurrence, which was significantly higher than the recurrence rate for R0 resections (3.4%)(p<0.001). Conclusion: The current study showed a vast discrepancy between surgical macroscopic- and actual pathological margins. Therefore a wide surgical margin is required to avoid irradical DFSP resection, where the width of the margin should be balanced against the need for reconstructions and surgical morbidity.

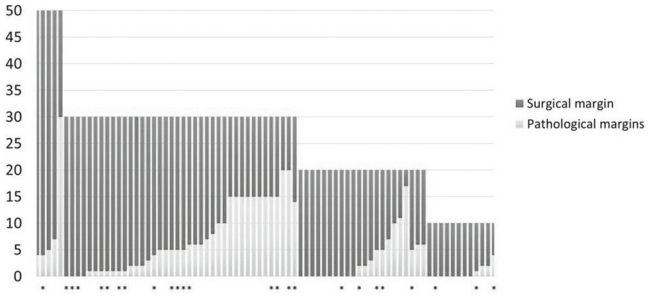


Figure 1. Analyses of differences in surgical margin (red) and pathological margin (blue). * resections margins of recurrent disease.

P348

Primary Site Surgery is Associated with Improved Survival in Metastatic Soft Tissue Sarcoma of the Extremity A.A. Gingrich,* S.B. Bateni, S. Thorpe, L. Jones, A.R. Kirane, A.M. Monjazeb, M.A. Darrow, R.J. Bold, R.L. Randall, R.J. Canter. *Department of Surgery, University of California Davis Cancer Center, Sacramento, CA.*

Background: Systemic therapy is viewed as the cornerstone of therapy for metastatic soft tissue sarcoma (STS) of the extremity, with a limited role for local surgical therapy. The objective of this study was to assess the impact of surgery on survival outcomes among patients with stage IV extremity STS. Methods: Utilizing the National Cancer Database, we identified 12,848 patients with extremity STS presenting with synchronous metastases from 2004-2015. Inclusion criteria included age ≥ 18, tissue diagnosis of extremity STS based on ICD-O-3 coding, and complete staging data. Patients were grouped by treatment modality (chemotherapy, radiotherapy (RT), surgery). Survival between groups was compared using the Kaplan Meier method and log rank test. Cox proportional hazard analysis was conducted to identify multivariate predictors of survival. Results: The mean age of the cohort was 57.6 years and 55.7% were male. The most common histologies were leiomyosarcoma (18.3%) and vascular sarcomas (7.8%). 59.0% of patients presented with lung metastases. 23.6% of patients had chemotherapy only, 11.4% primary site surgery only, and 8.3% RT only. 13.4% received surgery and chemotherapy, 10.6% chemotherapy and RT, 6.4% surgery and RT, and 7.7% tri-modality therapy. 18.5% received no treatment. Median survival for the entire cohort was 9.5 months, ranging from 9.1 – 10.9 months by year of diagnosis ($p > 0.05$). Survival for patients having primary site surgery was 15.2 months ($p < 0.001$). On multivariate analysis, surgery, RT, and chemotherapy were independently associated with significantly improved survival ($p < 0.05$). Among patients receiving chemotherapy, surgical resection of the primary site remained associated with improved survival ($p = 0.009$). Trends analysis revealed that the use of chemotherapy increased over the study period, while the use of surgery and RT decreased. Conclusions: Among patients with stage IV extremity STS, surgical resection of the primary site is associated with improved survival, especially in the context of multimodality therapy. Further evaluation of the potential for surgery to benefit patients with stage IV extremity STS appears warranted.

Table 1: Cox Proportional Hazard Analysis, All Patients

Variable*	Hazard Ratio	Standard Error	P-value	95% Confidence Interval	
Age < 65 years old	Referent				
Age ≥ 65 years old	1.2286	0.0937	0.007	1.0581	1.4266
Sex: Male	Referent				
Sex: Female	1.0153	0.0726	0.832	0.8825	1.1680
Facility Type: Community Center	Referent				
Facility Type: Comprehensive Cancer Center	0.9268	0.1339	0.599	0.6983	1.2301
Facility Type: Academic/Research	0.9412	0.1290	0.659	0.7195	1.2313
Facility Type: Integrated Network	1.0376	0.1718	0.823	0.7501	1.4353
Charlson-Deyo Score = 0	Referent				
Charlson-Deyo Score = 1	1.0626	0.0993	0.516	0.8848	1.2762
Charlson-Deyo Score = 2	1.0713	0.2224	0.740	0.7132	1.6093
Charlson-Deyo Score = 3	0.9211	0.3663	0.836	0.4225	2.0081
Grade: Well-differentiated	Referent				
Grade: Moderately differentiated	1.4363	0.3527	0.140	0.8877	2.3240
Grade: Poorly differentiated	1.4142	0.3070	0.112	0.9222	2.1622
Grade: Undifferentiated/anaplastic	1.4691	0.3257	0.083	0.9513	2.2687
Tumor Size: 0-4.99 cm	Referent				
Tumor Size: 5-9.99 cm	1.2880	0.1514	0.031	1.0229	1.6218
Tumor Size: 10-14.99 cm	1.1296	0.1446	0.341	0.8789	1.4518
Tumor Size: ≥ 15.00 cm	1.1034	0.1366	0.426	0.8658	1.4063
Surgery of Primary Site: No	Referent				
Surgery of Primary Site: Yes	0.7958	0.0618	0.003	0.6835	0.9265
Radiation Therapy: No	Referent				
Radiation Therapy: Yes	0.7885	0.0615	0.002	0.6767	0.9187
Chemotherapy: No	Referent				
Chemotherapy: Yes	0.8365	0.0646	0.021	0.7191	0.9732

*Histology, race and metastatic site also included in model, omitted for space. P > 0.05 for these variables.

P349

Cancer Risk in Patients with Neurofibromatosis Type 1 J.P. Landry,* K.L. Schertz, Y. Chiang, E.Z. Keung, B. Feig, K. Hunt, C. Roland, J. Cormier, A.E. Lazar, J.M. Slopis, I.E. McCutcheon, K.E. Torres. *The University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Neurofibromatosis type 1 (NF1) is a genetic and complex disorder with an increased susceptibility to develop both benign and malignant tumors. NF1 is associated with an increased risk of malignancies, both nervous-system and non-nervous system related. This study aimed to evaluate the prevalence, management, and outcome of malignancies in this population. Methods: Patients who met the clinical diagnostic criteria determined by the NIH consensus for NF1 and were evaluated at our institution from 2000-2015 were included (n=677). NF1-related clinical features, development of neoplasms, patient and tumor characteristics, treatments, and outcomes were analyzed. Prevalence, age at diagnosis, and survival in the NF1 cohort were compared to the published SEER Cancer Statistics Review 1975-2015 and Seer Participants Database. Results: Median follow-up was 5.8 years (range, 0.1-22.5 years). Thirty-seven percent (n=248) of patients developed malignancies of which 35 individuals (5%) developed multiple neoplasms. The most common malignancy developed by NF1 patients was glioma (n=116, 17.1%) followed by MPNST (n=83, 12.3%). One-hundred patients (14.8%) developed low-grade gliomas and 16 (2.4%) patients were diagnosed with high-grade gliomas. NF1 patients developed MPNST and high-grade gliomas at a younger age (median age = 29.5 and 25, respectively) compared to the general population (median age = 46 and 58, respectively). Patients with MPNST or high-grade glioma had significantly worse survival (5-year DSS = 43% and 33%, respectively) than NF1 patients with other malignancies ($p < 0.001$). NF1 patients developed other malignancies including neuroendocrine tumors (n=16, 2.4%), breast cancer (n=17, 2.5%), and soft tissue sarcomas (n=14, 2.1%) such as GIST, liposarcoma, leiomyosarcoma and undifferentiated pleomorphic sarcoma (UPS). NF1 patients develop MPNST, GIST, liposarcomas, rhabdomyosarcomas, UPS, gliomas, breast cancer, and melanoma at a younger age. Conclusions: Significant causes of death in NF1 patients are high-grade glioma and MPNST. Patients with NF1 develop most malignancies at a younger age. This information is useful for NF1 patient anticipatory guidance, prognosis, counseling, and follow-up.

P350

Immunohistochemical Markers Associated with Decreased Survival in Soft Tissue Sarcomas E.A. O'Halloran,* M. Hill, S. Murthy, F. Lambreton, S. Reddy, J. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Soft tissue sarcomas are a rare, heterogenous group of tumors composed of several distinct clinicopathologic entities. Immunohistochemical (IHC) and molecular profiling are often used to differentiate tumor types. Desmin, SMA, and HHF35 are all markers used to identify smooth and skeletal muscle when characterizing these lesions. We aim to analyze the patterns of these markers and determine their effects on survival and recurrence in our patient population. Methods: A retrospective chart review was conducted to identify patients with soft tissue sarcomas at a NCI designated cancer center between 2003 and 2017. Demographics, clinicopathologic characteristics, and pathology reports were collected. Primary endpoints were overall (OS) and disease free survival (DFS), with secondary endpoints related to recurrence. Groups were compared using Cox proportional hazard and multivariable logistic regression models. Results: Two hundred eight patients with soft tissue sarcomas of the extremities or retroperitoneum were studied, 55% of whom were female, with a median age of 59 years. IHC and molecular profiling were reported for 85 patients; 54 (63.5%) had tumors positive for desmin, SMA, or HHF35. Patients with any of these markers had decreased OS compared to the rest of the cohort, with an associated hazard ratio (HR) of 1.9 (95% CI 1.3-2.8, p=0.001). They also had a decreased DFS, with HR of 2.22 (95% CI 1.3-3.8, p=0.004), which persisted after controlling for pathologic stage of disease (HR 1.9, 95% CI 1.0-3.4, p=0.046). Additionally, patients with these markers were more likely to have a higher pathologic stage (OR 1.7, 95% CI 1.2-2.4, p=0.006). There was no difference between the groups in terms of frequency of recurrence (46.2% with these markers vs 60.1% without, p = 0.079), but patients with any of these tumor markers had greater odds of nodal or distant metastases as their site of primary recurrence (OR 3.3, 95% CI 1.2-9.7, p=0.027). Conclusions: Soft tissue sarcomas expressing the smooth and skeletal muscle markers desmin, SMA, and HHF35 were associated with higher pathologic stage, worse overall and disease free survival, and increased distant metastases.

P351

Outcomes Following Resection of Primary and Recurrent Retroperitoneal Liposarcoma E.A. Elder,* E.M. Gabriel, S.P. Bagaria. *Mayo Clinic Florida, Jacksonville, FL.*

INTRODUCTION Resection of primary and recurrent well-differentiated (WD) and dedifferentiated (DD) retroperitoneal liposarcoma (RPLPS) often requires complex resection and is associated with a high rate of local recurrence (LR). There is controversy surrounding the management of LR. We investigated the oncologic and post-operative outcomes following surgical resection of primary and recurrent RPLPS. METHODS Retrospective review of an institutional cancer registry identified patients who underwent surgical resection of a RPLS from 2000-2010. Data on oncologic and post-operative outcomes were collected. RESULTS A total of 99 patients underwent resection of primary RPLPS. The median age was 63 years, and 34 (34%) were female. There were 64 (65%) patients diagnosed with primary DDLPS and 35 (35%) diagnosed with WDLPS. R0/R1 resection was achieved in 87 (88%) patients. Approximately one-half of all patients (n=51) developed a LR (median time to first LR = 21 months). A LR was more likely to occur following resection of a primary DDLPS than WDLPS (61% vs. 34%, p=0.012). Resection of 1st LR was performed in 35 (69%) cases. Multifocality was more likely to be present with LR when compared to primary presentation (31% vs. 12%, p<0.01). R0/R1 resection was achieved in 33 (94%) 1st LR cases. A 2nd LR developed in 23 (66%) of patients (median time to second LR = 14 months) of which 16 (70%) underwent surgical resection. A third and fourth LR developed in 11 (48%) and 3 (27%) patients. Clavien-Dindo grade ≥ 3 adverse events and postoperative length of stay were similar between those who underwent resection of a primary and the 1st LR RPLPS (20% vs. 17%, p=0.26 and 9.4 days vs. 8.3 days, p=0.43). The transformation rate from WDLPS to DDLPS in subsequent LRs was 33%. The distant metastasis rate for all patients who underwent primary resection was 20%; the distant metastasis rate for patients with at least one LR was 27%. CONCLUSION Local recurrence occurs in approximately half of all patients treated for RPLPS and is more common following resection of DDLPS. Though a second LR is common following resection of a first LR, surgical morbidity is acceptable when compared to resection for primary disease.

	Primary RPLPS	1st Recurrence	2nd Recurrence
	Number (%)	Number (%)	Number (%)
N	99	51	23
Age, median years	63	60	59
Female	34 (34)	13 (26)	3 (13)
Follow up, median months	65	26	24
Time to recurrence, median months	N/A	21	14
Mean Charlson comorbidity score	4.3	4.6	4.7
Histologic subtype			
DDLPS	64 (65)	21 (41)	15 (65)
WDLPS	35 (35)	17 (33)	3 (13)
Unknown	0	13 (25)	5 (22)
Multifocal disease present*	12 (12)	11 (31)	5 (31)
Surgical resection			
Yes	99 (100)	35 (69)	16 (70)
Observed	0	16 (31)	7 (30)
Tumor size, median cm	21.5	8.5	4.9
Margins*			
R0/R1	87 (88)	33 (94)	14 (87)
R2	12 (12)	2 (6)	2 (13)
XRT administered	38 (38)	14 (28)	4 (17)
Clavian Dindo grade >=3	20 (20)	6 (17)	3 (19)
Length of stay, median days*	7	7	5
Median number organs resected*	1	0	0
Local recurrence**			
Yes	51 (52)	23 (70)	11 (79)
No	48 (48)	10 (30)	3 (21)
Distant metastasis			
Yes	20 (20)	14 (27)	4 (17)
No	79 (80)	37 (73)	19 (83)

*Percentage based on the number of patients who underwent surgical resection. **Percentage based on the number of patients who underwent R0/R1 resection.
RPLPS= retroperitoneal liposarcoma, DDLPS= dedifferentiated liposarcoma, WDLPS= well differentiated liposarcoma, XRT= radiation treatment

P352

Trends in Practice Patterns and Outcomes: A Decade of Sarcoma Care in the United States Y. Song,[1]* B. Ecker,[1] L. Maggino,[2] R.E. Roses,[1] R.P. DeMatteo,[1] D. Fraker,[1] G. Karakousis.[1] *1. Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA; 2. University of Verona, Verona, Italy.*

Background: Soft tissue sarcomas (STS) are a heterogeneous group of mesenchymal tumors for which there is significant variation in management across centers. Recent changes in practice patterns for STS with respect to centralization of care and the utilization and sequencing of multimodality therapy with impact on associated outcomes have not been well characterized at a national level. Methods: Adult patients with non-cardiac STS were identified in the soft tissue participant use file of the National Cancer Database (2005-2014). Diagnosis year was categorized into two eras (2005-2009 vs. 2010-2014). Chi-square test was used to analyze differences in treatment strategies. Overall survival (OS) was compared by Kaplan-Meier estimates. Factors associated with OS were determined using multivariate Cox proportional hazards model. Results: Of 69,162 patients, 31,680 (46%) were diagnosed in 2005-2009 and 37,482 (54%) were diagnosed in 2010-2014. There was a slight decrease in the rate of surgical resection (80.1% vs. 79.2%, P<0.001), but no change in the rate of amputation (3.6% vs. 3.5%, P=0.47). Surgical patients were more likely to be treated at an academic institution (41.6% vs. 45.5%, P<0.001). There was no difference in the rate of administration of radiotherapy (57.9% vs. 57.7%, P=0.53) or chemotherapy (73.4% vs. 73.7%, P=0.54). However, when utilized, there was an increase in neoadjuvant sequencing for both treatment modalities (radiotherapy: 8.4% vs. 11.2%, P<0.001; chemotherapy: 4.9% vs. 6.0%, P<0.001). Patients diagnosed in 2010-2014 had improved OS compared to those in 2005-2009 (5-year OS 55.5% vs. 56.2%, P=0.02), but this difference was not significant when adjusted for other prognostic factors in multivariate Cox regression analysis (P=0.054). Conclusions: Despite an increasing referral to academic centers and utilization of neoadjuvant therapy over the past decade, there has been lack of significant improvement in OS for patients diagnosed with STS overall, highlighting the need for rapid development of novel molecular or immunologic therapies.

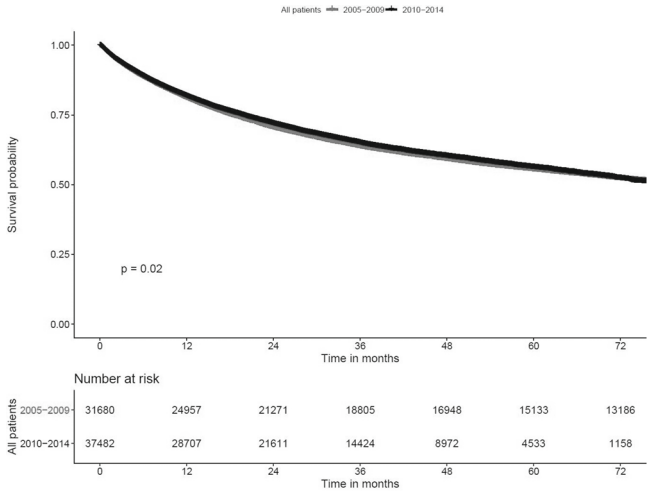


Figure 1. Kaplan-Maier estimates of overall survival in patients newly diagnosed with soft tissue sarcoma by diagnosis period

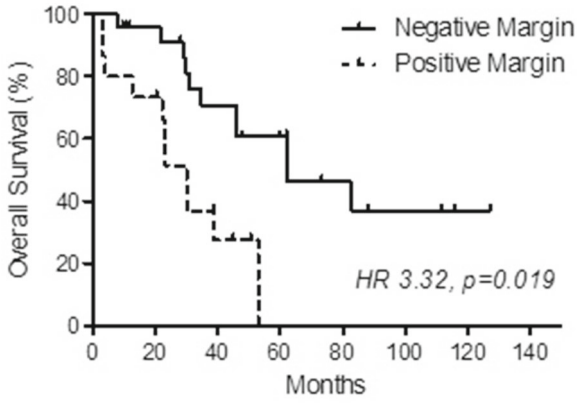


Figure 1. Kaplan-Meier overall survival plot of patients with extrapleural solitary fibrous tumors.

P353

In Extrapleural Solitary Fibrous Tumor Surgical Margins Matter

L.P. Suarez-Kelly,[1]* J.H. Howard,[1] T.B. Hughes,[1] R.D. Shelby,[1] P.Y. Yu,[1] C. Ethun,[2] T. Tran,[3] G. Poultsides,[3] J. Tseng,[4] K. Roggin,[4] K. Chouliaras,[5] K.I. Votanopoulos,[5] B.A. Krasnick,[6] R. Fields,[6] T. Gamblin,[7] M. Bedi,[7] A. Salem,[8] S. Weber,[8] R. Pollock,[1] K. Cardona,[2] V. Grignol.[1] *1. Surgery, The Ohio State University Wexner Medical Center, Columbus, OH; 2. Emory University School Of Medicine, Atlanta, GA; 3. Stanford University, Palo Alto, CA; 4. University of Chicago Medicine, Chicago, IL; 5. Wake Forest University School Of Medicine, Winston-Salem, NC; 6. Washington University School of Medicine, St. Louis, MO; 7. Medical College of Wisconsin, Milwaukee, WI; 8. Medical College Of Wisconsin, Madison, WI.*

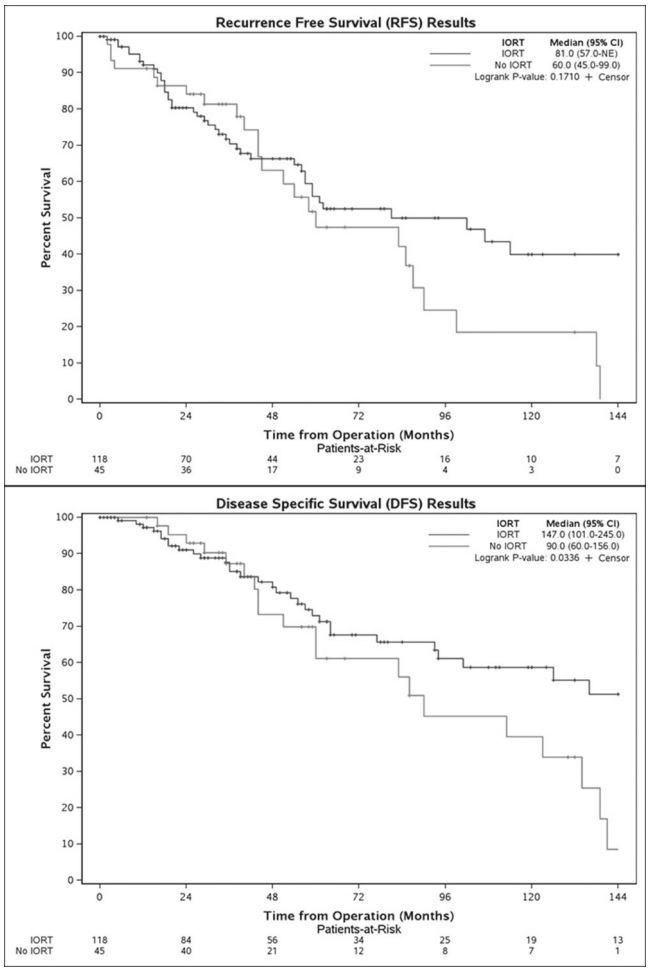
Background: Solitary fibrous tumors (SFT) are rare mesenchymal tumors that can arise in any anatomical location. Although SFT is often considered an indolent neoplasm, studies report aggressive and malignant behavior. This study evaluated the outcomes of surgically treated extrapleural SFT (ESFT) to determine factors associated with aggressive biology. Methods: A retrospective review of patients with resected ESFT between 2000-2016 at 8 US institutions was performed. Those with metastatic disease, meningeal, or head and neck tumors were excluded. Statistical analyses were performed using two-sample t-tests, chi-square tests, Kaplan–Meier curves and Cox proportional hazards analyses. Results: 40 patients had ESFT resected from either abdominal/retroperitoneal (n=17, 43%) or extremity/truncal (n=23, 57%) sites. At initial presentation, 25 patients had primary tumors and 15 had locally recurrent disease. Mean tumor size was 10.5 cm, 25% had multifocal disease, 48% were high-grade, 20% had ≥10 mitoses/HPF, 40% had tumor necrosis and 40% had microscopically positive margins. Mean follow-up was 41 months (mos). 23 patients (58%) developed recurrent disease and 22 (55%) died of disease with median recurrence free survival (RFS) of 30 mos and overall survival (OS) of 46 mos. Comparing resected recurrent disease to those with resected primary tumors, 67% vs 0% had multifocal disease ($p<0.001$), median RFS was 6 mos vs 50 mos ($p<0.001$) and median OS was 31 mos vs 62 mos ($p=0.004$), respectively, with no difference in tumor size, grade, mitosis, necrosis or margin status. On multivariate analysis, only recurrent disease at presentation was associated with subsequent recurrences (HR 5.16, $p=0.024$) and positive surgical margin was associated with death (HR 3.32, $p=0.019$). Median OS was 23 mos for positive margins vs 62 mos for those with a negative margin. Conclusion: Recurrence of ESFT is often multifocal and represents aggressive biology with high rates of disease related death. Survival for this disease appears to be impacted by negative margin resection of the primary tumor. For resected recurrent tumors, locoregional control with surgical resection may be poor while still attaining modest survival rates.

P354

Impact of Intraoperative Radiation Therapy on Local Recurrence in the Treatment of Retroperitoneal Sarcomas

T. Weidner,[1]* C. Stucky,[1] R. Gray,[1] J. Ashman,[1] M. Neville,[1] R. Butterfield III,[1] I. Petersen,[2] E.M. Gabriel,[3] L. Gunderson,[1] L. Yohanathan,[2] S.P. Bagaria,[3] T.E. Grotz.[2] *1. Mayo Clinic Arizona, Phoenix, AZ; 2. Mayo Clinic Rochester, Rochester, MN; 3. Mayo Clinic Florida, Jacksonville, FL.*

Background. Radical resection with radiation therapy (Surg-RT) is frequently used to treat retroperitoneal sarcoma (RPS) with a reported reduction in local recurrence (LR) rates. However, the benefits of using intraoperative radiation (IORT) as an adjunct to this combination are not well-defined. The purpose of this study was to examine the oncologic outcomes of Surg-RT and IORT. Methods. Retrospective chart review was performed of 228 patients with RPS undergoing R0/R1 resections across 3 institutional sites from 1998 to 2017. Univariate and multivariate analyses were performed to determine predictors of LR as were Kaplan Meier estimates for local recurrence-free (LRFS), disease-free (DFS) and overall survival (OS). IORT was directed at closest margin as indicated by the surgeon. Results. 160 patients (71%) were treated with Surg-RT. 63% of patients had high grade tumors and the median follow up was 44 months. Patients treated with Surg-RT were more likely to have recurrent disease at presentation to our institution ($p<0.0001$), smaller tumors ($p=0.003$), more organs resected ($p=0.003$) and IORT ($p<0.0001$). On univariate analysis, factors associated with LR included recurrent disease, dedifferentiated histology, dose of external beam RT and omission of RT. LR was also associated with decreased OS ($p=0.0001$). On multivariate analysis, dedifferentiated histology ($p=0.002$) was the only predictor of LR. A subset analysis examined association of LR and site of IORT. Of 118 IORT patients, 34 had LR with 47% outside IORT field and 53% within IORT field. LR was away from the pathologic closest margin (PCM) and IORT site in 10 patients, while 6 patients had LR at IORT/PCM site. The median LRFS was improved by 21 months for IORT vs. RT alone ($p=0.17$) and DFS was significantly improved with IORT vs. RT alone ($p=0.03$) (Figure 1). Conclusion. Use of Surg-RT and IORT is associated with a promising improvement in LRFS and DFS. Since LR is significantly associated with OS, aggressive multi-modality therapy to improve local control, particularly in high grade RPS, is warranted. Improvement in margin assessment and reporting may allow for more appropriately directed IORT.



P355

Epithelioid Sarcoma: A Nationwide Study of a Rare Tumor

A. Teng,[1]* S. Chang,[2] M. Goldfarb,[1] T.D. Fischer.[1] *1. John Wayne Cancer Institute, Santa Monica, CA; 2. Providence St. Vincent Medical Center, Portland, OR.*

Background Epithelioid sarcoma (ES) is a rare soft-tissue tumor described mainly in single institution case series. This study describes the largest collection of ESs and evaluates factors that impact survival utilizing a national database. Methods All patients diagnosed with ES from 2004 to 2015 were identified in the National Cancer Database (NCDB). Demographic, tumor, and treatment characteristics were examined; Kaplan-Meier and Cox proportional hazard models evaluated overall survival (OS). Results In 1106 patients, mean age at diagnosis was 44.9 years (78% ages 15-69) with ES more prevalent in males (61.6%) and White non-Hispanics (69.6%). Mean tumor size was 7.0 cm with the trunk (35.6%) being the most common primary site, followed by the upper and lower extremities. Regional lymph nodes were examined in 29% of patients of which 1/3 were positive, though overall known N1 disease was 11.7% and 13.1% presented with metastatic disease. Treatment was varied with surgery (79.7%), radiation (41.7%) and chemotherapy (31.1%). Median OS was 6.0 years with 5-year OS rates of 72.8%, 73%, 37.4%, and 6.8% for stages I-IV, respectively. Upper extremity lesions had superior 5-year OS (70.2%) compared to lower extremity (54.6%), truncal (41.9%), and head/neck tumors (34.3%). Age (40-69 HR 3.01; CI 1.38-6.57 and >70 HR 4.8; CI 2.06-11.2), tumor size (5-10 cm HR 1.64; CI 1.14-2.35 and >15 cm HR 3.01; CI 1.89-4.77), lymph node positivity (HR 1.74; CI 1.02-2.96), grade III/IV (HR 2.14; CI 1.31-3.5), and margin status (HR 2.04; CI 1.43-2.93) all significantly decreased OS whereas surgical resection (HR 0.53; CI 0.28-0.98) and receipt of radiation (HR 0.73; CI 0.55-0.95) were associated with improving OS. Conclusion This is the largest cohort of patients with ES that has been described to date. Although older patients and those with more aggressive tumor characteristics had a decreased OS, patients able to proceed with surgical resection and radiation may have improved survival outcomes.

P357

A Propensity-Matched Analysis of Open versus Minimally Invasive Transthoracic Oncologic Esophagectomy Using NSQIP Database

S.A. Naffouje,* G.I. Salti. *General Surgery, University of Illinois Hospital and Health Sciences System, Chicago, IL.*

Objective: to compare the surgical outcomes of open transthoracic esophagectomy (OTTE) minimally invasive transthoracic esophagectomy (MITTE) when performed for oncologic indications. Methods: The NSQIP esophagectomy-targeted database was used for the analysis. Only patients who underwent elective TTE for oncologic indications were included. Hybrid and hand-assisted techniques were excluded. We matched the patients per a propensity score for the likelihood of receiving OTTE vs. MITTE, which was based on a group of perioperative factors that would affect the surgical outcomes but are not dependent on the approach itself. The primary goal was to compare the short-term outcomes of OTTE vs. MITTE. Secondary goal was to compare laparoscopic vs. robotic approach. Results: 1,032 cases were reported, 308 of which met the inclusion criteria. We were able to match 109 patients from each group based on nearest-neighbor method of the propensity score with a caliper width of 0.1SD. OTTE had a significantly shorter mean operative time (329 vs. 414 minutes; p<0.001), but higher rates of superficial wound infections (12.8% vs. 2.8%; p=0.010), and a significantly longer median hospital stay (13 vs. 10 days; p=0.008). Otherwise, no difference was noted in intraoperative lymphadenectomy, postoperative complications including anastomotic leak, adequacy of oncologic resection, mortality, or readmission rates. Similarly, a 3:1 propensity match analysis was conducted to compare laparoscopic vs. robotic TTE. All outcomes were similar except in reported mediastinal lymphadenectomy which was significantly higher in robotic TTE (25.0% vs. 54.2%; p=0.009). Conclusion: MITTE is comparable in short-terms outcomes to OTTE and provides a shorter hospitalization

P358

Timing After Neoadjuvant Therapy Predicts Mortality in Patients Undergoing Esophagectomy

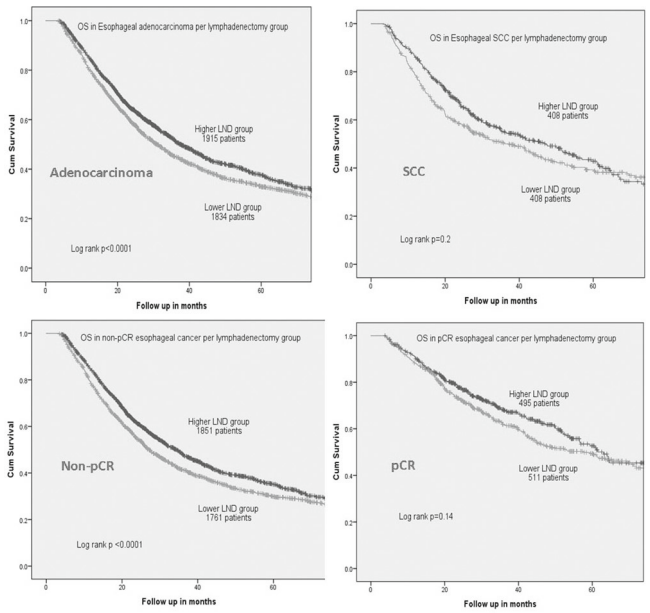
T. Maramara,[1] J. Huston,[2] R. Shridhar,[3] K. Meredith.[1]* *1. Surgical Oncology, Florida State University/ Sarasota, Sarasota, FL; 2. Sarasota Memorial Institute for Cancer Care, Sarasota, FL; 3. Florida Hospital Cancer Institute, Orlando, FL.*

Purpose: Neoadjuvant therapy (NT) prior to esophagectomy has dramatically improved survival in patients with esophageal cancer. Currently surgeons will allow 6-12 weeks after NT prior to esophagectomy. Given that complete pathologic response (pCR) correlates to an improvement in survival, some have advocated a longer interval should be entertained to increase the pathologic response. We sought to examine the impact of NT-surgery interval on outcomes. Methods: Utilizing the National Cancer Database we identified patients with esophageal cancer who underwent NT followed by esophagectomy. Patients were divided into 4 time intervals: <6 wks, 6-12 wks, 3-6 mo, and >6 mo. Mann-Whitney U, Kruskal Wallis, and Pearson's Chi-square test were used as appropriate. Survival analyses were performed using the Kaplan-Meier method and p<0.05 was considered significant. Results: We identified 9256 patients who received NT followed by esophagectomy. There were 8053 (87%) adenocarcinomas and N=1203 (13%) squamous cell carcinomas. 7858 (84.9%) were male and 1398 (15.1%) female with a median age of 62 (24-88). R0 resections decreased as the NT-Surgery interval increased: <6 wks, 6-12 wks, 2-6 mos, and >6 mos at 93%, 94.1%, 94.1%, and 86.2% p=0.004. Additionally, the median lymph nodes harvested decreased as timing increased: 12, 12, 10, and 9, p<0.001 and the median nodes positive decreased as timing increased 1.5, 1.3, 1.1, and 2.4, p=0.01. The complete response rates increased as timing increased 15.5%, 20.1%, 22.7%, and 25.8%, p<0.001. However, this improvement in pCR did not translate into an increase in median survival: <6 wks 40.9 mos, 6-12 weeks 38.5 mos, 3-6 mos 34.8 mos, and >6 mos 39.8 mos of survival, p=0.94. 90-day mortality increased as the timing from neoadjuvant therapy increased: 6.4%, 7.9%, 9.4%, and 16.0%, respectively p=0.001. Conclusion: Our data demonstrates that patients who have a prolonged NT-esophagectomy interval will have a substantial increase in 90-day mortality. While there was an increase in pathologic complete response rates, this did not translate into an improvement in survival. The current recommendations of a NT-surgery timing of 6-12 weeks should remain.

P359

The Value of Lymphadenectomy in Esophageal Cancer After Neoadjuvant Chemoradiation B. Azab,[2]* F. Macedo,[1] O. Picado,[1] C. Ripat,[1] D. Franceschi,[1] A.S. Livingstone,[1] D. Yakoub.[1] *1. University of Miami, Yorktown, VA; 2. Sentara Healthcare, Hampton, VA.*

Background: There are conflicting reports on the value of the extent of post neoadjuvant chemoradiation (NCRT) lymphadenectomy (LND) in locally advanced esophageal adenocarcinoma (E-ADC) and squamous cell carcinoma (E-SCC). We sought to study the impact of LND variables [positive and total lymph node (LN) number and LN ratio (LNR)]on oncological outcomes in these patients. Methods: The National Cancer Data Base 2004-2014 was queried for patients with NCRT followed by esophagectomy. The median examined LN number was used to divide the patients into a higher (>12) and lower (≤12) LND groups. The primary outcome was overall survival (OS) and secondary outcomes were 30- and 90-day postoperative mortality. Results: A total 4708 patients were included. The median of positive, negative LN, and LNR were and (0, 11, 0%). The median and 5-year OS for higher LND group were superior to the lower LND group (39 vs. 32 months, 38% vs. 34%), p<0.0001. OS was not significantly different among E-SCC subset or among those who achieved pathological complete response (pCR). The higher LND group had better 30- and 90-day postoperative mortality rates (61/2335=2.6%, 141/2308=6.1%) than lower LND group (86/2262=3.8%, 184/2251=8.2%), p=0.01 and 0.001, respectively. In multivariate Cox regression analysis, higher LND group (HR 0.88, 95% CI 0.81-0.96, p=0.004) and LNR (per 10% increase: 1.11, 95% CI 1.09-1.13, p<0.0001) were significant predictor of OS. Conclusion: The LND (>12 examined LN) remains as a crucial treatment goal after NCRT with potential survival benefit, especially among E-ADC and those did not achieve pCR.

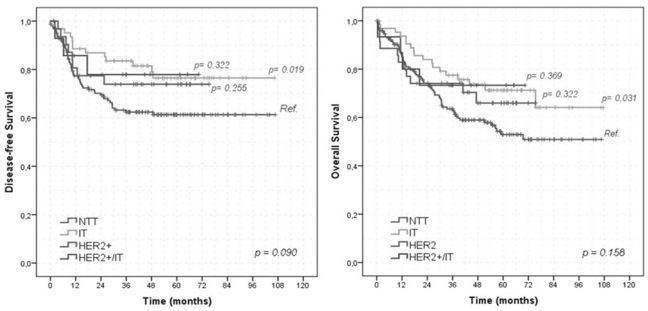


Overall survival among esophageal cancer patients according to their lymphadenectomy groups after neoadjuvant chemoradiation

P360

Clinicopathological Characteristics and Prognostic Value of HER2, PD-L1 and MSI Expression in Curative Resectable Gastric Cancer Patients M.A. Pereira,[1] M.F. Ramos,[1] S.F. Faraj,[1] A.R. Dias,[1] C.d. Cirqueira,[1] A.Z. Charruf,[1] F.S. Perrotta,[1]* E.S. Mello,[1] B. Zilberstein,[1] I. Cecconello,[1] O.K. Yagi,[1] V.A. Alves,[2] U.R. Junior.[1] *1. Instituto do Câncer do Estado de São Paulo, Hospital das Clínicas da Faculdade de Medicina de São Paulo (ICESP-HCFMUSP), Sao Paulo, Brazil; 2. Faculdade de Medicina da Universidade de São Paulo (FMUSP), Sao Paulo, Brazil.*

Introduction The importance of targeted therapy for gastric cancer (GC) has increased in recent years. The assessment of human epidermal growth factor receptor-2 (HER2) status is important for the selection and effectiveness of trastuzumab-targeted therapy, while immunotherapy with anti-PD1/PD-L1 is indicated for GC with microsatellite instability (MSI) or PD-L1 expression. However, the frequency of these profiles and its survival outcomes in Western GC remain unclear. The objective of this study was evaluate the frequency and clinicopathological characteristics of MSI, HER2 and PD-L1 expression in GC resected patients. Methods We retrospectively evaluated all GC patients who underwent gastrectomy with D2-lymphadenectomy from a prospective medical database. HER2, MSI status and PD-L1 expression were analyzed by immunohistochemistry (IHC) through tissue microarray technique. IHC-score of 2+/3+ was defined as HER2-positive group. MSI and/or PD-L1-positive GC constituted the immunotherapy group (IT). No patient was treated with targeted therapy. Results Among 284 enrolled patients, 50 (17.6%) were HER2+ and 79 (27.8%) MSI/PD-L1+. Fifteen CG presented both HER2+ and MSI/PD-L1 status. The remaining 155 (54.6%) cases were classified as non-targeting therapy (NTT) group. GCs HER2+ were predominant in men (p=0.019), well/moderately differentiated tumors (p=0.002) and intestinal Lauren type (p<0.001). Older age (p=0.016), pN0 (p=0.015), less advanced pTNM stage (p=0.023) were associated to IT GC. IT GC had longer disease-free survival (DFS), followed by HER2+/IT, HER2+ and NNT group. Similarly, HER2+/IT patients had better overall survival (OS) than IT, HER2+ and NTT groups. The DFS and OS of IT group were significantly better compared to NTT patients (p=0.019and p=0.031, respectively). There was no difference in DFS and OS for HER2+ compared to NTT group, (p=0.255and p=0.322, respectively). Conclusions Patients who may potentially benefit of known targeted therapy represent 45.4% of GC (17.6% and 27.8% for HER2 and IT, respectively). The IT group was associated to a better prognosis, while HER2+ had no significant survival impact.



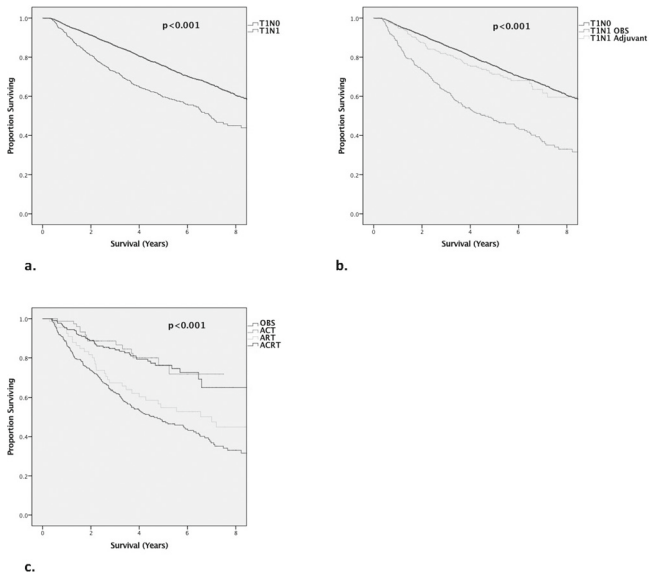
P361

Adjuvant Therapy is Associated with Improved Survival in pT1N1 Gastric Cancer in a Heterogeneous Western Patient Population C.A. Hester,* M. Augustine, J. Mansour, P.M. Polanco, A. Yopp, H. Zeh, S. Wang, M. Porembka. *University of Texas Southwestern, Dallas, TX.*

Background: Two recent studies from South Korea showed that adjuvant therapy was not associated with improved survival in pT1N1 disease in East Asian patients. We aimed to establish the prognostic utility of lymph node status in pT1N1 gastric cancers, determine the pattern of use of AT in pT1N1 disease, and compare survival amongst pT1N1 cancers stratified by the type of AT in a Western patient population. Methods: We identified patients with pT1N0 and pT1N1 gastric adenocarcinoma using the National Cancer Database (NCDB) from 2004-2012. Patient demographics, tumor characteristics, treatment regimens and overall survival (OS) were compared. Results: We identified 4,516 (86.6%) patients with resected pT1N0 and 696 (13.4%) pT1N1. pT1N1 tumors were larger (median size 2.5 cm vs 1.8 cm, p<0.001), more often poorly differentiated (56.2% vs 39.6%, p<0.001), and associated with higher median retrieved lymph nodes (RLN) (14 vs 12, p<0.001) compared to pT1N0. pT1N0 was associated with improved median OS of 9.9 years vs 6.9 years for pT1N1 (p<0.001). pN1 was independently associated with worse OS (HR 2.17 95%CI 1.84-2.56) as compared to pN0 and increased RLN was associated with improved OS (HR 0.73, 95%CI 0.65-0.83). Among pT1N1 patients, 330 (47.4%) underwent resection with observation (OBS), 77 (11.1%) received adjuvant chemotherapy (ACT), 68 (9.8%) received adjuvant radiation therapy (ART), and 221 (31.8%) received adjuvant chemoradiation therapy (ACRT). The median OS was 4.6 years for OBS, 7.0 years for ART, and was not reached for ACT and ACRT (p<0.001). Administration of ACT or ACRT was independently associated with improved OS (HR 0.37, 95%CI 0.22-0.65 and HR 0.40, 95%CI 0.28-0.57). Conclusion: pN1 was associated

with worse survival and RLN ≥ 15 was associated with improved survival in pT1 gastric cancer. The administration of ACT or ACRT was independently associated with improved survival in pN1 disease suggesting a valuable role in treatment of Western patients with pT1N1 gastric cancer.

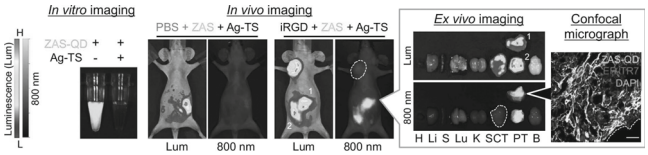
Figure 1: Overall survival for **a.** pT1N0 and pT1N1 gastric adenocarinoma, **b.** pT1N0, pT1N1 OBS, and pT1N1 Adjuvant gastric adenocarcinoma, **c.** pT1N1 gastric adenocarcinoma stratified by specific adjuvant therapy regimen



P362

Selective Detection of Peritoneal Tumors with Near-Infrared Quenchable Nanoprobes X. Liu,[1] G. Braun,[2] M. Qin,[3] M.D. Kluger,[1] A.M. Lowy,[3] K.N. Sugahara.[1]* *1. Surgery, Columbia University, New York, NY; 2. Sanford-Burnham-Prebys Medical Discovery Institute, La Jolla, CA; 3. University of California San Diego, La Jolla, CA.*

INTRODUCTION: Accurate detection of peritoneal tumors (PTs) is critical for effective cytoreduction prior to intraperitoneal (IP) chemotherapy. Here, we developed a system for highly specific in vivo PT detection. We used novel near-infrared (NIR) quantum dots (QDs) (Nat Commun 8:343, 2017) and the iRGD tumor-penetrating peptide (Science 328:1031-5, 2010; J Control Release 14:59-69, 2015). IP iRGD delivers co-injected QDs deep into PTs in a tumor-specific manner to produce NIR tumor signals, and the background from non-targeted QDs is quenched with a non-toxic chemical that exchanges cations with the QDs. METHODS: We synthesized ZAS-QDs using zinc (Zn), silver (Ag), selenide, and sulfide, and characterized the physical/chemical properties. We performed IP coinjection of the QDs and iRGD in mice bearing PTs created with luciferase-positive MKN45P human gastric cancer cells. The mice were subjected to whole body luminescent/NIR imaging, and tissues were analyzed by confocal microscopy. RESULTS: ZAS-QDs had a core diameter of 7 nm based on transmission electron microscopy. The photoluminescence emission peaked at 708 nm and extended beyond 800 nm making the QDs optimal for NIR imaging. The QDs lost their NIR signals upon treatment with a chemical made of Ag and thiosulfate (Ag-TS). Elemental analysis showed that the QDs received Ag from Ag-TS and lost Zn in exchange suggesting that cation exchange was involved in the QD quenching. IP injection of the QDs into PT mice led to a bright abdomen based on in vivo NIR imaging. Subsequent IP injection of Ag-TS caused effective quenching of the QDs that had not entered tissue. Minimal QD signal was noted in the PTs. When iRGD was coinjected, highly PT-specific NIR signals were obtained. The QDs entered the PTs in a circulation-independent manner as extraperitoneal tumors remained dark. Confocal microscopy showed strong QD signals extending from PT surfaces into the tumor interior. The QDs mainly colocalized with fibroblasts suggesting that they entered the PTs following the stroma. CONCLUSION: Tumor-penetrating etchable QDs allow specific in vivo PT detection and deserve further investigation as a companion to cytoreductive surgery.

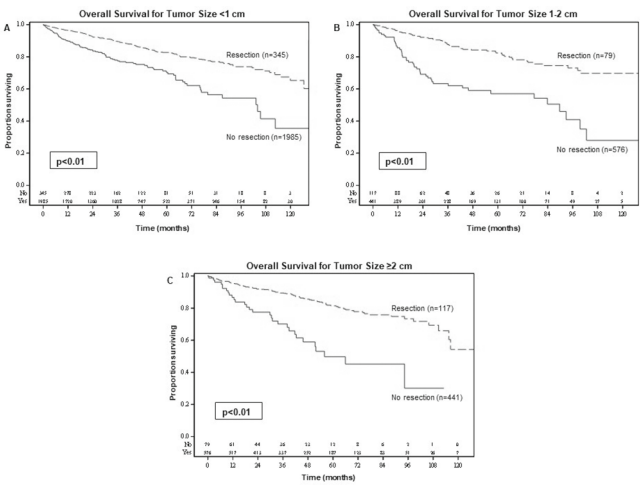


***In vitro* and *in vivo* quenching of ZAS-QDs with Ag-TS.** For the *in vivo* study, mice bearing MKN45P-luc PTs received IP iRGD or PBS with ZAS-QDs followed by Ag-TS. The iRGD group also had a subcutaneous tumor (SCT). *Ex vivo* images of iRGD group tissues and a confocal micrograph of one of the PTs from the group are shown. H, heart; Li, liver; S, spleen; Lu, lung; K, kidney; B, brain. Blue, DAPI; red, ER-TR7; green, ZAS-QDs; scale bar, 50 mm; dotted lines, SCT or PT surface.

P363

Duodenal Neuroendocrine Tumors: Somewhere Between the Pancreas and Small Bowel? A.C. Gamboa,[2]* Y. Liu,[1] M.Y. Zaidi,[2] R.M. Lee,[2] C. Staley,[2] D.A. Kooby,[2] M.C. Russell,[2] K. Cardona,[2] S. Maithel.[2] *1. Winship Cancer Institute, Emory University, Atlanta, Georgia; 2. Winship Cancer Institute, Emory University, Atlanta, GA.*

Background While sub-2cm pancreatic neuroendocrine tumors (NETs) are often observed given their indolent behavior, small bowel NETs are routinely resected with a regional lymphadenectomy regardless of size given their malignant potential. Considering this variability, our aim was to define the natural history of duodenal (D-NETs) and determine the role of resection. Secondary aim was to define factors associated with overall survival (OS) in pts who undergo resection. Methods Pts in the National Cancer Database (2004-14) diagnosed with non-metastatic, non-functional D-NETs were included. Local resection (LR) was defined as local excision, polypectomy, or excisional biopsy. Anatomic resection (AR) was defined as removal with radical surgery. Tumor size was divided into three categories (<1cm,1-2cm,2cm). Propensity score weighting analysis was used to create balanced cohorts between resection and no-resection pts; this was maintained in all size categories. Primary endpoint was OS. Results Of 5502pts, median age was 65yrs; 52% were male. Median f/u was 51mos. Median tumor size was 0.8cm. Resection was performed in 72%(n=3954) of which 61% were LR and 39% were AR. Lymph (LN) node resection was performed in 25% of pts, of which 44% had LN metastasis. 74% had negative margins. Resection and no-resection cohorts were propensity score weighted for age, gender, race, Charlson-Deyo score, and tumor grade, all of which were independently associated with OS on MV Cox regression analysis, thus creating balanced cohorts. Resection was associated with improved median OS compared to no-resection (MNR vs 94mos, p<0.01); this persisted for all three size categories (<1cm: MNR vs 194mos; 1-2cm: MNR vs 56mos; >2cm: MNR vs 90mos; all p<0.01; Fig1 A,B,C). Subset analysis of each size cohort who underwent resection showed that neither type of resection, LN retrieval, LN positivity, or margin status was associated with OS (all p>0.05). Conclusion All pts with non-metastatic non-functional D-NETs should be considered for resection regardless of tumor size. Given their lack of prognostic value, the type of resection and extent of LN retrieval should be tailored to the patient's clinical picture and safety profile.



P364

Adhesions are Derived from Hypoxia Responsive Mesothelin-Positive Mesothelial Cells and are Resolved via Targeted Therapies G.W. Krampitz,[1]* J. Tsai,[2] J.A. Norton,[3] I.L. Weissman,[3] Y. Rinkevich.[4] *1. Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX; 2. Brigham and Women's Hospital, Boston, MA; 3. Stanford University School of Medicine, Stanford, CA; 4. Helmholtz Zentrum München, Munich, Germany.*

Peritoneal adhesions are fibrous tissues that tether organs to one another or to the peritoneal wall and are a significant cause of post-surgical and infectious morbidity. The primary molecular chain of events leading to the initiation of adhesions has been elusive, chiefly due to the lack of identifiable cells of origin. Using clonal analysis and lineage tracing we identify cells of origin of the injured surface mesothelium that express podoplanin (PDPN) and up-regulate mesothelin (MSLN), as the primary instigators of peritoneal adhesions. A targeted anti-MSLN antibody mediated immunotherapy diminishes preformed adhesions, and combinations of anti-MSLN and anti-CD47 are even more effective. RNA sequencing and bioinformatics analyses on purified injured mesothelial cells, reveal aspects of the pathological mechanism of adhesion development and some of its candidate regulators. Specifically, we show that $PDPN^{+}MSLN^{+}$mesothelium responds to hypoxia through early upregulation of hypoxia inducible factor 1 alpha (HIF1α), a necessary regulator of adhesion development. Inhibition of HIF1α largely ameliorates the injury program in damaged mesothelial cells, and is sufficient to diminish adhesion severity. Analyses of human adhesion tissue suggest that similar pathways and surface markers contribute to human disease. These results highlight the critical role mesothelial cells play in adhesion formation and demonstrate multiple new and promising therapeutic approaches for treatments of adhesions.

P365

Teaching D2 Lymph Node Dissection for Gastric Cancer to Practicing Surgeons: An Evaluation of Knowledge and Educational Needs V. Palter,[1]* S. Brar,[1] H. Canaj,[2] V. Delibasic,[2] L. Davis,[2] N. Coburn.[1] *1. Surgery, University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Health Sciences Centre, Toronto, ON, Canada.*

Introduction: Recently, guidelines for the management of gastric cancer have changed, with national societies recommending a D2 lymph node dissection (LND) be performed rather than a D1. Our group has shown that less than 10% of gastrectomies for cancer occur with a D2 LND in Ontario, Canada. The objective of this study was to evaluate surgeons' knowledge and educational needs prior to participating in a course to learn D2 LND. Methods: We developed a two-day short course to provide practicing surgeons an update regarding current guidelines for the management of gastric cancer, and teach the technique for D2 LND. At the outset of the course, participants completed a survey designed to assess their knowledge regarding the management of gastric cancer, and determine their educational needs. Results: 23 surgeons participated in the course, and 20 completed the survey (response rate of 87%). The majority were in the early stages of their career (range <1year to 11years in practice). On average, participants performed 8 gastrectomies per year for gastric cancer (range 2-18). Despite this, only 50% of our participants 'strongly agreed' that they have a good understanding of when to perform a D2 LND. Moreover, only 5 (25%) 'strongly agreed' that they know how to perform a D2 LND. Our participants also had significant knowledge gaps relating to the management of patients with both early and advanced gastric cancer. Only 50% of participants said they found short courses helpful (11/20) and practice changing (10/20). Cited barriers to implementing techniques learnt in short courses into practice include issues related to lack of appropriate equipment, and lack of mentorship from experienced colleagues. Conclusions: These results highlight the learning needs of a group of surgeons attending a course for D2 LND. Although the attendees were mostly recent graduates, there was a gap between participants' knowledge and ability to perform a D2 LND, and what the current guidelines recommend. Finally, our results highlight the importance of ensuring that surgeons are mentored as they incorporate new techniques learnt from short courses into their practice.

P366

Gastric Cancer Staging in the Era of Neoadjuvant Therapy and its Prognostic Implications G. Kim,* P. Friedmann, J. McAuliffe, P. Muscarella, H. In. *Surgery, Montefiore Medical Center, Bronx, NY.*

Background: Increasingly, patients are undergoing neoadjuvant therapy for gastric cancer. The relationship between stage-based prognostic information available prior to treatment (cStage), after surgery (ypStage), and difference between cStage and ypStage (delta) remains unclear. We aim to describe the relationship between cStage and ypStage as relates to survival for gastric cancer patients. Methods: Data from the National Cancer Data Base (NCDB) from 2004-2015 was used for the analysis. Patients with gastric adenocarcinoma who received neoadjuvant therapy then underwent surgery were included. Kaplan Meier curves were used to model survival. Harrell's C-statistics obtained from Cox Regression models were reported. Results: 9,959 patients met our inclusion criteria. Increases in cStage, ypStage and delta (ypStage-cStage) were associated with worse survival. Median overall survivals for cStages 1-4 were: 53.8, 39.5, 29.2, 20.9 months (logrank test, $p < 0.0001$). Median survivals for ypStage 0-4 were: 95.4, 89.7, 36.9, 23.4, 16.0 months (logrank test, $p < 0.0001$). Survival was further stratified by delta. A representative figure comparing cStage 2 and ypStage 2 is shown below. A cox regression model with cStage as predictor of survival yielded a Harrell's C-statistic of 0.555; when delta was added to the model, the C-statistic increased to 0.638. Separately, a Cox-regression model with ypStage as predictor yielded a C-statistic of 0.632; when delta was added to this model, the C-statistic increased negligibly to 0.638. Conclusions: Prognostic accuracy using cStage prior to treatment improved when tumor responsiveness was considered while this was not the case for ypStage. Pre-surgical prognostic information should be provided with a caveat that treatment response will influence survival. Post-surgery, the clinical stage is less relevant and ypStage can be used alone in providing prognostic information.

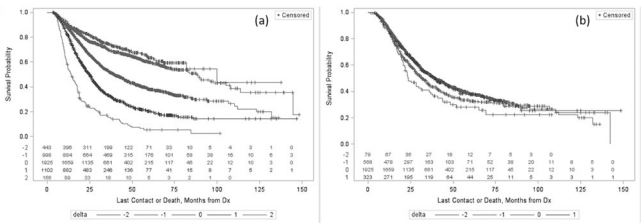


Figure: Kaplan Meier survival estimates of (a) cStage 2 and (b) ypStage 2 stratified by delta. Prognosis differed by tumor responsiveness for cStage 2 tumors, but not for ypStage 2 tumors.

P367

Cultural and Ethnic Variables Improve a Survey's Ability to Identify Individuals at High Risk for Gastric Cancer I. Solsky,[1]* M. Parides,[1] C. Schechter,[2] B. Rapkin,[2] H. In.[1] *1. Department of Surgery, Montefiore Medical Center, Bronx, NY; 2. Department of Epidemiology and Population Health, Albert Einstein College of Medicine, New York, NY.*

BACKGROUND: Absence of national US gastric cancer (GC) screening necessitates alternative methods like surveys to identify high-risk populations. Identification of high-risk persons may be enhanced by adding ethnic and cultural variables to more conventionally known risk factors for GC. METHODS: Data from a prior case-control study of 40 GC cases and 100 controls were used. A "conventional" risk factor model (age, gender, family history of GC, body mass index, excessive salt intake, alcohol, smoking, blood type, H pylori) was compared to one incorporating ethnic and cultural variables (race, immigration, generation, cultural food at ages 15-18 years, acculturation and education) using model fit, sensitivity, specificity and expected positive predictive values (PPV). Stepwise regression was then used to create a model from this pool of variables. PPV was calculated using Bayes' Theorem applied to the baseline GC incidence in the US (7.2 per 100,000). RESULTS: The "conventional" model required 14 questions and resulted in 25% sensitivity, 94% specificity, 28 per 100,000 PPV at the 70% probability cut-off, and AUC=0.871. The model incorporating ethnic and cultural variables required 38 questions and resulted in 48% sensitivity, 91% specificity, 38 per 100,000 PPV, and AUC =0.965. After eliminating items less predictive at p=0.2, age, gender, family history of GC, excessive salt intake, immigration, generation

and race remained in the model. This model required 7 questions and resulted in 45% sensitivity, 96% specificity, 81 per 100,000 PPV and AUC=0.914. CONCLUSION: The model with the greatest ability to identify persons at risk of GC included ethnic and cultural variables. This model can be translated into a survey with few items that can serve as a highly scalable tool to identify high-risk individuals. Support: UG1CA189823

Final Model Items to Identify Individuals at Higher Risk of Gastric Cancer

1. Age
2. Gender
3. Race/ethnicity
4. Were you or your parents born in the US?
5. Did your mother, father, brother or sister ever have stomach cancer?
6. How many meals per week do you eat at restaurants or have take-out food?
7. How many meals per day do you eat processed meats (such as bacon, sausage, salami, ham)?

P368

Hispanic Ethnicity is Associated with Early Presentation and Advanced Stage of Gastric Adenocarcinoma S. Paul,* Y. Liu, C.A. Hester, S. Wang, P.M. Polanco, A. Yopp, M. Augustine, J. Mansour, H. Zeh, M. Porembka. *Department of Surgery, Division of Surgical Oncology, University of Texas at Southwestern Medical Center, Dallas, TX.*

Introduction: Gastric adenocarcinoma (GA) is a heterogeneous disease with variable presentation and progression between ethnic groups. We aimed to assess factors related to the early age of GA presentation (< 45 years) between racial and ethnic groups. Methods: Using the National Cancer Database, patients with GA and upfront surgery were selected. Those receiving neoadjuvant therapy were excluded to ensure accurate pathologic stage. Clinicopathologic data was correlated to factors associated with age at diagnosis. Ethnicity was classified into Non-Hispanic White (NHW), Hispanic (HS), African American (AA) and Asian (AS). Univariate and multivariate linear regression models were used to determine factors associated with age of presentation. Overall survival was estimated using the Kaplan–Meier method and compared using log-rank tests. Results: Between 2006 and 2013, 18504 patients with GA and upfront surgery were identified. Median age was 67 years (IQR: 57-76) and 60% were male. Mean age at diagnosis was variable between ethnicity (NHW: 10838, 59%, 68 years, HS: 2319, 13%, 61 years, AA: 3619, 20%, 64 years and AS: 1728, 9%, 65 years; p<0.001). HS and AA presented with more advanced stage (Stage 4: HS 13.7%, AA 14.1%, NHW 12.5%, AS 10.1%; p<0.05). On univariate analysis, female gender, HS/AS race, uninsured status, Medicaid, advanced pathologic stage, and poorly differentiated tumor grade were associated with young presentation (p<0.001). On multivariate analysis, factors associated with young presentation included female gender (1.51, 95%CI: 1.31-1.74), minority race compared to NHW (HS: 2.34 95%CI: 1.96-2.86; AA: 1.41 95%CI: 1.17-1.71), and poorly (2.65, 95%CI: 1.49-4.71) or undifferentiated grade (3.53, 95%CI: 1.82-6.87). Median survival was significantly different between races (NHW 24 months, HS 39 months, AA 25 months, AS 47 months, p<0.001). Conclusion: Young presentation of GA is associated with HS/AS, female gender, and advanced tumors. Despite HS presenting at a young age with more advanced disease, median survival was prolonged compared to AA/NHW. Further research is necessary to determine underlying biologic basis of ethnic variation observed in GA.

P369

Impact of Skeletal Muscle Mass on Short- and Long-term Outcomes After Gastrectomy for Elderly Patients with Gastric Cancer K. Sakurai,[1]* N. Kubo,[1] Y. Tamamori,[1] T. Tamura,[2] T. Toyokawa,[2] H. Tanaka,[2] K. Muguruma,[2] Y. Masakazu,[2] K. Maeda,[1] M. Ohira.[2] *1. Gastroenterological surgery, Osaka City General Hospital, Osaka City, Japan; 2. Osaka City University Graduate School of Medicine, Osaka, Japan.*

Objective: The aim of this study was to elucidate the impact of sarcopenia in elderly patients with gastric cancer (GC) on short- and long-term outcomes after surgery for GC. Methods: A total of 569 patients subjected to gastrectomy for GC at our institution between January 2007 and December 2013 were reviewed. We defined areas of muscle that were normalized by height in meters squared, at the level of the third lumbar vertebral body (L3) in CT images, as the lumbar skeletal muscle index (SMI). Patients were divided into two groups according to age (younger than 65 years and 65 years or older group) and the presence of sarcopenia (low SMI and high SMI group) with the first quartile serving as the cut-point of SMI for both men and women. Clinicopathologic features and short- and long-term outcomes were compared. Results: The overall survival (OS) rate in 65 years or older patients with low SMI correlated with a significantly poor prognosis than the rate in patients with high SMI (5 year OS rate; 39% vs. 63%, P < 0.01). In terms of OS in the65 years or older group, univariate analysis indicated that pT≧3, lymph node metastasis, total gastrectomy, Prognostic nutrition index (PNI) (<45) and low SMI were independent predictors. In multivariate analysis, low SMI, PNI (<45) and lymph node metastasis were independently associated with unfavorable outcomes. The hazard ratio for low SMI was 1.53 (95% confidence interval: 1.01-2.29; p=0.045). OS rates in younger than 65 years patients with low or high SMIdid not differ significantly(5 year OS rate; 66% vs. 77%, P=0.441). In terms of postoperative complications, the incidence of anastomotic leak and mortality was similar in the low or high SMI group in the 65 years or older (8.7% vs. 5.3%, P=0.231, 1.9% vs. 0.4%, P=0.161). In younger than 65 years group, the incidence did not differ significantly in the low or high SMI group (0% vs. 5.0%, P=0.159, 0% vs. 1.1%, P=0.514). Conclusion: low SMIand worse long-term outcomes were significantly associated with patients in GC aged 65 years or older but not in those younger than 65 years. SMIand postoperative morbidity showed no correlation in this study.

Clfinicopathologic characteristics in the low and high SMI group

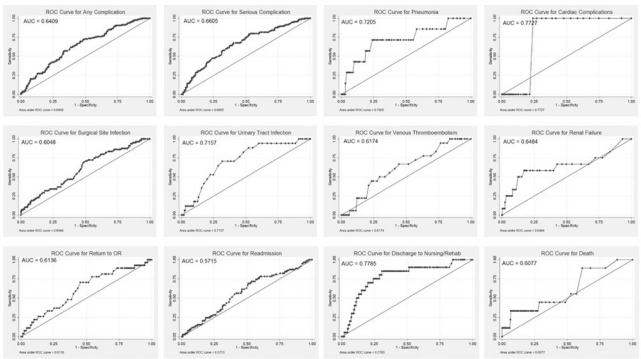
	All patients N=569	Low SMM N=142	High SMM N=427	P value
Age	66.7±11.2	70.0±10.3	65.6±11.2	<0.0001
BMI	21.9±3.4	19.3±2.6	22.8±3.2	<0.0001
Male Female	396 (69.6) 173 (30.4)	99 (69.7) 43 (30.3)	297 (69.6) 130 (30.4)	0.9327
PNI	48.2±6.0	45.6±6.5	49.1±5.6	<0.0001
pT1 2 3 4	240 (42.2) 74 (13.0) 91 (16.0) 64 (28.8)	42 (29.6) 18 (12.7) 26 (18.3) 56 (39.4)	198 (46.4) 56 (13.1) 65 (15.2) 108 (25.3)	0.0017
pN0 1 2 3	328 (57.5) 75 (3.2) 73 (12.8) 93 (16.3)	69 (48.6) 17(12.0) 23 (16.2) 33 (23.2)	259 (60.7) 58 (13.6) 50 (11.7) 60 (14.1)	0.0179
pStage1 2 3 4	264 (46.4) 121 (21.3) 126 (22.1) 58 (10.2)	50 (35.2) 29 (20.2) 35 (24.4) 28 (19.7)	214 (50.1) 92 (21.6) 91 (21.3) 30 (7.0)	<0.0001
Total gastrectomy Partial gastrectomy	203 (35.7) 366 (64.3)	54 (38.0) 88 (62.0)	149 (34.9) 278 (65.1)	0.4995
Complication				
Leakage	31 (5.4)	9 (6.3)	22 (5.2)	0.5897
CD grade 3 or more	64 (11.2)	15 (10.5)	49 (11.5)	0.7465
Mortality	5 (0.8)	2 (1.4)	3 (0.7)	0.4398
Postoperative days	18.1±13.7	19.1±15.2	17.8±13.1	0.0613

P370

Evaluating the ACS-NSQIP Risk Calculator in Primary Gastrointestinal Neuroendocrine Tumor: Results from the United States Neuroendocrine Tumor Study Group E.W. Beal,[1]* J. Kearney,[1] E. Lyon,[1] A.G. Lopez-Aguiar,[2] G. Poultsides,[3] J. Cannon,[3] F. Rocha,[4] Z. Kanji,[4] S. Weber,[5] A. Fisher,[5] R. Fields,[6] B.A. Krasnick,[6] K. Idrees,[7] P. Marincola Smith,[7] H. Nathan,[8] M. Beems,[8] S. Maithel,[2] T. Pawlik,[1] M. Dillhoff.[1] *1. The Wexner Medical Center at the Ohio State University, Columbus, OH; 2. Emory University, Atlanta, GA; 3. Stanford University, Palo Alto, CA; 4. Virginia Mason University, Seattle, WA; 5. University of Wisconsin, Madison, WI; 6. Washington University, St. Louis, MO; 7. Vanderbilt University, Nashville, TN; 8. University of Michigan, Ann Arbor, MI.*

Background: The American College of Surgeons (ACS) established an online risk calculator to help surgeons make patient specific estimates of postoperative morbidity and mortality. Our objective was to assess the accuracy of the ACS NSQIP calculator for estimating risk after curative intent resection for primary gastrointestinal neuroendocrine tumors (GI-NET). Methods: Adult patients with GI-NET who underwent complete resection from 2000-2017 were identified using a multi-institutional database including data from 8 academic medical centers. The ability of the NSQIP calculator to accurately predict a particular outcome was assessed using ROC curves and area under the curve. Results: 703 patients were identified who met inclusion criteria. The most commonly performed procedures were resection of small intestine with anastomosis (N=193, 26%) and partial colectomy with anastomosis

(N=136, 18%). The majority of patients were less than 65 years of age and ASA Class III. The most common comorbidities were hypertension (395, 56%) and diabetes (N=128, 18%). Complications among these patients based on ACS NSQIP definitions included any (N=132, 19%), serious (N=118, 17%), pneumonia (N=7, 1.0%), cardiac complication (N=1, 0.01%), surgical site infection (N=80, 11.4%), urinary tract infection (17, 2.4%), venous thromboembolism (N=18, 2.5%), renal failure (N=16, 2.3%), return to the OR (N=27, 3.8%), discharge to nursing/rehab (N=23, 3.1%) and 30-day mortality (9, 1.3%). The calculator provided reasonable estimates of risk for pneumonia (AUC=0.7205), cardiac complication (AUC=0.7727), urinary tract infection (AUC=0.7157) and discharge to nursing/rehab (AUC=0.713) and performed poorly (AUC < 0.7) for all other complications (Figure 1). Conclusions: The ACS NSQIP Risk Calculator estimates similar proportion of risk to actual events in patients with GI-NET but has low specificity for identifying the correct patients for many types of complications. The risk calculator may require modification for some patient populations.



P371

Comparison of Outcome of Esophagectomy Versus Nonsurgical Treatment for Resectable Esophageal Cancer with Clinical Complete Response to Neoadjuvant Therapy S. Koga,* Y. Ohkura. *gastroenterological surgery, Toranomon hospital, Minato-ku, Tokyo, Japan.*

Background. Treatment for patients who have achieved clinical complete response (cCR) after neoadjuvant therapy has not been established, and there is no consensus regarding the indications for either esophagectomy or nonsurgical treatment. Methods. Among 1,545 patients with esophageal cancer at Toranomon Hospital between January 2006 and August 2017, 39 who achieved cCR after neoadjuvant treatment were divided into two groups according to treatment: esophagectomy group (n = 18) and nonsurgical treatment group (n = 21) for comparison. Results. No significant intergroup difference was observed in baseline characteristics. Pathological complete response was confirmed in 13 (72.2%) of the 18 patients who underwent esophagectomy, whereas residual tumor was detected at the location of primary tumor in 2 (11.1%) patients, and lymph node metastasis was found in 3 (16.7%) patients. Recurrence-free survival (RFS) was significantly longer in the esophagectomy group than in the nonsurgical group (p = 0.002). Disease-specific survival (DSS) was significantly longer in the esophagectomy group (p = 0.007). However, no significant intergroup difference was observed in overall survival estimated based on all deaths, including respiratory failure and aspiration pneumonia (p = 0.451). Conclusions. With improved diagnostic accuracy, nonsurgical treatment can be an option for patients estimated as cCR after treatment administered in a neoadjuvant setting. However, surgical resection is considered more appropriate because of residual tumor in some patients with cCR and because of superior DSS and RFS following esophagectomy compared with nonsurgical treatment. Future studies must focus on ameliorating late postoperative complications, such as respiratory failure and aspiration pneumonia.

P372

Small Bowel Adenocarcinomas: Impact of Location on Survival T.C. Lee,* M.C. Morris, L.K. Winer, V.K. Dhar, K. Wima, J.J. Sussman, S.A. Ahmad, S.H. Patel. *Surgery, University of CIncinnati, Cincinnati, OH.*

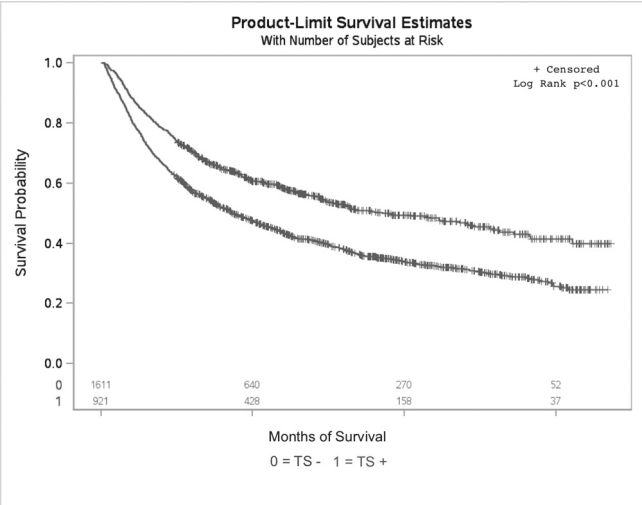
Introduction: Proximal (duodenal) small bowel adenocarcinomas have been noted to have worse prognosis compared to distal (jejuno-ileal) tumors, but comparisons of patient and tumor factors or treatment strategies between locations are unclear. We hypothesized that proximal and distal tumors represent separate disease processes resulting in different outcomes and may warrant distinct approaches to treatment. Methods: The National Cancer Database was queried for patients with clinical stage I-III small bowel adenocarcinomas who underwent surgical resection between 2004-2015. Of 64,756 small bowel entries, 2765 met the inclusion criteria. Baseline characteristics were studied using univariate and multivariate analyses. Kaplan-Meier and Cox regression analyses were performed for overall and stage-specific survival. Results: Proximal small bowel adenocarcinomas were associated with worse overall and stage-specific survival than distal (overall median survival 3.7 vs 5.9 yr, p<0.01). For both proximal (p<0.01) and distal tumors (p=0.01), better survival was associated with neoadjuvant (4.0 and 6.2 yr) and adjuvant (4.5 and 7.1 yr) chemotherapy compared to surgery alone (3.4 and 4.6 yr). Cox regression for the entire cohort showed higher clinical stage and grade, positive nodal and margin statuses to be associated with worse survival, while distal location and chemotherapy were associated with better survival. Cox regression for the proximal cohort showed tumor grade was no longer associated with survival, while for the distal cohort, stage and chemotherapy were no longer associated. Distal tumors were more likely to be higher pathologic stage than proximal (OR 2.2-3.4 for stage II-III, p<0.05), but less likely to be higher grade (OR 0.61 for moderate and 0.47 for high, both p<0.01) or node positive (OR 0.30, p=0.02). Conclusions: Proximal small bowel adenocarcinomas are associated with worse overall and stage-specific survival. This may be due to tumor biology differences as proximal tumors were more likely to have higher grade and nodal disease than distal. Future studies should investigate biologic tumor differences between proximal and distal tumors to guide targeted treatment algorithms.

P373

Textbook Surgery is a Strong Predictor of Survival in Patients with Stomach Cancer: An Analysis of a Population Registry of Esophageal and Stomach Tumors of Ontario (PRESTO) J. Levy,[1]* V. Gupta,[1] Q. Li,[3] O. Saarela,[1] A. Mahar,[2] C. De Mestral,[1] N. Coburn.[1] *1. General Surgery, University of Toronto, Toronto, ON, Canada; 2. University of Manitoba, Winnipeg, MB, Canada; 3. Institute of Clinical and Evaluative Sciences, Toronto, ON, Canada.*

Background Surgical outcomes for gastrectomies in North America are variable and poor. While post-operative mortality is an important quality marker, Textbook Surgery, a composite measure of post-operative complications, re-interventions, ICU admissions, prolonged admissions and readmissions represent a more patient-centric and comprehensive outcome for this complex surgery. Objectives To characterize what proportion of patients achieve Textbook Surgery and determine the association between Textbook Surgery and overall survival. Design A population-based retrospective analysis of routinely collected administrative data. Methods Adult patients with gastric adenocarcinoma undergoing gastrectomy between 2004 and 2016 were identified and followed up until May 31, 2018. Post-operative outcomes were analyzed, and patients were assigned to Textbook vs. Non-Textbook Surgeries. A marginal cox proportional hazards model regressed over patient confounders was used to assess the association between Textbook Surgery and overall survival. Results In total, 2,703 patients were deemed eligible for analysis and Textbook Surgery was achieved in 34% of patients (n=930). This group was younger (mean 65.9 vs. 68.9 years, p<0.001), healthier (p<0.001), had less residential instability (p<0.001), underwent surgery in more recent years (p<0.001) and received more neoadjuvant and adjuvant therapy (p<0.001). But otherwise had similar proportions of male patients (p=0.057), material deprivation (p=0.11), proportions of signet ring/mucinous tumours (p=0.35) and underwent surgeries at hospitals with similar volumes (p=0.061). The Textbook Surgery group had superior median survival (p<0.001) and achieving textbook surgery was associated with a 24% decrease in the relative rate of death (HR 0.76, p<0.001). Conclusion Textbook Surgery is a valid proxy for

high quality surgery. It remains a rare outcome in most patients, which is all the more significant given its strong impact on survival. Textbook Surgery should be considered as the new benchmark in oncology surgery.



KM Curves - Months of Survival by Textbook Surgery Groups

P374

Inflammatory and Nutritional Markers as Prognostic Factors in Gastric Cancer K.E. Padilla-Leal, L. Mejía-Fernandez, H. Medina-Franco.* *SURGICAL DEPARTMENT, INSTITUTO NACIONAL DE CIENCIAS MEDICAS Y NUTRICION SALVADOR ZUBIRAN, Mexico City, Mexico.*

Background:Cancer is associated to an elevation of various systemic inflammatory markers and in turn to a reduction of albumin level; some of their calculated indices can predict long-term outcomes. The aim of this study was to evaluate new elements, mainly the prognostic nutritional index (PNI), and platelet/lymphocyte ratio (PLR) as predictors of survival in gastric cancer without metastatic disease. Methods: A retrospective study was conducted enrolling patients with resectable gastric cancer treated through potentially curative gastrectomy in our institution, a tertiary referal center in Mexico City. PNI (10x serum albumin (g/dL) + 0.005 x total lymphocyte count /mL) and PLR was calculated. Demographic, pathological and clinical variables were registered. Univariate and Cox regression analysis was performed for identification of variables associated with disease-specific survival (DSS). p<0.05 was considered significant. Results: A total of 214 subjects with a median follow-up of 20 months were included. High PNI (>40) was established as a good prognostic factor for DSS (HR:0.524; 95% CI 0.308-0.892; p=0.017). Other inflammatory markers such as platelet-lymphocyte ratio (PLR) weren't statistically significant (HR: 0.573, 95% CI 0.327-1.006; p=0.53). Previously known prognostic factors (clinical stage [HR 5.966, 95% CI 1.848-19.262; p=0.003], pathological characteristics like positive nodes [HR 3.166, 95% CI 1.739-5.763; p <0.001] in-hospital stay [HR 1.89, 95% CI 1.126-3.172; p=0.016]) were identified as risk factors for worse outcomes. The Kaplan-Meier analysis demonstrated that patients with low PNI had a poorer DSS (p = 0.015); the same result was obtained when matched with the clinical stage, having a lower survival as the stage increased (p = 0.005). Conclusions: Having a good nutritional status expressed by an increased PNI is associated to a better DSS in patients with resectable gastric cancer. PLR was not associated to long- term prognosis.

P375

Prognostic Value of Nutritional Status for Esophageal Cancer Patients Undergoing Neoadjuvant Therapy and Resection S. Saeed,[2]* J. Fontaine,[1] L. Pena,[2] S. Hoffe,[3] J. Frakes,[3] R. Metha,[4] E. Gurd,[5] J. Pimiento.[1] *1. Moffitt Cancer Center and Research Institute, Department of Surgical Oncology, Tampa, FL; 2. Moffitt Cancer Center and Research Institute, Department of Gastrointestinal Oncology, Tampa, FL; 3. Moffitt Cancer Center and Research Institute, Department of Radiation Oncology, Tampa, FL; 4. Moffitt Cancer Center and Research Institute, Department of Medical Oncology, Tampa, FL; 5. Moffitt Cancer Center and Research Institute, Department of Nutrition, Tampa, FL.*

Background: Malnutrition, linked to decreased patient tolerance to chemotherapy and increased rates of therapy-related toxicity, negatively affects cancer prognosis. Esophageal carcinomas (EC) frequently present with dysphagia and significant weight loss which may be exacerbated by neoadjuvant chemoradiation, placing EC patients at an increased risk of malnutrition. We therefore aim to assess the prognostic value of pre-operative malnutrition for esophageal cancer patients undergoing neoadjuvant therapy (NAT). Methods: Query of our institution's IRB approved database of 1113 EC patients (pts) identified 725 individuals who underwent NAT followed by resection from 1994-2018. Seventy-six pts were considered to be at higher nutritional risk during NAT, as indicated by significant weight loss and enteral feeding tube requirement (ETF+), while 644 did not receive pre-operative feeding tube placement (ETF–). Clinicopathologic characteristics, post-operative outcomes, and survival were compared between ETF+ and ETF– using various statistical methods. Results: Of the included pts, 83% were male with a median age of 64.5 (28-86) years. Between ETF+ (n=76) and ETF– (n=644), pt characteristics were balanced in terms of initial stage, age, histology and tumor location. A higher percentage of ETF+ pts had >5% weight loss before NAT (32 vs. 6%; p<.01). ETF+ was associated with a significantly worse median survival (27 vs. 77 m; p<.01), but not with increased post-operative length of hospital stay (p=.69), complications (p=.20) or tumor recurrence (p=.89). Although completion of chemotherapy (p=.46) and radiation (p=.49) were comparable between ETF+ and ETF–, tumor response was worse in the ETF+ group (71 vs. 60% non-complete response; p=.02). Conclusion: Our results suggest that baseline malnutrition is a risk factor for poor survival and negatively impacts the efficacy of neoadjuvant therapy in EC patients. Poor response to NAT in malnourished patients may stem from impaired immune function. Future prospective studies should evaluate other parameters for nutritional assessment to further assess the impact of malnutrition on tumor regression and survival after NAT.

P376

Preoperative Factors Predictive of Pathologic Upstaging in Clinical Stage I Gastric Cancer Patients H. Thuppal,[1]* P. Friedmann,[2] J. McAuliffe,[1] P. Muscarella,[1] H. In.[1] *1. Surgery, Montefiore Medical Center, Bronx, NY; 2. Albert Einstein College of Medicine, Bronx, NY.*

Background: In patients with stage 1 gastric cancer, surgical resection without neoadjuvant therapy is offered as the first line treatment. However, some of these patients are found to have higher stage after resection and miss the opportunity for neoadjuvant therapy. Pre-operative patient and tumor characteristics may be predictive of the likelihood of pathological upstaging in stage 1 gastric cancer patients who have not received neo-adjuvant therapy. Methods: The National Cancer Database was queried for patients diagnosed from 2004-2015 with clinical stage 1 gastric adenocarcinoma who had undergone surgical resection without neoadjuvant therapy. Univariate analysis and multivariable logistic regression were conducted to determine pre-operative factors associated with pathological upstaging. Candidate variables examined included age, sex, race, tumor size, histology, grade, tumor location, days to surgery, and lymphovascular invasion. Results: Analysis was conducted on 8,015 clinical stage 1 patients. Overall 1,981 (25%) patients were upstaged. On multivariable logistic regression analysis, significant predictors of upstaging included increasing tumor size [ref: size<1cm, 1-2cm aOR=3.8 (95% CI 2.3-6.1); 2-4cm aOR=12.4 (7.9-19.5); >=4cm aOR=25.9 (22.9-56.4)], younger age [ref: >=75, <50 aOR=1.7 (1.4-2.1), 50-65 aOR=1.4 (1.2-1.6), 65-75 aOR=1.2 (1.1-1.5)], male gender [aOR=1.16 (1.0-1.3)], presence of diffuse type gastric cancer [aOR=2.3 (1.7-3.2)], mucinous type [aOR=1.7 (1.1-2.5)], or signet ring cell histology [aOR=1.6 (1.3-2.0)] compared to intestinal histology, presence of lymphovascular invasion [aOR=6.0 (5.0-7.1)], and increasing grade [ref: grade

1, grade 2 aOR=2.30 (1.7-3.5); grade 3 aOR=4.9 (3.6- 6.7)]. Conclusions: A quarter of all patients thought to have stage 1 gastric cancer prior to surgery had higher pathologic stage at time of resection. Patients with the above risk factors may be understaged with currently available diagnostic tools. The addition of neoadjuvant therapy should be considered when the above risk factors are present in clinical stage 1 patients.

P377

Impact of Perineural and Lymphovascular Invasion on Survival Following Gastrectomy for Gastric Cancer T. Newhook,* C.J. Allen, T.J. Vreeland, N. Ikoma, J. Estrella, M. Blum, P. Das, B. Minsky, P. Mansfield, J. Ajani, B. Badgwell. *MD Anderson Cancer Center, Houston, TX.*

Background: The effect of perineural invasion (PNI) and lymphovascular invasion (LVI) on outcomes following gastrectomy for gastric adenocarcinoma (GA) is unclear and the prognostic significance of these variables together is underreported. We aimed to evaluate the impact of PNI and LVI on survival following gastrectomy for GA. Methods: Demographic and clinicopathologic data was abstracted from a prospectively-maintained database for patients who underwent gastrectomy for GA between 1/2000-7/2018. Univariate analyses were used to compare patient groups, and Kaplan-Meier survival analyses evaluated disease-free (DFS) overall survival (OS). Results: A total of 474 patients underwent gastrectomy: 219 total (46.2%), 224 subtotal/distal (47.3%), and 31 proximal gastrectomy (6.5%). Most patients had poorly-differentiated tumors (n=326, 68.9%). The presence of signet ring morphology was found in 49.3% (n=233). A total of 283/474 (59.7%) received preoperative therapy. Patients were AJCC 8th edition pathologic stage I 36.7% (n= 174), stage II 26.5% (n=126), stage III 27.4% (n=130), and stage IV 5.9% (n=28). Both PNI/LVI were present in 22.8% (n=108), LVI-alone in 17.7% (n=84), PNI-alone in 5.1% (n=24), and neither in 258 (54.4%). Patients with both PNI/LVI were more likely to have undergone preoperative therapy (71.7% vs. 57.2%, p=0.009), have pT stage ≥T3 (89.8% vs. 35.5%, p<0.001), have node-positive (76.9% vs. 32.2%, p<0.001), and ≥ stage III disease (79.6% vs. 20.8%, p<0.001). There was no difference in OS or DFS between patients without LVI/PNI, with PNI-alone, and LVI-alone. Patients with both PNI/LVI had worse median DFS (1.5 years vs. 2.2 years, p=0.001) and OS (1.7 years vs. 2.4 years, p=0.006; Fig 1) than those with PNI-alone, and LVI-alone, or neither LVI nor PNI. Conclusions: The presence of both PNI/LVI is associated with advanced stage tumors and significantly decreased DFS and OS following gastrectomy for GA. Patients with tumors having both PNI and LVI may be candidates for more aggressive postoperative therapy and surveillance.

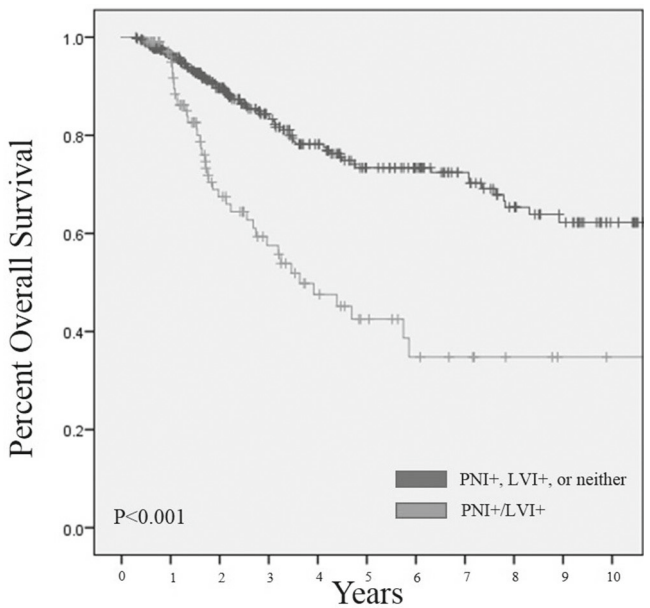


Figure 1. Kaplan meier survival analysis of overall survival for patients with both PNI/LVI

P378

Aggressive Tumor Phenotype and Increased Gastric Cancer Mortality in Hispanics B.D. Babcock,* L. Ji, M.J. Selleck, M.M. Kwong, J. Morgan, J. Namm, M. Reeves, S. Lum, C. Garberoglio, M. Senthil. *Surgery, Loma Linda University Medical Center, Loma Linda, CA.*

Introduction: Recent studies have shown an increasing incidence of advanced stage gastric cancer in Hispanics in the U.S. It is critical to understand the biologic and survival differences of gastric cancer in Hispanics compared to other race/ethnic groups to make meaningful screening recommendations in this high-risk population. Methods: California Cancer Registry (CCR) data was used to identify patients diagnosed with gastric adenocarcinoma from 2004-2015. Univariate logistic regression analyses were performed to determine odds ratios (OR) for T-stage, tumor location, grade, histology, and peritoneal carcinomatosis (PC) contrasting Hispanics with other race/ethnic groups (Table 1). Multivariable mortality hazard ratios (HR) were used to determine independent effects of demographic and tumor characteristics. Results: From 2004-2015, 15,798 patients were diagnosed with gastric adenocarcinoma. Of these patients, 6,185 (39.2%) were non-Hispanic white (NHW), 4,967 (31.4%) were Hispanic, 949 (6.0%) were non-Hispanic black (NHB), and 3,697 (23.4%) were Asian/other. Hispanics were more likely to have T4 tumors, poorly differentiated histology, and signet ring adenocarcinoma compared to other races (Table 1). Peritoneal carcinomatosis was also seen with higher prevalence among Hispanics as compared to NHW (OR 1.66, 95% CI 1.21-2.29). Hispanics had poorer survival compared to NHW (HR 1.07, 95% CI1.00-1.13) and Asian/other (1.20, 95% CI 1.13-1.28). The only race that had poorer survival than Hispanics was NHB (HR 1.18, 95% CI 1.07-1.29). Conclusions: Hispanic race is an independent predictor of increased gastric cancer mortality. Hispanics are also more likely to develop aggressive gastric cancers and present with advanced disease at the time of diagnosis. Results of this study highlight the need for GC screening in Hispanics. Ongoing tumor genomic studies in Hispanics may help understand the biologic differences of gastric cancer in this group.

Tumor characteristics in Hispanics compared to other ethnic groups.

Race	T4 tumor	Poorly differentiated tumor	Signet ring adenocarcinoma
Hispanic vs NHW	1.93 (95% CI 1.63-2.28)	1.47 (95% CI 1.35-1.59)	1.13 (95% CI 1.01-1.27)
Hispanic vs NHB	1.40 (95% CI 1.02-1.90)	1.23 (95% CI 1.06-1.43)	1.42 (95% CI 1.16-1.73)
Hispanic vs Asian /other	1.81 (95% CI 1.50-2.19)	1.23 (95% CI 1.12-1.35)	1.38 (95% CI 1.22-1.56)

NHW (Non-Hispanic white); NHB (Non-Hispanic black)

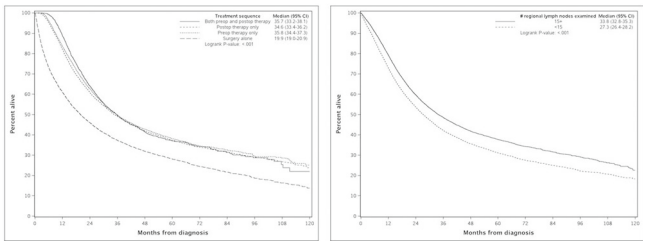
P379

Utilization of Adjunctive Therapies for Resectable Gastric Cancer in the United States C.A. Thiels,* K.T. Hanson, E.B. Habermann, D.M. Nagorney, R.L. Smoot, S.P. Cleary, M.J. Truty, T.E. Grotz. *Surgery, Mayo Clinic, Rochester, MN.*

Background: Numerous trials have significantly impacted gastric cancer management over the last 2 decades. However, how these findings have affected care in the broader population is less understood. We aimed to assess utilization of adjunctive therapies in the management of patients with gastric cancer. Methods: The National Cancer Data Base was queried for patients with stage >1a gastric (including gastroesophageal) adenocarcinoma (2006-2015) undergoing curative intent resection. Patients missing treatment sequence data (n=3482) were excluded. Patients were categorized by treatment modality received and sequence. Trends in utilization of MIS were assessed from 2010-2015. One-sided Cochran-Armitage test was used to assess for increases in utilization of therapies over time. Kaplan-Meier analysis evaluated overall survival. Results: 28,678 patients were included with 9,038 (31.5%) receiving surgery alone, 7,298 (25.5%) pre-operative therapy, 9,592 (33.5%) post-operative therapy, and 2,750 (9.6%) peri-operative therapy. Within individual treatment modalities, the majority of patients undergoing chemotherapy received it pre-operatively (44.6%) or post-operatively (37.9%, vs 17.6% peri-operatively). Conversely, the majority (50.9%) of radiation was given post-operatively (vs 37.3% pre-operatively and 11.8% peri-operatively). Utilization of any chemotherapy increased (39.1% 2006 to 67.2% 2015) while utilization of chemoradiation increased more slowly (40.5% 2006 to 48.3% 2015). MIS was utilized in 26.4% of cases, increasing from 17.1% 2010 to 34.6% 2015 (p<0.001). The percent of patients with >15 LN harvested also increased (44.3% 2010 to 61.6% 2015, p<0.001). Overall survival was improved for patients undergoing each form of adjunctive therapy vs. surgery alone. Additionally, patients with ≥15 LN examined had superior survival

(Figure). Conclusion: The utilization of adjunctive therapies in the management of resectable gastric cancer has increased, primarily driven by chemotherapy in the pre-operative setting. These findings, plus improved quality of oncologic surgery as demonstrated by increased rate of lymphadenectomies, may explain overall improvements in survival.

Figure. Overall survival in patients with resectable gastric cancer using Kaplan Meier analysis.



P380

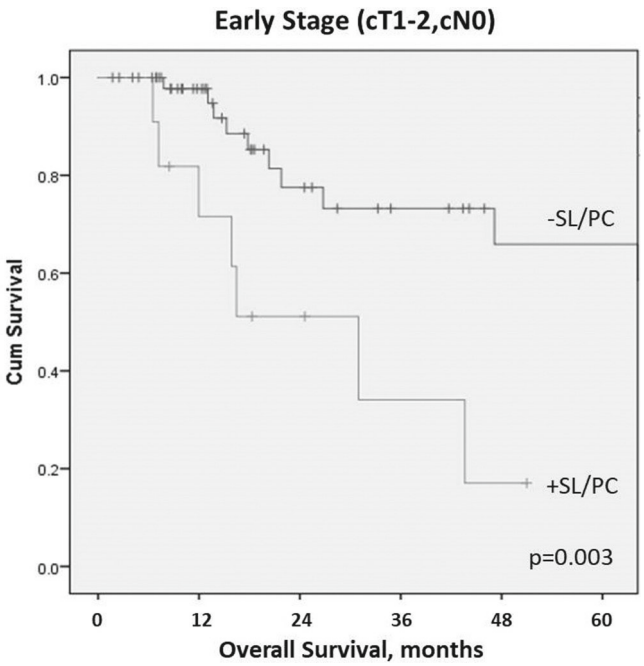
Inaccurate Pretreatment Staging Can Significantly Impact Survival in Early Stage Esophageal Carcinoma A.J. Scholer,[1]* A. Uppal,[1] D. Ghosh,[2] M. Garland-Kledzik,[1] T.D. Fischer,[1] M. Goldfarb.[1]
1. John Wayne Cancer Institute, Santa Monica, CA; 2. Department of Information Technology, Rutgers Business School, Newark, NJ.

Introduction: Neoadjuvant chemoradiation (NCXR) is known to improve survival in patients with stage II/III esophageal adenocarcinoma. However, inaccurate pre-treatment staging may have some patients inadvertently forego NCXR and select upfront esophagectomy (UFE), though the frequency and distribution of pathologic upstaging and the impact on survival is unknown. Methods: Patients diagnosed with non-metastatic esophageal adenocarcinoma between 2004 and 2013 were identified in the National Cancer database. The kappa index evaluated which patient and tumor characteristics influenced concordance between clinical (c) and pathologic (p) T and N staging (p>0.05 non-concordance) in patients that had UFE without NCXR. After propensity score matching, 3- and 5-year overall survival (OS) was compared between c-stage I patients that had UFE followed by adjuvant CXR (because of upstaging to p-stage II/II), and c-stage II/III patients that had NCXR followed by esophagectomy. Results: Of 1943 c-stage I patients, 11.5% were upstaged after UFE; this included 32% of T1 (n=88), 41% of T2 (n=110), and 59% of N0 (n=398) that were found to have a higher p-T or N-stage. T-stage was more non-concordant in females (kappa=0.41, p=0.06) and Blacks (kappa=0.023, p=0.07), whereas N-stage was most non-concordant in White Hispanics (kappa=0.67, p=0.16). After propensity score matching, 3- and 5-year OS was significantly decreased (p<0.001) in patients with c-stage I (3-year 61.6%, 5-year 57.6%) that had UFE and were upstaged compared to p-stage II (3-year 72.8%, 5-year 65.5%) or p-stage III (3-year 76.4%, 5-year 70.6%) patients after NXCR and esophagectomy. After controlling for other clinical factors, failure to receive NCXR conferred a decreased OS in p-stage II (HR:0.66, p=0.006) and p-stage III (HR:0.64, p=0.002) patients. Conclusion: Inaccurate preoperative staging affects >10% of patients with c-stage I esophageal adenocarcinoma, and is more likely in certain patient demographics. Lack of NCXR in c-stage I patients that are upstaged to p-stage II/III after UFE leads to a significantly decreased OS, which should be disclosed to patients when discussing treatment options before UFE.

P381

Staging Laparoscopy and Peritoneal Cytology in Patients with Early Stage Gastric Adenocarcinoma C.J. Allen,* T. Newhook, T.J. Vreeland, P. Das, B. Minsky, M. Blum, S. Roy-Chowdhuri, J. Ajani, N. Ikoma, P. Mansfield, B. Badgwell. *Surgery, MD Anderson Cancer Center, Houston, TX.*

Introduction In patients being considered for curative resection for gastric adenocarcinoma (GA), staging laparoscopy (SL) and peritoneal cytology (PC) may be useful in detecting radiographically occult metastatic disease in patients. However, the yield of SL and PC in patients with early stage disease is lacking. Therefore, we assessed the yield of SL and PC in patients with early stage GA. Methods Demographic and clinicopathologic data were abstracted from a prospectively-maintained database of patients who had undergone SL and PC for GA at our institution between 1/2000-7/2018. Patients with early stage gastric cancer (cT1-2, cN0) on staging EUS were assessed. Rates of positive PC and gross carcinomatosis at time of SL were obtained. Univariate analyses were used to compare patient groups and Kaplan-Meier survival analyses were used to examine the implication of positive SL/PC on overall survival (OS). Results A total of 1188 patients underwent SL and PC, with 66 being performed in patients with early stage GA (cT1-2, cN0). Age was 62±13y, 39.4% were male, and 45.5% were white. Of all patients who underwent SL with early stage GA, 18.2% were found to be either grossly positive for carcinomatosis (12.8%) and/or positive PC (10.8%). These patients were more likely to be have poorly differentiated (91.7% vs 66.0%, p=0.05) and signet ring cell (83.3% vs 58.5%, p=0.09) histology. There were no differences in age, gender, or race between the groups (all p>0.05). As depicted in the figure, positive SL/PC in patients with early clinical stage disease significantly affects overall survival (p=0.003). Conclusions SL and PC identify metastatic disease in a significant number of patients with early stage GA, particularly in those with poorly differentiated histology. Given the poor prognosis associated with peritoneal disease, SL and PC should be considered in patients with GA at all clinical stages.

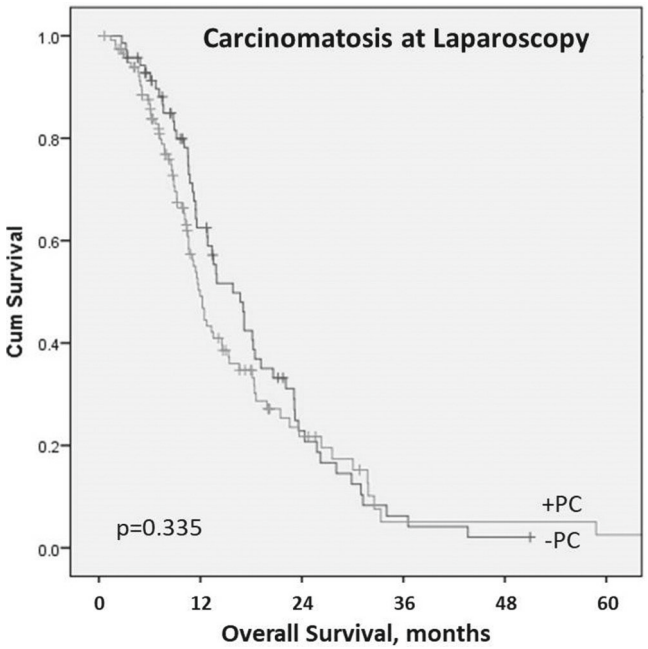


P382

Yield of Peritoneal Washings and Cytology in Staging Patients with Gastric and Gastroesophageal Cancer C.J. Allen,* T. Newhook, T.J. Vreeland, P. Das, B. Minsky, M. Blum, S. Roy-Chowdhuri, J. Ajani, N. Ikoma, P. Mansfield, B. Badgwell. *Surgery, MD Anderson Cancer Center, Houston, TX.*

Introduction National Comprehensive Cancer Network guidelines for gastric and gastroesophageal (GE) cancer recommend staging laparoscopy (SL) with cytology for clinical stage T1b or higher malignancies. However, the sensitivity of peritoneal cytology (PC) is unknown. The purpose of this study was to determine the sensitivity of peritoneal washings with cytological analysis in patients with established carcinomatosis. Methods We analyzed data from a prospectively maintained database of patients who had undergone SL and PC for gastric and GE cancer at our institution. Rates of positive PC were determined in patients with biopsy proven carcinomatosis at time of SL. Assuming those with both a negative SL and PC did not have peritoneal disease at time of surgery, test sensitivity of PC for detecting peritoneal disease was assessed. Kaplan Meier survival analyses were used to examine the implication of negative PC on overall survival (OS) in patients with carcinomatosis. Results A total of 1186 patients underwent SL and PC for gastric and GE cancer, with 282 (24%) being found with carcinomatosis. In these patients, age was 59±13y, 160 (57%) were male, and 175 (62%) were white. PC was sent in 214 (76%) of these patients and 77 (36%) were found to have no atypical cells. In this setting, PC carried a sensitivity of 32.4% for detecting peritoneal disease. There were no differences in age, gender, race, histology, or AJCC 8th edition stage based on PC in patients with gross peritoneal disease

(all p>0.05). The figure depicts 5y OS based on PC in patients with carcinomatosis. Conclusions Although PC serves as an adjunct to SL, it has a low sensitivity for detecting peritoneal disease. PC has no additional implications of disease state in patients with carcinomatosis. As peritoneal disease from gastric and GE cancer carries a very poor prognosis, novel biomarkers or improved assessment techniques are needed for the identification of microscopic disease in peritoneal washings.



P383

Neoadjuvant Therapy for Foregut GIST: Where Do We Stand? Trends from the National Cancer Data Base C. Hague,[1]* B. Fisher,[2] M. Fluck,[2] M. Hunsinger,[2] M. Shabahang,[2] J. Blansfield,[2] T. Arora.[2]
1. Geisinger Commonwealth School of Medicine, Scranton, PA;
2. Geisinger Medical Center, Danville, PA.

Background: Neoadjuvant therapy (NAT) of GISTs with tyrosine kinase inhibitors has been reported to facilitate tumor regression, decrease surgical morbidity, facilitate complete surgical resection and improve long-term survival in small studies. The goal of our study was to assess the survival benefits of NAT in foregut GIST and assess the trends of use. A lack of data and few guidelines exist for the management of GIST tumors in the neoadjuvant setting. Methods: This is a retrospective study of patients in the National Cancer Database (NCDB) diagnosed with GISTs of the esophagus, stomach and small intestine, from 2004–2014. Multivariate logistic regression was utilized to predict patient, tumor, and facility factors that were associated with receipt of NAT, and downstaging. Overall survival was analyzed using Cox proportional hazard analysis and the Kaplan-Meier Estimate. Results: The study included 3,372 patients total and were divided into those who received NAT (463 patients, 14%) and those who did not (2,909 patients, 86%). The use of NAT increased in usage from 2004–2014 (0% in 2004, 17.7% in 2014; $p < 0.0001$). More than half (54%) of patients who received NAT had ≥ T3 tumors and the average duration of treatment was about 180 days. Adjusted and unadjusted models for overall survival showed no significant difference between patients receiving NAT versus those who did not. Multivariate logistic regression showed no significant difference in age, gender, or insurance type. Significant factors associated with receiving NAT are shown in Table 1. NAT resulted in 19.9% of patients having tumor size downstaging and a longer post-surgical hospital stay (7.1 vs 6.5 days; $p < 0.0001$). Conclusions: Despite having larger tumors, patients who received NAT had similar overall survival to those who did not. Currently patients are more likely to receive NAT in high volume, academic centers. As this treatment, now integrated into NCCN guidelines, gains more widespread use and trial data become available, the surgical outcomes and survival will mandate further study. Key Words: Neoadjuvant, Tyrosine kinase inhibitors, Gastrointestinal Stromal Tumor

Table 1

Factors Associated with Neoadjuvant Chemotherapy					
Variable		Odds Ratio	95% Confidence		p value
			Lower	Upper	
Facility Type	Community	0.555	0.323	0.955	0.017
	Comprehensive	0.669	0.509	0.879	
	Academic/Research	ref	ref	ref	
	Integrated Network	1.013	0.712	1.44	
	Unspecified	1.117	0.31	4.018	
Race	White	ref	ref	ref	0.005
	Black	1.296	0.981	1.713	
	Other	1.748	1.212	2.521	
Income Quartile	Less than $38,000	ref	ref	ref	0.013
	$38,000 - $47,999	0.598	0.425	0.84	
	$48,000 - $62,999	0.886	0.647	1.214	
	$63,000 +	0.956	0.698	1.309	
	Unreported	0.259	0.033	2.054	
TNM Clinical T Stage	Unreported	1.558	1.035	2.344	<0.0001
	TX/0	ref	ref	ref	
	T1	2.47	0.993	6.139	
	T2	2.311	1.402	3.808	
	T3	3.004	1.96	4.605	
	T4	5.918	3.898	8.987	
Facility Highest Volume Quartile		1.665	1.3	2.13	<0.0001
TNM Clinical N1 (ref. NX/0)		2.457	1.168	5.167	0.018

P384

Pathologic Aggressiveness in Curatively Treatable Esophageal Cancer is More Likely Associated with Local Tumor Enhancement than with the Standardized Uptake Value (SUV) Derived from 18-F-FDG-PET J.Th.M. Plukker,* J. Hulshoff, M. Nicolai, W. Noordzij. *Universitair Medisch Centrum Groningen, Groningen, Netherlands.*

Introduction: Standardized uptake value (SUV) derived from ^{18}F-FDG-PET measures intra-tumoral FDG uptake and is used in prognosis of esophageal cancer (EC). Higher SUV is related to recurrent disease and poorer survival. Therefore, it could be related to tumor aggressiveness and pathologic features that contribute to this aggressiveness. This study assessed the association between SUV as a semi-quantitative parameter and pathologic features and survival, which could be useful in the decision-making of treatment. Patients and methods: Patients underwent curative intended treatment for a stage T2-4N0-3M0 esophageal tumor and had a baseline FDG-PET in the University Medical Centre Groningen. Treatment consisted of primary surgery, possibly preceded by neoadjuvant chemoradiotherapy (nCRT). Primary outcomes were pathologic features (perineural invasion, lymphovascular invasion, ≥ 4 lymph node metastases and LN ratio > 0.2) and overall survival (OS), disease free survival (DFS). Baseline SUV_{max}/SUV_{peak} and $\Delta SUV_{max}/SUV_{peak}$ (percentage decrease of SUV after nCRT) were assessed. Analyses were performed in the whole study group, the nCRT group and the surgery-alone group. Results: 150 of the 176 patients were treated by nCRT followed by surgery. No association between SUV and pathologic features was found. Pathologic features were often related to advanced T and N-stage, higher clinical tumor length and involvement of resection margins. SUV was not an independent prognostic factor for OS and DFS, whereas a higher clinical T-stage was. Conclusion: In patients with advanced EC, pathologic features and survival were not associated with SUV, but with local tumor enhancement and involvement of the resection margins.

P385

Gastro-entero-pancreatic Neuroendocrine Tumors (GEP-NETs) in Young Adults A.H. Nguyen,* C.J. LaRocca, C.L. Stewart, P. Ituarte, B. Lee, S. Chang, J. Kessler, D. Li, G. Singh. *City of Hope, Duarte, CA.*

INTRODUCTION While patients who are treated for GEP-NETs tend to be in their 6th and 7th decades of life, there is a minority of patients who face this diagnosis earlier in life. Herein we query in a population-based study, clinical and pathologic features and survival of patients of ages 18-29 with a diagnosis of a primary GEP-NET. METHODS A retrospective study from the National Cancer Data Base including patients from 2004 to 2014 with a primary gastrointestinal or pancreatic neuroendocrine tumor was performed. Patients were stratified by age. Kaplan-Meier and multivariate Cox proportional hazards analyses were performed. RESULTS We identified 131,012 patients with a diagnosis of a primary gastro-entero-pancreatic neuroendocrine in the National Cancer Data Base. The median age of diagnosis was 62 years

and less than 2% of patients were under the age of 30. While 5-year overall survival for all patients was 53%, for those patients with ages 18-29, 5-year survival was 82%, which was higher than any other age group ($p<0.001$). We then looked at distributions of stage and grade across age groups. 37.6% of patients ages 18-29 had stage 1 disease, whereas those in groups ages 30-44, 45-59, and ≥60, had frequencies of stage 1 disease of 22.7%, 20.9%, and 18.9%, respectively. Similarly, young patients had greater low grade disease where 44.2% of patients ages 18-29 had well-differentiated grade, whereas those in age groups 30-44, 45-59, and ≥60 had frequencies of grade 1 of 34.1%, 31.3%, and 24.8%, respectively. We then performed a multivariate analyses for survival including age, gender, race, grade, and stage in our model. We found that young age, low grade, and early stage to be associated with lower risk of mortality. Female gender and non-white race had modest associations of risk reduction. CONCLUSIONS Two percent of patients with GEP-NETs are under the age of 30. These patients tend to have earlier stage disease and lower grade tumors, which contribute to a much better survival compared to older patients. These findings suggest that younger patients are ideal candidates for an aggressive surgical approach when deemed resectable.

P386

Derived Neutrophil-to-Lymphocyte Ratio Predicts Disease Specific Survival in Patients Undergoing Curative Intent Resection for Gastric Cancer within a Racially and Socioeconomically Diverse Population M. Tsao,* L.J. Magnotti, O. DeLozier, M. Bright, E. Glazer, J.L. Deneve, S.W. Behrman, M.D. Fleming, D. Shibata, P.V. Dickson. *University of Tennessee Health Science Center-Memphis, Memphis, TN.*

Background Inflammatory biomarkers have been demonstrated to correlate with prognosis in gastric cancer (GC); however, most studies have been performed in Asian populations. The purpose of this study was to evaluate the prognostic value of the derived neutrophil-to-lymphocyte ratio (dNLR) for patients having curative intent resection for GC within a diverse population in a US center. Methods Patients were identified from an institutional database. dNLR was determined from peripheral blood obtained at diagnosis (white blood cell count – neutrophil count). Youden's index determined the optimal cut-point value for dNLR based on disease specific survival (DSS). Significant predictors of DSS on univariable analysis were evaluated by multivariable analysis using Cox's proportional hazards model. Results From 2003-2018, 153 patients had curative intent gastrectomy, median follow up 26.4 months. Median age 65, 55% male, 68 % African American, 27% Caucasian, 4% Hispanic, and 1% Asian. Insurance status: 46% Medicare; 35.3% private; 18.7% state-sponsored/ no insurance. Based on income by zip code, 77.1% were below the median for the state. For patients with >6 months follow up, median DSS for AJCC stage I, II, III disease was 54, 36.4, 20.5 months, respectively ($p=0.009$). The optimal cut-point value for dNLR was 2.86. Elevated dNLR was not significantly associated with any demographic, socioeconomic, or tumor related factor. On univariable analysis, T4 tumor (HR 2.05), LN+ disease (HR 3.77), LVI (HR 1.95) and elevated dNLR (HR 3.91) were significantly associated with worse DSS. In a multivariable model, only LN+ disease (HR 3.53) and elevated dNLR (HR 3.20) remained predictive of worse DSS. Conclusions Within a racially and socioeconomically diverse population in a US center, elevated dNLR was an independent predictor of DSS for patients having curative intent resection for GC. This simple surrogate for systemic inflammation offers prognostic value in patients with GC at the time of diagnosis, regardless of race, socioeconomic status, and independent of tumor related factors.

P387

Incisional Hernia Following Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy M.C. Morris,* L.K. Winer, T.C. Lee, S.A. Ahmad, J.J. Sussman, S.H. Patel. *Surgery, University of Cincinnati, Cincinnati, OH.*

Introduction: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS+HIPEC) for peritoneal carcinomatosis is associated with increased morbidity. Incisional hernia is a known complication following laparotomy, but there is little evidence examining the association between incisional hernias and CRS+HIPEC. This is the first study evaluating the incidence of and risk factors for hernia following CRS+HIPEC in a US population. Methods: This study was a retrospective analysis of 141 patients undergoing CRS+HIPEC between 2012-2018 at a high-volume academic institution. Incisional hernias were identified on postoperative physical exam or cross-sectional imaging. Results: After a median follow-up period of 20.5 months, incisional hernias were found in 14.2% of CRS+HIPEC patients (n=20). Median age was 54 years old, 55% were women, and median BMI was 28.3 kg/m^2. On multivariate analysis, CAD/CHF (OR 5.54, CI 1.16-26.58, $p=0.03$) and SSI (OR 5.92, CI 1.05-33.52, $p=0.04$) were associated with hernia formation. Incisional hernias were not associated with patient age, BMI, preoperative albumin, smoking status, or diabetes (all $p>0.05$). Similarly, there were no differences in peritoneal disease burden, intraoperative blood loss, chemotherapy use, or extent of bowel resections ($p>0.05$). Hernia repair occurred in 60% of cases (n=12). At index operations, fascia was uniformly closed with running looped #0 or #1 PDS. Repair technique consisted of component separation and/or underlay mesh placement. No hernia recurrences were identified after a median follow-up of 11.4 months. Conclusion: Despite anecdotal data, the incidence of incisional hernia after CRS+HIPEC is comparable to that reported in the literature following standard laparotomy. Cardiac comorbidities and surgical site infections are significant risk factors for incisional hernia after CRS+HIPEC. However, as CRS+HIPEC patient selection and overall survival continue to improve, the rate of hernia occurrence may increase. Prospective studies are needed to characterize the true prevalence of incisional hernia and to determine measures for decreasing this complication in this complex population.

P388

Adjuvant Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Patients at High-risk of Peritoneal Metastases M.C. Morris,[1]* V.K. Dhar,[1] M. Stevenson,[2] L.K. Winer,[1] T.C. Lee,[1] J. Wang,[1] S.A. Ahmad,[1] S.H. Patel,[1] J.J. Sussman,[1] D. Abbott.[3] *1. Surgery, University of Cincinnati, Cincinnati, OH; 2. University of Louisville, Louisville, KY; 3. University of Wisconsin, Madison, WI.*

Background: Selection of patients for hyperthermic intraperitoneal chemotherapy (HIPEC) continues to evolve. We hypothesized that adjuvant HIPEC for patients at high-risk of peritoneal progression is safe and associated with favorable outcomes. Methods: The institutional database of a high-volume center was queried for patients with high-risk disease undergoing HIPEC with a peritoneal carcinomatosis index (PCI) of 0. High-risk patients were defined as those with ruptured primary tumors or locally advanced (T_4) disease. Results: 37 patients underwent adjuvant HIPEC, with a median follow-up of 5.2 years. 54% had low-grade (LG) tumors while 46% had high-grade (HG) tumors. Five patients (14%) underwent neoadjuvant chemotherapy, while eight patients (22%) received adjuvant chemotherapy. There were no perioperative mortalities, and the overall complication rate was 43%. For the entire cohort, five year recurrence-free survival (RFS) and overall survival (OS) were 77% and 100%, respectively. Five year RFS and OS were 75% and 100% for LG patients and 81% and 100% for HG patients, respectively. Conclusions: Adjuvant HIPEC for patients at high-risk of peritoneal progression, with PCI 0, is safe and associated with favorable long-term survival. Additional prospective investigation is needed to identify patient populations who may benefit most from HIPEC.

P389

Lymph Node Retrieval is Influenced by Self-Reported Race in U.S. Patients Undergoing Gastrectomy for Gastric Cancer M.C. Tee,* D. Kermode, S. Raman, S.R. Kraemer, N. Pirozzi, J. Franko. *Surgery, Mercy Medical Center, Des Moines, IA.*

BACKGROUND: Gastric cancer lymph node (LN) retrieval during gastrectomy differs significantly between Asian and Western studies. It is unclear whether such disparities are the result of variances in surgical technique, patient population, or both. We aimed to determine whether surgical LN retrieval analyzed pathologically differs among Caucasian American, African American, and Asian American gastric cancer patients undergoing gastrectomy. METHODS: 73,842 patients undergoing gastrectomy for gastric cancer were identified in the National Cancer Data Base (2000-2015) and stratified by self-reported race. Three race groups were selected: Caucasian Americans (n=57,871), African Americans (n=12,580), and Asian Americans (n=3,391). Differences in demographics, cancer characteristics, receipt of neoadjuvant therapy, and surgical lymphadnectomy were compared between these groups. RESULTS: Asian Americans were least likely to receive neoadjuvant chemotherapy (12.9%) or radiation (2.2%), compared to Caucasian (28.0% chemo, 14.9% radiation) and African (15.5% chemo, 3.1% radiation) Americans, $p<0.001$. When restricting our analyses to cases of upfront gastrectomy only, Asian Americans were most likely to have undergone adequate

lymphadenectomy with ≥ 16 LNs retrieved (57.5%) compared to Caucasian (36.3%) and African (36.3%) Americans, p<0.001. Asian-Americans have the highest total LN retrieval, positive LNs, negative LNs, but lowest LN ratio (defined as positive LNs / total LNs) [Table]. CONCLUSIONS: Asian Americans with gastric cancer undergoing gastrectomy at accredited US cancer centers are less likely to receive neoadjuvant therapy, but more likely to have adequate lymphadenectomy, higher LN retrieval, and consequently lower LN ratio. These data suggest factors outside of surgical technique and related to patient population may be responsible for gastric surgery outcome differences seen between Asian and Western studies.

LN Retrieval, Positive LNs, Negative LNs, and LN ratio by Self-Report Race

Variable	Asian Americans	Caucasian Americans	African Americans	P-Value (Kruskal-Wallis)
Total LN Retrieval	18.3 ± 13.5 (16)	12.3 ± 11.5 (10)	12.4 ± 11.8 (10)	0.0001
Positive LNs	4.2 ± 7.5 (1)	3.2 ± 7.5 (0)	3.2 ± 5.9 (0)	0.0001
Negative LNs	14.1 ± 12.4 (12)	9.1 ± 9.9 (6)	9.1 ± 10.1 (6)	0.0001
LN Ratio	0.22 ± 0.31 (0.06)	0.25 ± 0.32 (0.08)	0.25 ± 0.32 (0.10)	0.0003

LN ratio = positive LNs / total LNs. Values are stated as mean ± standard deviation and (median)

P390

Associations Between Patient and Hospital Factors and Margin Positivity in Resectable Esophageal Cancer C.R. Schlick,* D.D. Odell, R. Khorfan, R.P. Merkow, D.J. Bentrem. *Surgery, Northwestern, Chicago, IL.*

INTRODUCTION: Esophageal cancer is a common and lethal condition, with a 5-year survival rate of less than 15%. Positive resection margins are associated with worse survival in patients who undergo esophagectomy. The rate of margin positivity is being evaluated as a quality measure in rectal and gastric cancer, and has been proposed in esophageal cancer, however risk factors for esophageal margin positivity are less well defined. Our objectives were 1) to evaluate rates of margin positivity in resected esophageal cancer 2) to identify patient and hospital factors associated with higher rates of margin positivity. METHODS: The National Cancer Database was used to identify patients who underwent esophagectomy for esophageal cancer with documented margin status from 2004-2015. Univariate analysis was used to identify factors that may impact margin positivity. Associations between patient/hospital factors and margin positivity were assessed by multiple logistic regression. RESULTS: Among 34,783 patients who underwent esophagectomy for esophageal cancer, 7.7% had positive margins. Both patient and hospital factors were found to be associated with margin positivity. African Americans were more likely than non-Hispanic Whites to have positive margins (10.9% vs. 7.4%; OR 1.29 [95% CI 1.07-1.55]), as were Medicare, Medicaid and uninsured patients (8.1-11.8% vs. 7.1% in patients with private insurance; ORs 1.16-1.45). With regard to treatment factors, neoadjuvant therapy was associated with lower margin positivity (6.1% vs. 10.1%; OR 0.44 [95% CI 0.40-0.49]), as was robotic approach (3.6% vs. 7.0% in open cases; OR 0.54 [95% CI 0.38-0.75]). Higher esophagectomy volume at the hospital level was associated with lower margin positivity rates (5.4% in 4th quartile versus 9.7% in 1st; OR 0.63 [95% CI 0.52-0.73]). CONCLUSION: In addition to patient factors, hospital and treatment factors are associated with variability in margin positivity rates in esophageal cancer. Knowledge of these associations will be beneficial in treatment planning and patient counseling, while margin positivity rates can be utilized by hospitals as a quality measure.

P391

Commission on Cancer Center Type is Associated with Overall Survival in Patients with Gastric Adenocarcinoma S. Banerjee,[1]* B. Zhao,[2] F. Vaida,[2] K.J. Kelly.[2] *1. UC Los Angeles/UC San Diego, La Jolla, CA; 2. UC San Diego, La Jolla, CA.*

Introduction: This study aimed to identify factors associated with Commission on Cancer (CoC) treatment center type for patients with gastric cancer, and whether center type is associated with long-term oncologic outcome. Methods: The National Cancer Database (NCDB) was queried for patients presenting with gastric adenocarcinoma between 2004 and 2015. Demographic and clinical factors were analyzed by multivariate logistic regression to identify factors associated with presentation to Academic / Research Programs (ARP) compared to Non-Academic Programs (NAP). Log-rank and Cox regression were utilized to identify factors associated with overall survival (OS). Results: A total of 133,226 patients were identified, of which 39.1% were treated at an ARP. Treatment at an ARP was associated with younger age, lower Charlson-Deyo Comorbidity Score (CDS), higher "Crowfly" distance, urban location, race/ethnicity, and highest income bracket. Patients with AJCC stage 2 & 3 disease presented to either CoC type equally, while patients with stage 4 disease were less likely to present to an ARP than a NAP (P<0.016, OR=0.76, 95%CI 0.73-0.79) relative to stage 0 & 1 disease. Presentation to an ARP was associated with superior median OS than NAP (17.3 months, 95%CI 17.0-17.6 vs 11.1 months, 95%CI 10.9-11.3, respectively) overall, and stage-for-stage (stage 0 & 1: 59.4 months, 95%CI 55.8-63.1 vs 31.4 months, 95%CI 29.9-33.0; stage 2 & 3: 22.9 months, 95%CI 22.1-23.7 vs 17.4 months, 95%CI 16.9-17.8; and stage 4: 6.8 months, 95%CI 6.6-7.0 vs 4.7 months, 95%CI 4.6-4.8, respectively) (Figure 1). Lastly, presentation to an ARP was an independent predictor of improved OS (P<0.011, HR=0.81, 95%CI 0.79-0.82) after adjustment for patient age, CDS, race and stage. Conclusion: Despite CoC efforts to ensure availability of high-quality cancer care at all accredited facilities, there is a survival discrepancy between ARPs and NAPs in gastric cancer. Treatment at an ARP was associated with younger age, lower CDS, urban location, race/ethnicity, highest income bracket and disease stage. Future studies should focus means of improving outcomes at NAPs, and on increasing access to ARPs.

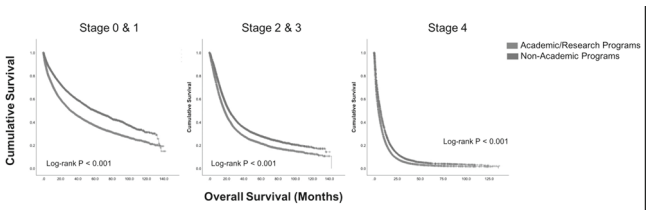


Figure 1: Overall survival of patients with gastric adenocarcinoma presenting to Academic / Research Programs compared to Non-Academic Programs by AJCC disease stage

P392

Disparities Associated with the Receipt of Palliative Care in Patients with Metastatic Gastric Cancer S. Paul,* C.A. Hester, S. Wang, P.M. Polanco, A. Yopp, M. Augustine, J. Mansour, H. Zeh, M. Porembka. *Department of Surgery, Division of Surgical Oncology, University of Texas at Southwestern Medical Center, Dallas, TX.*

Introduction: Metastatic gastric adenocarcinoma (mGA) is frequently associated with debilitating symptoms that negatively impact quality of life. We aim to determine the rate of palliative care (PC) use in mGA and the factors which are associated with receipt of PC. Methods: Using the National Cancer Database, mGA patients were selected. Receipt of PC as defined by the NCDB participant use file was correlated to demographic and clinicopathologic factors. As defined according to NCDB, PC treatment included surgery, radiation, systemic therapy, and pain management to alleviate symptoms. Logistic regression was performed to assess the impact of factors on the likelihood of receiving PC. Overall survival was estimated using the Kaplan-Meier method and compared using log-rank tests. Results: Between 2004 and 2013, 45519 patients with mGA and reported PC status were identified. Median age was 66 years (IQR: 55-76 years) and 64% were male. 7365 (16.2%) patients received PC. PC utilization increased over time (2004-6 13.4%, 2007-10 15.8%, 2011-13 19.1%; p<0.001). Factors associated with PC on univariate analysis included insurance status, education level, income, sex, race, Charlson/Deyo comorbidity score, and year of diagnosis (all p<0.001). On multivariate analysis, female sex (0.87, 95%CI: 0.83-0.92) and minority race were associated with less receipt of PC (Hispanic 0.73, 95%CI: 0.66-0.80, Black 0.87, 95%CI: 0.80-0.95, Asian 0.89, 95%CI: 0.77-0.98 compared to non-Hispanic White patients). Higher education level was associated with greater receipt of PC (1.46, 95%CI: 1.31-1.62). Receipt of PC was associated with decreased overall survival (PC 4.8 months vs no PC 6.0 months; p<0.001). Conclusion: Although use of PC has increased over time, PC is underutilized in mGA. Disparities exist in receipt of PC in regard to race, gender, and education. Additional research is necessary to better optimize PC use in mGA and mitigate potential disparities.

P393

Lymphovascular Invasion is a Bad Actor in Small Bowel Neuroendocrine Tumors J. De Andrade,* A.M. Blakely, A.H. Nguyen, P. Ituarte, D. Li, B. Lee, G. Singh. *Surgery, City of Hope National Medical Center, Duarte, CA.*

INTRODUCTION: Lymphovascular invasion (LVI) has prognostic value in neuroendocrine tumors (NETs) of the appendix, however, its association in small bowel NETs is unknown. METHODS: The National Cancer Database (NCDB) was reviewed for patients with small bowel NETs beginning in 2010, when LVI data became available, to 2013. Clinical data were analyzed for associations with p<0.001 set for statistical significance. RESULTS: 6285 patients with known LVI status were included in analysis. LVI was absent (LVI-) in 3367 (53.6%) and present (LVI+) in 2918 (46.4%). LVI- and LVI+ patients were of similar age (61.6 vs 63.1 years, p=0.225) and male sex (48.2% vs 50.9%, p=0.038) [see table]. LVI- NETs were duodenal 41.5% of the time whereas LVI+ NETs were duodenal only 7.6% (p<0.001). Distal small bowel NETs were more likely to be LVI+ (84.4%). LVI- NETs were more likely to be well-differentiated: 85.8% compared to 79.9% for LVI+ NETs (p<0.001). The median T stage for LVI- tumors was T2 compared to T3 for LVI+ tumors (p<0.001). LVI- patients underwent lymph node resection (LNR) only 60.3% of the time at surgery. LVI+ patients had a more complete lymphadenectomy (92.9%, p <0.001). More lymph nodes were likely to be positive in LVI+ patients vs LVI- patients (median 3 vs 1, p<0.001). Because of the relatively short time frame and follow up, overall survival was similar between the two groups, but subgroup analysis showed LNR in both LVI- and LVI+ patients was associated with improved overall survival, most pronounced when comparing LVI- patients with LNR (mean 58.9 months) to LVI+ patients without LNR (42.0 months, p<0.001). DISCUSSION: When compared to LVI+ tumors, LVI- NETs are more likely to be duodenal, well-differentiated, and less likely to have nodal metastases, suggesting earlier detection rate or more indolent nature. The data suggest that LNR is important, as LNR was associated with improved survival in both LVI- and LVI+ NETs.

		LVI- (n=3367)	LVI+ (n=2918)	P
Age, mean		61.6	63.1	0.225
Male sex (%)		1624 (48.2)	1484 (50.9)	0.038
Site of primary	Duodenum	1083	147	<0.001
	Jejunum	167	152	0.687
	Ileum	1316	1630	<0.001
	Meckel's	41	3	<0.001
	Overlapping	25	52	<0.001
	Not specified	738	937	<0.001
Lymph node status known		n=2030	n=2740	
	Zero nodes resected (%)	810 (39.9)	195 (7.1)	<0.001
	Any nodes resected (%)	1220 (60.1) median positive 1	2545 (92.9) median positive 3	<0.001
Survival, mean (median not met)				
	Without LND	55.6 months	42.0 months	
	With LND	58.9 months	57.6 months	

Clinical and pathologic characteristics associated with lymphovascular invasion. LVI-: no lymphovascular invasion LVI+: lymphovascular invasion present LNR: lymph node resection

P394

The Costs of Gastric Cancer Care at Institutions with and without Cancer Surgery Center Designation Y. Jeong,[1]* J. Hallet,[1] A. Mahar,[2] N. Mittmann,[1] V. Gupta,[1] L. Bubis,[1] N. Coburn.[1] *1. University of Toronto, Toronto, ON, Canada; 2. University of Manitoba, Winnipeg, MB, Canada.*

Intro: Gastric cancer is a clinically and economically expensive cancer to treat. While improved outcomes have been described for designated cancer surgery centers, costs of care at these specialized centers are expected to be increased. We therefore conducted a cost analysis comparing the costs of care for non-metastatic gastric cancer patients treated with gastrectomy between institutions with and without cancer surgery center designation. Methods: Patient-level, population-based data was used from a payer perspective with a 38-month time horizon. Multivariable linear regression with log-transformed costs analyzed cancer surgery center designation and costs of care with adjustment for clinically relevant covariates. Parameter estimates with 95% confidence intervals (CI) were derived to represent proportional changes in median costs, and mean per-patient costs per month alive. Costs were inflated to 2016 United States dollars. Results: A 4% decrease in median monthly costs of care was found for institutions with cancer surgery center designation compared to institutions without cancer surgery center designation, however this difference did not reach statistical significance. Adjusted mean per-patient costs per month alive were $2,400 (95% CI $1,728-$3,332) while the adjusted mean monthly costs of care for patients treated at institutions without cancer surgery center designation was $2,487 (95% CI $1,790- $3,455);(p=0.36). Conclusion: Gastric cancer care is costly, however, specialized cancer surgery care may be provided to patients without increased costs to the healthcare system.

P395

Distant Metastasis from Small Bowel Adenocarcinomas: A National Cancer Data Base Analysis A. Dodd,* B.R. Zambetti, Z. Stiles, F.W. Williard, J. Raine, E. Glazer, P.V. Dickson, S.W. Behrman, D. Shibata, M.G. Martin, J.L. Deneve. *The University of Tennessee Health Science Center, Memphis, TN.*

Introduction: Small bowel adenocarcinoma (SBA) often presents at an advanced stage at initial diagnosis and has a poor prognosis. We examined treatment factors and determinants of outcome for patients who present with distant disease using a national dataset. Methods: The 2004-2015 National Cancer Database (NCDB) was queried for patients with small bowel adenocarcinomas (histologic codes 8140 & 8144). Trends in treatment and outcomes for distant metastasis were examined. Factors affecting overall survival (OS) were assessed with the log-rank test and Cox regression. Results: 16,372 patients were identified. 4928 (30.1%) presented with AJCC pathologic stage IV disease. The most common location of distant metastasis was the peritoneum in 3561 (21.8%), liver 1685 (10.3%), lung 484 (3.0%) and bone 154 (0.9%). Duodenal primary tumors (N=9916) most commonly spread to the liver (N=1137, 21%) and peritoneum (N=2062, 22%). Jejunal tumors (N=2247) metastasized most commonly to the peritoneum (N=532, 24%) followed by the liver (N=176, 14%) which was similar for ileal tumors (N=1619, peritoneum N=316, 20%; liver N=120, 14%). The OS for patients who presented with liver and lung metastasis was poor (6.0 months vs 24.2 months, p<0.0001) and (6.2 months vs 19.1 months, p<0.001), respectively, when compared to those without. Patients with peritoneal metastasis had a worse OS (7.4 months vs 24.3 months, p<0.0001) while patients who had bone metastasis had the worst OS (3.9 months vs 18.1 months, p<0.0001) when compared to those without. For patients with peritoneal metastasis, surgery with chemotherapy improved OS over chemotherapy alone or surgery alone (19.1 months vs 9.1 months vs 4.0 months, p<0.0001, respectively). Conclusions: Approximately 1/3 of SBA patients will present with stage IV disease. The outcome is poor with those having bone metastasis faring the worst. Patients presenting with peritoneal and liver metastasis may benefit from multimodality therapy.

P396

Increasing Lymph Node Yield is Not Associated with Improvement in Survival in Gastric Cancer S.T. Aubry,* P. Strassle, K. Stitzenberg, M. Meyers. *Surgery, University of North Carolina at Chapel Hill, Chapel Hill, NC.*

Background: The impact of lymphadenectomy in gastric cancer has long been debated. Previous work has suggested a relationship between lymph node (LN) yield at the time of gastrectomy. We sought to examine this relationship in the era of increasing utilization of neoadjuvant chemotherapy. Methods: All National Cancer Database (NCDB) patients undergoing gastrectomy with curative intent from 2004 to 2015 were examined. Trends in LN yield over time were assessed using Poisson regression. 5-year survival differences were compared using Kaplan-Meier curves and multivariable Cox proportional hazards regression. Interaction terms were used to assess potential effect measure modification of the LN yield/mortality relationship by T stage, N stage, and neoadjuvant therapy status. Results: 29,741 patients were included. Neoadjuvant chemotherapy use increased significantly over the study period from 24.1% to 43.8%. 44% had ≥15 LN reported (median 13, IQR 5 – 21). The median LN yield increased from 11 LN to 17 LN between 2004 and 2015; however, the median number of positive lymph nodes remained relatively stable. Among those included in the survival analysis, median follow-up time was 34 months (IQR 20 – 57). While there was an association with LN yield and survival in unadjusted data, when adjusted for mulitiple variables, no association was seen between LN yield and survival (Table). This was true for node-negative and node-positive patients. In addition, no effect was seen when LN yield was treated as a continuous variable; HR for an 5 LN increase (1.00, 95% CI 0.99, 1.00) The receipt of neoadjuvant chemotherapy had no impact on whether LN yield was associated with survival. Conclusions: Both the use of neoadjuvant chemotherapy and the LN yield in patients with gastric cancer treated with curative intent have increased over time, although more than half of all patients have less than the recommended 15 LN examined. As opposed to prior reports, there is no association with LN yield and survival when adjusted for clinical and pathologic variables.

	Crude		Adjusted[a]	
Number of LN Examined	HR (95% CI)	p-value	HR (95% CI)	p-value
0 – 4 LN	ref	–	ref	–
5 – 15 LN	0.70 (0.66, 0.74)	<0.0001	1.01 (0.95, 1.07)	0.74
15 – 19 LN	0.81 (0.76, 0.86)	<0.0001	0.98 (0.92, 1.05)	0.62
>20 LN	0.86 (0.82, 0.91)	<0.0001	0.97 (0.91, 1.03)	0.28

Abbreviations: HR, hazard ratio; CI, confidence interval
[a] Adjusted for race, primary insurance type, facility type, region, population density, median residential income, residential education level, and distance to care; age (modeled as a restricted cubic spline), sex, Charlson-Deyo Score, clinical stage, neoadjuvant therapy, surgery type, and year of diagnosis

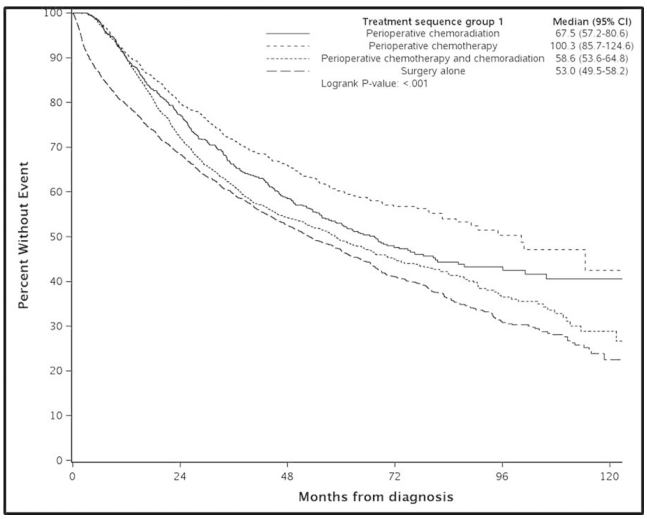
Crude and Adjusted Effect of Lymph Node Yield on Survival

P397

Determining Which Patients with Resectable Gastric Adenocarcinoma Benefit from Adjunctive Therapies C.A. Thiels,* K.T. Hanson, E.B. Habermann, D.M. Nagorney, R.L. Smoot, S.P. Cleary, M.J. Truty, T.E. Grotz. *Surgery, Mayo Clinic, Rochester, MN.*

Background: Based on recent trials, both perioperative chemotherapy and chemoradiation are acceptable treatment modalities for gastric cancer. Our aim was to identify which subsets of patients might benefit more from each particular therapy. Methods: The American College of Surgeons National Cancer Data Base (NCDB) was queried for patients with stage ≥Ib gastric (including gastroesophageal) adenocarcinoma (2006-2015) undergoing curative intent resection. Patients missing treatment sequence data (n=3482) were excluded. Patients were divided into groups based on treatment modality received. Kaplan Meier analysis and Cox proportional hazards models compared overall survival between patients who received surgery only, chemotherapy only, chemoradiation only, or both, regardless of treatment sequence. As the effect of treatment modality on survival varied across patient subsets, separate models were used to assess survival within each subgroup after controlling for age, sex, treatment modality, procedure type, Lauren classification, T-stage, N-stage, margin status, and completeness of LN dissection (>15). Results: 28,678 surgical patients with gastric adenocarcinoma were included with 9,038 (31.5%) receiving surgery only, 6,682 (23.3%) chemotherapy, 3,981 (13.9%) chemoradiation, and 8977 (31.3%) both. Adjunctive therapies were associated with improved overall survival compared to surgery alone (median 33-40 months vs 20 months surgery alone, log rank p<0.001). Kaplan Meier analysis (Figure) and multivariable Cox proportional hazards models demonstrated that improved overall survival was independently associated with chemoradiation, compared to chemotherapy across all clinicopathological subsets except for N0 patients (HR 1.08, p=0.28). Conclusion: Improved OS from multimodality therapy compared to surgery alone was found across all clinicopathological subgroups. However, patients without lymph node metastasis benefited most from the perioperative chemotherapy treatment than the other subgroups. Prospective, randomized trials are needed to further elucidate which subgroups of patients with gastric cancer benefit most from each adjuvant treatment modality.

Figure. Kaplan Meier analysis in patients with node negative gastric cancer comparing chemotherapy only, chemoradiation only, both, and surgery only.



ABSTRACTS

Accepted for
POSTER PRESENTATIONS

GLOBAL PARTNER POSTERS PROGRAM

SSO's Global Partner Posters Program is an important component of the Society's efforts to advance its Mission to improve multidisciplinary patient care by advancing the science and practice of cancer surgery worldwide. Top abstracts from international surgical oncology and relevant cancer surgery meetings and their presenters are invited to be a part of the SSO Annual Cancer Symposium. These posters are identified by the leadership and program committees of the societies as the top abstracts presented at their various meetings in 2018.

72nd Annual Cancer Symposium
Society of Surgical Oncology
March 27–30, 2019
San Diego, California

GPP1

DNA Methylation of SHOX2 as Plasma Marker for Lung Cancers
Z. Liang,* Z.R. Chuan, X. Qi. *National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College*.

Aim: Lung cancer has already been the most frequent malignant tumor in the world, however, some patients with advanced stages diseases were not candidates for surgical treatment for the reason of delayed detection. Although, the LDCT screening project has done a lot in detection of small sized lung nodules, its value in discriminating the benign and malignant diseases may not be very strong. On the other hand, value of aberrant DNA methylation as diagnostic markers for lung cancers has been widely confirmed. Thus, it`s of important potential to combine new tumor markers and LDCT for early detection of lung cancers. Method: A triplex real-time PCR assay for methylated DNA of SHOX2, and ACTB as control assay was developed. Total DNA was extracted from 3.5ml plasma samples and bisulfite converted utilizing a commercially available kit. After purification DNA was assayed in PCR triplicates, cycle threshold values were aggregated utilizing a predefined algorithm. Receiver operating characteristic and the area under the curve (AUC) were analyzed. Result: 101 samples were collected in the study, and 13 patients were diagnosed with benign lung diseases, the left 88 patients were with lung cancers. Specifically, 53 patients were in the pT1 group, 29 lung cancer patients were in the pT2 group and 6 lung cancer patients were diagnosed with pT3 stage. In lung cancer patients, the methylation levels of SHOX2 were elevated significantly ($p < 0.05$) with increasing of T stages. While, higher but not significantly methylation levels of SHOX2 were observed in positive lymph nodes group compared with negative lymph nodes group ($p > 0.05$). ROC of SHOX2 in this studied population was concluded with AUC of 0.573 (95% CI, 0.403 to 0.743). Conclusion: Although, methylation levels of SHOX2 in lung cancer patients with advanced T stages and N stages were higher than early stages lung cancer patients, its diagnostic value in distinguishing lung cancers from non-malignant diseases still needs to be studied with more enrolled candidates.

GPP2

Integrated Analysis of Trefoil Factor Family Members in Breast Cancer: Tumor Suppressor or Oncogene? *R. Ge,* J. Li, G. Wang, S. Siddharth, Q. Wu, C. Chen, S. Zhu, S. Sun. Huadong Hospital Affiliated to Fudan University, Renmin Hospital of Wuhan University, Johns Hopkins School of Medicine.*

Background: Trefoil factor family (TFF) peptides are often found abnormally expressed in numerous solid malignancies, including breast cancer. TFFs are widely known for epithelial healing and protection. However, during tumorigenesis, a variety of studies demonstrated that TFFs could act as a tumor suppressor or as an oncogene in different types of tumor. However, the role of TFFs in breast cancer is not clear where both an oncogenic and a tumor suppressor function have been attributed. Materials and methods: We evaluated the expression profiles of three members of TFF peptide genes in breast cancer using transcript quantification data obtained from the Oncomine and CCLE database, as well as the co-expression patterns in breast cancer. Furthermore, we performed GOBO analysis to deeply mine TFF's expression in different molecular subtypes and a collection of breast cancer cell lines. TFFs expression and methylation were retrieved from TCGA database, the correlation between methylation and expression was analyzed using the MEXPRESS tool. Finally, associations between overall survival(OS) and TFFs were analyzed using Kaplan-Meier Plotter. Results: The mRNA expression levels of TFF1, TFF2, TFF3 were significantly elevated in breast cancer tumor tissue. Data mining analysis revealed that the expressions of TFF1 and TFF3 were significantly higher in ER+ tumors with respective to ER- tumors or normal tissue. The co-expression analysis from Oncomine revealed that TFF1 and TFF3 were significantly co-expressed with ESR1. In addition, the expressions of TFF1 and TFF3 were associated of different genes of the ER pathway in ER+ tumors. We also disclosed that TFF1 and TFF3 are significantly methylated in basal like tumors. In survival analysis, Kaplan-Meier analysis demonstrated that low TFF1 and TFF3 expression levels were associated with poor overall survival in patients with ER positive patients. These over-expressed genes in tumor tissues of breast cancer could significantly prolong the patients' overall survival. Conclusion: These results indicated that TFF1 and TFF3 are potential predictive and prognostic biomarkers for ER+ breast cancer, probably due to the interaction with key genes of the ER pathway.

GPP3

A Comparison of Machine Learning Algorithms for Outcome Prediction in Neoadjuvant Chemotherapy for Esophageal Squamous Cell Carcinoma X. Kang,* C. Huang. *Peking University Cancer Hospital, College of Cybersecurity Sichuan University*.

Background: Accurate measurement of neoadjuvant therapeutic outcomes is highly desirable to optimize surgical decision-making. Machine learning algorithms for prediction of treatment response are becoming more popular in surgery literature. The purposes of this study are to compare such algorithms specifically for locally advanced esophageal squamous cell carcinoma (ESCC) patients and to estimate their discriminative performance for neoadjuvant chemotherapy outcome prediction. Methods: The study used a prospective database of 1,523 consecutive patients with ESCC undergoing esophagectomy between 2000 and 2016. Eligible locally advanced ESCC patients undergoing neoadjuvant chemotherapy followed by surgery were selected. The treatment outcome, tumor regression grade (TRG), assessed as the percentage of residual primary ESCC cells in resection specimens, was classified histologically by pathologists. Three common classification algorithms with built-in feature selection (random forest, support vector machine, naïve Bayes) were employed for data analysis. Performance metric (area under the curve [AUC]) was computed. We ranked classifiers by AUC to determine which classifier is likely to perform well in future studies. Results: In total, 270 ESCC patients were included. The overall follow-up rate and median follow-up duration were 92.6% and 38.6 months, respectively. Twenty-six patients (9.6%) had no residual primary tumor (ypT0), 56 (20.7%) had 1% to 10% residual cancer, 49 (18.2%) had 11% to 50%, 139 (51.5%) had more than 50%. Survival was worse with increasing residual primary ESCC, plateauing at 50%. The support vector machine (AUC 0.69), naïve Bayes (AUC 0.68) and random forest (AUC 0.67) showed the similar overall best discrimination, but there was no single best classifier. Conclusions: Better TRG in response to preoperative chemotherapy is associated with a linear increase in survival after esophagectomy for locally advanced ESCC. Machine learning algorithm classifiers could be the choice for investigators when building classification models or to benchmark one's own modeling results against.

GPP4

A Prospective Colorectal Liver Metastasis Database with an Integrated Quality Assurance Program (CLIMB): Primary Analyses of Variations in European Clinical practices and surgical complications after complex liver metastasis surgeries S. Evrard.* *Institut Bergonié Université de Bordeaux.*

CLIMB, the first project launched by SURCARE, the EORTC & ESSO surgical quality assurance infrastructure, is a prospective study to benchmark quality of practices for unresectable or borderline resectable colorectal liver metastasis (CRLM) surgery. CLIMB included 14 specialized centers in 9 countries. Eligible patients were registered after MDT & pre-surgery. Primary endpoint was 30 & 90 day surgical complication rate (Clavien-Dindo Classification). Data about quality indicators such as practice of multidisciplinary team (MDT), use of biomarker testing, type of chemotherapy regimen, imaging used pre-surgery and post-operative (to day 90) complications rates were collected. Among 210 patients registered, 126 (60%) had at least one liver surgery: of these 73% had left-sided or rectal primary tumor, 95.2% had synchronous primary and liver metastasis, 19.8% had extra-hepatic lesions and CRLM. An MDT with liver surgeon, oncologist and radiologist assessed patients with a median of 30.5 days from last MDT to surgery. 122 (96.8%) received pre-surgery chemotherapy with a median duration of 4.9 months. Among those, 86.9% used only 1 regimen, usually FOLFOX. Only 65.1 % received targeted therapy. Median time interval of last pre-surgery imaging was 34.5 days. Among those with pre-surgery image data (87.7%), 54.1% received less than CT scan with MRI while 45.9% received at least CT with MRI. Most patients (N=95, 75.4%) had one stage liver surgery while 30 (23.8%) had two stage liver surgery, 10 of whom had ALPSS. Over-all complication rates for one stage surgery were 53.7% (95% CI 43%- 64%), 17.9% (95% CI: 11%-27%) with grade ≥3 and 93.3% (95% CI: 78%- 99%) for two stage surgery, 46.7% (95% CI:28%- 66%) with grade ≥3 including two deaths. Infections, bile leak, post hepatectomy liver failure grade A, fluid retention and anemia were most commonly reported. CLIMB prospectively collected data on upfront unresectable CRLM surgery. Two-stage surgery had more Clavien-Dindo grade≥3 complications. Harmonizing standards in MDT evaluation, biomarker testing and imaging may improve outcomes. SURCARE

will use these indicators to develop trials with enhanced QA methods to improve cancer surgery.

GPP5

Pancreaticojejunostomy Versus Pancreaticogastrostomy Following Whipple's Procedure: A Comparative Study A.A. Mirza.* *Regional Cancer Centre*.

Pancreatoduodenectomy (PD) remains gold standard for management of patients with Carcinoma head of pancreas (HOP) and periampullary neoplasms. The procedure is considered safe when performed in high volume centers with mortality of 3-5%. Despite low mortality, morbidity remains high, usually due to development of postoperative pancreatic fistula, ranging 2-28%. Although several trials have studied the efficacy of anastomotic techniques, there is no clear consensus on which technique is superior in terms of decreased rate of pancreatic fistula. This study aims to compare the anastomotic techniques of pancreaticojejunostomy [PJ] versus pancreaticogastrostomy [PG] following Whipple's Procedure performed in a Surgical Oncology department of a tertiary cancer centre in South India. Method: A cohort study of patients who underwent Whipple's Procedure in Department of Surgical Oncology in Regional Cancer Centre from 2015 to 2017 was carried out. The primary outcome studied was the rate of post-op pancreatic leak, while peri-operative outcomes of blood loss, operative time, length of hospital stay, etc were compared. The International Study Group of Pancreatic Fistula (ISGPF) definition of pancreatic fistula according to the 2016 update was used to define pancreatic fistula. Results: 85 patients underwent Whipple's procedure during the study period. 42 PG and 43 PJ were performed. There were 62 periampullary carcinomas and 23 carcinoma HOP. Grade A leaks were seen in 13 patients in PG group and 10 in PJ (P value 0.83). Incidence of Grade B leaks was 3 in both groups. Grade C leaks were seen in 2 patients in PJ and 1 in PG group. There was no significant difference in perioperative outcomes between the two groups. On logistic regression analysis; soft pancreas, duct size less than 3mm and presence of preoperative cholangitis were significantly associated with leak. Conclusion: Our study shows that the type of enteric anastomosis (PG vs PJ) following Whipple's procedure are equivalent in terms of development of clinically relevant post-operative pancreatic fistula. The choice of reconstruction should be left to the discretion of the surgeon and institutional protocol.

GPP6

Immunological Effects of Laparoscopic Versus Open Colorectal Surgery: A Leap in Lap S. Kulkarni.* *Regional Cancer Centre*.

Introduction: Laparoscopic approach in colorectal surgery has developed into an interesting therapeutic alternative as it allows for rapid recovery with early return to preoperative activity with significantly shorter hospital stay due to limited surgical trauma. Despite promising clinical results, only limited information is available regarding perioperative immunological effects of laparoscopic surgery when compared to open colorectal surgery. This is the first study to be conducted in India. Aims & Objectives: The objective of our study was to compare the immunological effects of laparoscopic surgery with open colorectal surgery. Comparison of surgical and post-operative outcome of open versus laparoscopic surgery. Methods: A prospective study was conducted on 52 patients. All were above 18 years and had non-metastatic colorectal malignancy treated with curative intent. Patients with known immunological dysfunction, on immunosuppressants were excluded. Informed consent was taken. Blood samples were taken from all eligible patients on pre-op day and POD (Post-operative day) 1, 3 and 5. CRP (C- Reactive Protein) was done and NK (Natural Killer) cells were quantified by profiling of CD3-CD16+ and CD56+. Minimally invasive colorectal surgery was performed as a laparoscopic-assisted procedure with removal of the resected specimen via a horizontal mini-laparotomy or perineum in case of APR. Conventional colorectal surgery was performed via a vertical midline incision.After removal of the resected specimen, stapler or hand sewn anastomosis was performed. Results: Serum CRP showed trend of return to normal value early in laparoscopic compared to open arm with a significant p value of 0.041, 0.001 on POD 3 & 5. Drop in NK cells percentage was less in laparoscopic arm with a significant p value of 0.003, 0.002 on POD 1 & 3 indicating preserved cellular immunity. Conclusion: Immune function seems to be well preserved after laparoscopic approach compared to open approach. This study highlights that immunological effects seen post-operatively with benign conditions is consistent with malignancy also. Long term follow-up is required to assess whether preserved immunological effects translate into overall survival advantage.

GPP7

Analysis of Critical Complications Following Upfront Verses Re-do Surgery for Thyroid Cancer N. Kumar.* *All India Institute of Medical Sciences*.

Background: Thyroid cancer is the most common endocrine malignancy with a rapid world-wide rise in incidence in the past few decades. Total thyroidectomy with or without neck dissection is the mainstay of treatment with good long-term survival. Sub-optimal or incomplete surgical interventions are common at community level practice. Re-do surgery for thyroid cancer carries a higher risk of morbidity especially related to parathyroids and recurrent laryngeal nerve. We present our experience of thyroid surgery related morbidity in upfront versus redo thyroid surgeries. Methods: All the cases of biopsy proven differentiated thyroid cancer (DTC) undergoing surgery between 2009 to 2016 were analyzed from prospectively maintained computerized database. An analysis was performed for clinical spectrum, Patterns of surgical intervention, and critical morbidities in patients undergoing upfront surgery (Group-1) and re-do surgery (Group-2). Results: A total 270 patients fulfilled inclusion criteria. Group-1 had 151 patients and group-2 119 patients. Median age at presentation was 40 years with female predominance. Among all histological variants of thyroid cancer, PTC was the commonest variant followed by FTC. Majority of the patients had Total thyroidectomy in both the groups: group-1 (92.7%); group -2 (81.5%) and almost two thirds of patients had neck dissection in both the groups. Reported complications in the patients who operated outside were transient hypocalcemia (5.88%), permanent hypocalcemia (10.08 %) and RLN related vocal cord palsy (7.56%). The patients who operated at IRCH, the reported complications were transient hypocalcemia (3.31%), permanent hypocalcemia (1.98 %) and RLN related vocal cord palsy (0.66%) in group-1 and in group-2 (3.36%, 2.56%, 2.5% respectively). Conclusion: Surgical morbidity is one of the key determinants of outcome and in general higher rates of parathyroid and recurrent laryngeal injuries were reported in patients undergoing redo surgeries. How ever results of the current study indicate the possibility of achieving comparable morbidity in redo cases in high volume centers with experienced surgeons.

GPP8

Microvascular Free Flap Reconstruction in Recurrent Head and Neck Squamous Cell Cancers A.H. Pareek.* *Asian Cancer Institute*.

Background & Introduction: Squamous cell carcinoma of the head and neck presents a treatment challenge since it is often aggressive and has a high rate of recurrence. Recurrent tumor at the primary site is the most common pattern of failure, occurring in approximately 20-30% of patients. Regional recurrence in the neck occurs in 10-15%. Free flap reconstruction in previously irradiated patients decreases local wound complications by bringing non-irradiated well-vascularised tissue into the wound. In this study, we present our experience with free single as well as multipaddled microvascular free flaps for functional and aesthetic reconstruction of complex head and neck soft tissue defects after excision of recurrent oral cancer. Methods: 26 patients with recurrent squamous cell carcinoma of the oral cavity underwent salvage surgical treatment. Microvascular free flaps including free anterolateral thigh flap, free radial forearm flap and free fibula osteocutaneous flap were used for the reconstruction of the extensive defects caused by excision of the tumors. The complications of the flap and the prognosis of the patients were analyzed with a follow-up from 1 to 14 months. Results: The overall success rate of the flap was 92.3%. Flap related complications occurred in 6 patients (23.07%). Major complications occurred in 2 patient (7.6%) and minor complications occurred in 4 patients (15.38%). Conclusion: Microvascular free flaps are a reliable choice for reconstruction of complex soft tissue defects caused by excision of recurrent oral cancer because it can provide several independent skin paddles for multiple separate defects with minimal donor site morbidity.

GPP9

Cytoreductive Surgery & HIPEC for Peritoneal Surface Malignancy: Clinical Spectrum, Morbidity and Mortality in 102 Cases
B. Bansal.* *All India Institute of Medical Sciences*.

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) has recently emerged as a viable management option for peritoneal surface malignancy (PSM). However, review of literature reveals a steep learning curve and high morbidity and mortality. We present our experience of first 100 cases of CRS and HIPEC. Methods: All patients

of PSM undergoing CRS & HIPEC between January, 2015 to June, 2018 were identified from a prospectively maintained surgical oncology database and analyzed for clinical spectrum, surgical morbidity and peri-operative mortality. Results: A total of 102 cases of PSM were identified from the database. 77.5% of the patients were females. Epithelial ovarian carcinoma (56.9%) was the most common pathology, followed by colorectal carcinoma (15.7%), pseudomyxoma peritonei (14.7%), malignant mesothelioma (7.84%). Total peritonectomy was performed in 50.9% of cases and disease specific peritonectomy in 49.1%. Optimal CRS could be achieved in 90.2% of patients. Cisplatin and mitomycin were the most common drugs used. A total of 35% of patients had morbidity including deep vein thrombosis (7.8%), sub-acute intestinal obstruction (5.9%), wound dehiscence (3.9%), lymphocele (3.9%), ureteric injury (3.9%), acute renal failure (3.9%), entero-cutaneous fistula (3.9%). The overall treatment related mortality was 2.9% (3/102). The incidence of major morbidities was relatively less and there was no mortality in last 50 cases in comparison to first 50 cases. Conclusions: The most common indication for CRS and HIPEC was carcinoma ovary followed by colorectal and appendicular neoplasms with PMP. Overall morbidity and mortality of the current series are comparable to global rates reported from high volume centers. A protocol based multidisciplinary team approach plays an important role for successful outcome in executing complex treatments like CRS and HIPEC.

GPP10

Diagnostic Accuracy of F18-FDG PET/CT in Preoperative Nodal Staging of Esophageal Cancer: A Comparison with Histopathological Findings N.V. Gulavani*. *Apple Cancer Institute*.

Background: Purpose of this study is to more accurately assess the diagnostic accuracy of PET/CT for Lymph node metastasis of carcinoma. We prospectively compared the preoperative lymph nodal staging findings on PET/CT to the postoperative histopathological examinations in patients undergoing esophagectomy with 2/3 field lymphadenectomy. Methods: The data of 61 patients with squamous or adenocarcinoma esophagus undergoing F18-FDG PET/CT and surgery with or without neoadjuvant treatment was analyzed prospectively. In principle, a SUVmax of 5.0 or more in the tracheal bifurcation and pulmonary hilum or a value of 2.0 or more in other sites was considered metastatic. Lymph nodal metastasis by PET/CT and its pathological examination were compared across different nodal levels to calculate diagnostic accuracy. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of PET/CT was calculated using statistical software SPSS version 15.0, IBM and Open Epi ver. 2.3. Results: In patients undergoing primary surgery, sensitivity, specificity, PPV, NPV and diagnostic accuracy were 61.54%, 90%, 42.11%, 95.19% and 86.99% respectively. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of PET/CT scan done before neoadjuvant treatment were 35.29%, 76.89%, 25.71%, 83.98% and 69.2% and after neoadjuvant treatment they were 27.12%, 89.08%, 34.04%, 85.47%, and 78.43% respectively. The diagnostic accuracy of PET/CT in squamous carcinoma was 91.01%, 76.16% and 82.67 % and in patients with adenocarcinoma was 76.47 %, 57.69 % and 70.34 % respectively, for primary surgery, before neoadjuvant treatment and after neoadjuvant treatment groups. Thus accuracy was better for squamous carcinoma, which is consistent with the international literature. Conclusion: Our study showed higher diagnostic accuracy of PET/CT in squamous carcinoma than adenocarcinoma. Higher specificity of PET/CT for preoperative nodal assessment, as shown in our study may help in surgical decision-making pertaining to the extent of lymph node dissection during surgery of esophageal carcinoma, especially in patients with co-morbidities. Although the diagnostic accuracy is good, PET/CT alone may be insufficient in surgical decision making, due to its lower sensitivity. Lower sensitivity may indicate the presence of inflammatory mediastinal nodes (e.g tuberculosis/ sarcoidosis), especially found in the Indian subgroup of patients, which can be false positive on PET/CT.

GPP11

A Prospective Two Arm Comparative Study of Indo Cyanine Green (ICG) Enhanced Fluorescence Imaging Versus Conventional Methods (Blue Dye and Radiocolloid/Hand Held Gamma Probe) for Sentinel Lymph Node Detection in Early Breast Cancer: Going Beyond the Horizon R.C. Kumar.* *MANIPAL COMPHRENSIVE CANCER CENTRE*.

Objectives: The objective of the present study was to assess the performance of sentinel lymph node (SLN) biopsy using indocyanine green (ICG) fluorescence method compared with that using the conventional method in detection of sentinel lymph nodes. Materials & Methods: 60 patients diagnosed with early breast cancer underwent the SLNB procedure using technetium-99m radio colloid (R), methylene blue dye (MB), and ICG. All SLNs that were removed during surgery were labelled as hot, blue or/and fluorescent and sent for pathological examination. The detection rate of SLNs and positive SLNs, and the number of SLNs of ICG, MB+ R were compared. Injection safety of ICG and MB was evaluated. Modified Delphi consensus developed quality indicators for SLNB questionnaire was also used to assess the quality of SLNB. Results: Sentinel Lymph Node was identified in all 60 cases. Total Sentinel lymph nodes removed was 145 (Mean=2, Range 2-5), ICG was able to identify more nodes than the dual dye technique. The identification rate with the dual dye technique was 95%, with blue dye alone 93.6% and with radioisotope alone 96.8% whereas with ICG alone was 100%. 28(46.6%) out of 60 patients had positive nodes which was identified by both dual dye & ICG. We are in par with all the quality indicators mentioned in the modified Delphi consensus. None of the patients had any local or systemic reaction with ICG, 3 patients with blue dye had tattooing & staining of skin. Conclusion: ICG is as effective as the dual dye for SLNB. In addition, as a near-infrared dye, it has the advantages of real-time visualization, lower cost, and wider availability, since no radioactive material needs to be handled. It can be a boon for developing countries & second tier centers of developed country where there is limited access to nuclear medicine department facility & the cost involved in its establishment.

GPP12

The Adequate Resection Margin of Hepatocellular Carcinoma According to the Tumor Microenvironment S.H. Kim,* Y.T. Kim. *Yonsei University Wonju College of Medicine*.

Background: There is no consensus on the safe resection margin in patients with hepatocellular carcinoma (HCC). Surgeons decide the extent of resection according to residual liver function and tumor location. We investigated the change of tumor microenvironment according to the resection margin. Methods: We prospectively collected the specimen of 60 patients with HCC from April, 2012 to Jan. 2016. We selected three portions of specimens as follows: tumor, 1cm and 2cm margin normal tissue. We investigated the expression status of tumor microenvironment genes by using real-time polymerase chain reaction. We compared the expression status according to the stemness marker expression status, recurrence, HCC gross type and positron emission tomography (PET) positivity. We divided the patients into two groups based on the classification of The Korean Liver Cancer Study group as follows: group 1 included expanding and vaguely nodular types whereas group 2 included nodular with perinodular extension, multinodular confluent and infiltrative types. Results: Group 2 had a higher prevalence of PET positive [6 (37.5%) vs 10 (62.5%)] and recurrence [5 (16.7%) vs 17 (56.7%)]. However, in cases with more than 1cm resection margin, there was no difference of recurrence rate [9 (75%), p=0.017 vs 8 (44.4%), p=0.06]. Beta-catenin was significantly decreased and E-cadherin was significantly increased according to the resection margin in group 1. These expression patterns were similar in PET negative group. Group 2 and PET positive patients did not show any significant change of beta-catenin and E-cadherin until 2cm resection margin. Conclusions: Although our study has the limitation of a small number of cases, the data suggest that patients with HCC of expanding and vaguely nodular gross types may safely undergo surgical resection with a narrow resection margin and patients with HCC of nodular with perinodular extension, multinodular confluent and infiltrative gross type must undergo surgical resection with more than 2cm resection margin because of tumor microenvironment condition.

GPP13

Comparisons of Cancer-Associated Fibroblasts (CAFs) on the Intratumoral Stroma and Invasive Front in the Colorectal Cancer Patients G.M. Son.* *Pusan National University Yangsan Hospital*.

Aim: The aim of this study was to evaluate the cytomorphologic maturity and molecular activation of cancer-associated fibroblasts (CAFs) in the intratumoral stroma and invasive front in colorectal cancer and how they affect cancer invasion and long-term oncologic outcomes. Methods: The cytomorphologic maturity of and α-smooth muscle actin (α-SMA), fibroblast activation protein α (FAPα), and fibroblast-specific protein 1 (FSP-1) expression in CAFs in the intratumoral stroma (CAF[IT]) and the

invasive front (CAF[IT]) of colorectal cancer tissues were compared. The correlations between CAF maturation, molecular activity markers, and cancer invasion were evaluated by network analysis. Overall survival and systemic recurrence were analyzed to assess the oncological effects of CAF properties. Results: The cytomorphologic maturation rate was comparable between CAF[IT] and CAF[IF]. The presence of mature CAFs was related to epidermal growth factor receptor overexpression on cancer cells. Expression rates of α-SMA and FAPα were not different between CAF[IT] and CAF[IF]. FSP-1 expression was more frequent in CAF[IT] than in CAF[IF]. There was a significant decrease in FSP-1 expression in CAF[IT] and CAF[IF] in higher stages. Immature CAF[IT] were related to infiltrating growth. FSP-1 expression on CAF[IF] was inversely related to perineural invasion and lymph node metastasis. FSP-1 expression and immature CAF[IF] were favorable prognostic factors of survival, but CAF maturity did not significantly affect survival and systemic recurrence for non-metastatic colorectal cancer patients. Conclusions: Cytomorphologic maturity and molecular activation markers were not different in CAFs in the intratumoral stroma and invasive front of colorectal cancer. CAF maturation types were bi-directionally related to cancer invasion.

GPP14

Feminizing Adrenal Adenoma: Case Report F. Silva.* *Hospital Juarez de México*.

Introduction: Adrenal tumors that secrete sex hormones are quite rare, but are almost always symptomatic. The term feminizing adrenal adenoma describes those tumors that secrete estrogens, especially in adult males. Bilateral gynecomastia is the main symptom in almost all patients with or without other manifestation of gonadal deficiency. Presentation of the case: Male patient of 58 years, presents tumor-like lesion in the right inguinal region, performing a resection of the same with a report of Dermatofibrosarcoma Protuberans with positive surgical margins for neoplasia. It is referred to complete surgical treatment. During its initial approach, bilateral gynecomastia was evidenced, which required study protocol: hormonal profile with hypogonadotropic hypogonadism, normal thyroid profile, and hyperprolactinemia (prolactin: 20.4ng/dl). CT reports 1.2x0.8 inch left suprarenal incidentaloma as well as 8mm hypophyseal microadenoma. It is cataloged as a feminizing adrenal producer of estrogen. The case was discussed and it was determined to carry a laparoscopic adrenalectomy, which was performed without incident; concomitantly resected and gave margin to the lesion in groin. Histopathological report: adenoma of adrenal cortex of 1 inch, without capsular or venous sinusoidal invasion, non-neoplastic gland; focal residual dermatofibrosarcoma and lymph node negative to neoplasia. No postoperative complications, endocrinology and genetics determine it is Multiple Endocrine Neoplasia Syndrome 1. MRI shows an 8mm hypophysis adenoma with extension outside the diaphragm and erosion of the floor of the chair without affecting the optic system, for which it receives treatment with bromocriptine. He was taken to a bilateral subcutaneous mastectomy with preservation of the nipple, finding breasts of 400gr without palpable tumors. Currently in follow-up and control, clinically and paraclinically without evidence of tumor activity. Last control of prolactin in 19ng / dl and rest of hormonal profile without alterations. Conclusions: Due to the rarity of adrenocortical sex hormone-producing tumors, evidence-based data regarding diagnosis, classification, therapy and prognostic factors are hardly available. Surgery is the only therapeutic option with curative intent for patients with tumors that produce sex hormones. Laparoscopic adrenalectomy has become the operation of choice, with shorter hospitalization, less postoperative pain and fewer complications compared to open adrenalectomy

GPP15

Renal Cancer with Thrombus in the Inferior Vena Cava According to the Neves Classification S.I. Gamboa Hoil,* M.C. Andres, H.T. Narciso. *Oncology Hospital, National Medical Center, Mexican Institute of Social Security*.

Renal cancer represents 4.7% of all tumors treated in our Oncology Hospital. Renal cancer has a unique feature, vascular invasion, which occurs in 4-15% of patients. Our objective is to describe the characteristics of patients with renal cancer and thrombus in inferior cava according to the Neves classification. Methods. All patients with renal cancer and thrombus in the inferior vena cava of the Oncology Hospital, treated with surgery, at the National Medical Center, in Mexico City, from January 2003 to August 2016. Results. Of the 134 patients, the male gender was observed in 51.4%, M:F ratio of 1.06: 1, with an average age of 68.5 for level I and 60.4% for level IV ($p = 0.49$ for all levels). The triad hematuria, tumor and pain (7%), as well as the site affected right (67%) and left (33%) did not present significant differences according to the thrombus level. The Chevron and thoracoabdominal approaches, as well as liver mobilization, were observed more frequently in levels III and IV (36.5% and 31.3% respectively), with statistical significance. The size of the tumor, bleeding and surgical time were progressively greater, being 8.5 cm, 1033 ml and 3.1 hrs in level I; and of 16.1 cm, 3 064 ml and 6.5 hrs in level IV. The most frequent histology was clear cells in 86% ($p = 0.27$ for all levels) A higher frequency of positive lymph nodes was observed in levels III and IV with 20.1% ($p = 0.001$) Distant metastases were observed in 27% of patients ($p = 0.36\%$) When comparing free thrombus and adhered to the wall vs invasion to the wall in levels I and II (91%) vs III and IV (12%) we found a p 0.00001. Mortality of 4.5% was observed due to hypovolemic and septic shock. Survival in patients with inferior vena cava thrombus according to the Neves classification showed no significant differences at 3 years ($p = 0.09$) and 5 years ($p = 0.347$). Conclusions. The global survival of 60% at 5 years justifies the surgical treatment of this pathology, although a multidisciplinary approach is required.

GPP16

Relation of cancer-related gene mutations and clinico-pathological factors in oral squamous cell carcinoma N. Batta,* M. Pandey. *IMS, BHU Varanasi*.

Background & Introduction: Oral squamous cell cancer (OSCC) is the most common malignancy among males in India and the eighth most common cancer worldwide occurring as a result of an interaction between the habits/environmental (tobacco, betel quid, etc.) and genetic (EGFR, TP53, etc.) factors. This study was carried out to evaluate the frequency of functional and non-functional gene mutations in OSCC in the background of tobacco and other habits. Methods: A single group prospective study including 36 operable OSCC was carried out to elucidate relationship between 50 selected gene mutations and tobacco habits, clinico-pathological factors and their survival outcomes. Pathological staging was done according to TNM AJCC 8th. Genetic profiling was done by using semiconductor based Next Generation Sequencing, performed on Formalin fixed paraffin embedded tissue block. Results: The mean age of patients was 46.6 years, 94.4% being males. Most common site was buccal mucosa (44.4%) followed by tongue (30.6%), lower alveolus (16.7%), lower lip (5.6%) and upper alveolus (2.8%). Patients presenting with stage IV, II and III were 44.4%, 38.9%, 13.9% respectively. Genetic mutations were present in 25 patients out of which 14 had >1 mutation. Tp53 mutation was the most common (41.7%) and had significant association with tumor size >4 cm ($p=0.032$), followed by CDKN2A (19.4%), HRAS (13.9%), PIK3CA (8.3%), KIT, EGFR, BRAF (2.8% each) etc. Depth of Invasion >10mm was present in 16 patients, out of which 8 had Tp53 mutation ($p=0.320$). The 18 months disease free survival for TP53 mutation present and absent were 66.7% and 81.0% respectively. PIK3CA and HRAS had significant association with site of tumor, i.e., lower alveolus ($p=0.015$) and lower lip (0.016) respectively. Conclusions: EGFR downstream mutation pathways play a definitive role in tumorigenesis of various sites of oral cavity, especially the role of TP53 mutation in advanced stage tumors. Future study of the molecular biology and pathogenesis of OSCC can help in stratification of groups in predicting biomarkers, treatment selection and choosing novel therapeutic approaches.

GPP17

Impact of microsatellite instability status and programmed death-ligand 1 expression on tumor response after neoadjuvant chemoradiation therapy in locally advanced rectal cancer S.U. Bae,* W.K. Jeong, S.K. Baek. *Keimyung University Dongsan Medical Center*.

Purpose: We designed this study to evaluate relations between microsatellite instability (MSI) status and programmed death-ligand 1 (PD-L1) and tumor response following neoadjuvant concurrent chemoradiation therapy (CCRT) in locally advanced rectal cancer. Materials and methods: In the prospective study, we collected 54 rectal adenocarcinoma patients who underwent neoadjuvant concurrent chemoradiation therapy between August 2016 and December 2017. With exclusion criteria, we finally included 24 patients and evaluated the PD-L1 expression using immunohistochemistry (IHC) and tested the MSI status with pre- and post- CCRT samples. Human colorectal cell lines DLD 1, HT-29 and HCT116 were obtained and cell morphology, cell viability, and PD-L1 expressions were evaluated using

flow cytometry 24, 48 and 72 hours after irradiation. Using 4-fields box technique, 50.4 to 54 Gy in daily 1.8Gy fractions of radiation was delivered to pelvis including rectal mass and surgery was performed 6 to 8 weeks after completion of neoadjuvant CCRT. Tumor response was estimated by using Mandard grading system. Results: According to the tumor regression grade, patients were classified into two groups; responder (grade 0, 1 or 2; 9 patients, 37.5%) and non-responder (grade 3 or 4; 15 patients, 62.5%). Between the two groups, there was no statistically significant differences in several tumor characteristics including histologic type, lymphocytic response, tumor budding, BRAF or K-ras mutations except tumor stage; more patients with advanced T stage in non-responder ($p = 0.019$). MSI-high status was reported in two responders (25%), but no one with pre-CCRT MSI-high status in non-responder group (relative risk = 3.143, 95% CI = 1.705 - 5.794). High PD-L1 expression on tumor marginally significantly increased from 16.7% before CCRT to 45.0% after CCRT by IHC ($P = 0.053$), especially in non-responder group. PD-L1 gene expression by irradiation in three human cell lines using flow cytometry analysis was increased, mostly in radio-resistant cell line, DLD 1. Conclusion: This prospective study verified the chemoradiation-induced immune-oncologic shift toward increases in PD-L1 expression that may be associated with radio-resistance. MSI status was associated with tumor response after chemoradiotherapy for locally advanced rectal cancer.

GPP18

Vertical Rectus Abdominis Myocutaneous (VRAM) flaps for reconstruction in pelvic exenteration surgery: complications and impact on quality of life G. van Ramshorst,* J.M. Young, M.J. Solomon. *Royal Prince Alfred Hospital*.

Aims: Pelvic exenteration for malignancy occasionally requires reconstruction with vertical rectus abdominis myocutaneous (VRAM) flap. We investigated flap-related morbidity. Methods: Review of prospective tertiary referral unit database covering 2003-2016. Patient data and follow-up records until May 2017 were reviewed. Primary outcome was flap-related complications; secondary outcomes were quality of life, hospital stay, and readmission. Results: 87/519 patients were included, median follow-up was 20 months (range 1-161). Median age was 60 years (IQR 51-66). Flap-related complications occurred in 59 patients (68%), with minor recipient-site complications occurring in 33 patients (38%). Fifteen patients suffered major recipient-site complications (17%), including flap separation (n=7), partial (n=3) or complete necrosis (n=4). One patient required flap removal. Obesity was the only independent risk factor for short term flap-related complications ($p=0.02$). Hospital stay was significantly longer in patients with short term major flap complications (median 65 days $p<0.001$) and these patients reported lower QOL scores for role physical at 6 months ($p=0.016$). In the long term, 12 patients developed minor flap-related complications and 11 patients developed major donor-site complications. Fourteen patients developed major recipient-site complications (16%), including enterocutaneous fistulas, sacral collections, perineal hernia or ulcer. Conclusions: VRAM flaps should be used selectively in pelvic exenterations.

Global Partner Posters Program
Disclosures

Relevant Financial Disclosures

The Global Partner Posters Program Abstract Authors and Presenters have reported that they have no relevant financial relationships with commercial interests to disclose.

Author Index

Relevant Financial Disclosures
Oral and Video Abstracts
72nd SSO Annual Cancer Symposium
March 28-30, 2019
San Diego, CA

Disclosures Policy and Disclosures
As required by the Accreditation Council for Continuing Medical Education (ACCME) and in accordance with the Society of Surgical Oncology (SSO) policy, all educational planners, presenters, instructors moderators, authors, reviewers and other individuals in a position to control or influence the content of an activity must disclose all relevant financial relationships with any commercial interest that have occurred within the past 12 months. This includes the disclosure of all financial relationships with a commercial interest of a spouse or partner. A commercial interest is any entity producing, marketing, reselling, or distributing health care goods or services consumed by, or used on, patients. ACCME does not consider providers of clinical service directly to patients to be commercial interests. The ACCME considers financial relationships to create conflicts of interest when individuals have both a financial relationship with a commercial interest and the opportunity to affect the content of CME about the products or services of that commercial interest. All identified conflicts of interest must be resolved and the educational content thoroughly vetted for fair balance, scientific objectivity, and appropriateness of patient care recommendations. It is required that disclosure be provided to the learners prior to the start of the activity. Individuals with no relevant financial relationships must also inform the learners that no relevant financial relationships exist. Learners must also be informed when off-label, experimental/investigational uses of drugs or devices are discussed in an educational activity or included in related materials. Disclosure in no way implies that the information presented is biased or of lesser quality. It is incumbent upon course participants to be aware of these factors in interpreting the program contents and evaluating recommendations. Moreover, expressed views do not necessarily reflect the opinions of the SSO.

The following Oral Abstract and Video Abstract Authors and Presenters have disclosed financial relationships with commercial interests:

Callegaro, Dario, 129
Honorarium: Eli Lilly

DeMore, Nancy, 135
Other: Enci Therapeutics, Inc., Officer and Shareholder

Hallet, Julie 55
Honorarium: Ipsen; Honorarium: Novartis

Hunt, Kelly, 1
Advisory Board: Armada Health; Advisory Board: Merck; Research Grant: Endomag

The following Oral Abstract and Video Abstract Authors and Presenters have reported that they have no relevant financial relationships with commercial interests to disclose:

Aggarwal, Piyush, V1
Ajkay, Nicolas, 125
Allen, Casey, 142
Altman, Ariella, 67

Aquina, Christopher, 117
Auer, Rebecca Ann, 36
Ayabe, Reed, 83
Azab, Basem, 144
Bae, Sung Uk, 50
Banerjee Sudeep, 138
Blakely, Andrew, 34, 57
Bubis, Lev, 118
Burke, Erin, 131
Burkheimer, Erica, 18
Burns, William, 105
Campf, Jessica, 41
Cass, Richard, 130
Cavnar, Michael, 139
Cohen, Noah, 77
Court, Colin, 64
Crown, Angelena, 149
Datta, Jashodeep, 72
De Andrade, James, 150
de la Cruz, Lucy, 20
Dogeas, Epameinondas, 65
Downs-Canner, Stephanie, 16
Ecker, Brett, 91
Egger, Michael, 101
Ellis, Ryan, 113
Ellsworth, Rachel, 27
Eng, Oliver, 107
Essner, Richard, 88
Ferrantella, Anthony, 82
Gajardo, Jorge, 143
Gamboa, Adriana, 134
Gerstenhaber, Fabian, 148
Good, Meghan, 37
Gunn, Jinny, 15
Gyorki, David, 98
Hendrix, Ryan, 94
Hieken, Tina, 19
Ho, George, 55
Höppener, Diederik, 45
Hwang, Rosa, 84
Ikoma, Naruhiko, 140
Jadeja, Priya, 14
Jajja, Mohammad Raheel, 6
Jogerst, Kristen, 111
Jrearz Ricky, 128
Judge, Sean, 137
Kang, S. Thomas, 126
Kantor, Olga, 29
Katsuta, Eriko, 23
Kelly, Kaitlyn, 42
Klemen, Nicholas, 106
Konishi, Tsuyoshi, 3
Kotha, Nikhil, 42
Kranker, Lindsay, EHV2
Krasnick, Bradley, 90
Kumar, Naveena, 48
Kupstas, Amanda, 19
Kwak, Minyoung, 102
Lahat, Guy, 148
LaRocca, Christopher, EHV1
Lazarus, Jenny, 43
Lee, Ann, 103
Lee, David, 126
Leick, Katie, 89
Liao, Ning, 21
Lillemoe, Heather, 122
Liu, Jessica, 62
Lofthus, Alexander, 132
Look Hong, Nicole, 93
Louie, Raphael, 13
Lu, Jun, 141, V6
Luna-Perez, Pedro, 49
Luu, Shelly, 146
Macedo, Francisco Igor, 66
Madsen, Sarah, 4
Mahuron, Kelly, 8
Malekzadeh, Parisa, 38
Manguso, Nicholas, 58
Marco, Michael, 31
Margonis, Georgios Antonios, 71
Masoud, Sabran, 99
McEvoy, Christian, 40
McIntyre, Caitlin, 75
Merchant, Shaila, 121
Merle, Evan, EHV2
Minami, Christina, 26
Miura, John, 96, 100
Moaven, Omeed, 52
Moldoveanu, Dan, 24
Moncrieff, Marc, 95
Moo, Tracy-Ann, 10

Morency, Dominique, 12
Nassour, Ibrahim, 85
Newhook, Timothy, 123
Nguyen, Trang, 120
Nicholson, Kristina, 63
Nijhuis, Amanda, 104
Nijhuis, Amanda, 92
Nizri, Eran, 133
Nuckles, Brandon, 109
Okamura, Ryosuke, 70
Oxner, Christopher, 40
Paniccia, Alessandro, 80
Paredes, Anghela, 78
Park, Young Suk, 145
Pawlik, Timothy, 78
Peng, June, V3, V4, V5
Philipp, Lucas, 60
Polanco, Patricio, 74
Popat, Saurin, 54
Pyfer, Bryan, 110
Quezada, Felipe, 46
Rahnemai-Azar, Amir A., 68
Ramanathan, Rajesh, 32, 79
Rand, Jamie, 97
Rosenberger, Laura, 11
Ross, Merrick, 4
Santamaria-Barria, Juan, 5
Saunders, Neil, 60
Scally, Christopher, 116
Showalter, Shayna, V8
Schuitevoerder, Darryl, EHV3
Scott, Aaron, 56
Selleck, Matthew, 147
Smith, Margaret, 108
Solomon, Daniel, 39
Song, Yun, 115
Sorrells, William, 59
Spanheimer, Philip, 61
Srour, Marissa, 22
Steenhoven, Julia, 28
Sturm, Emily, 124
Sun, Susie, 30
Sun, Virginia, 34, 119
Swords, Douglas, 127
Takahashi, Hideo, 73, 87
Terhune, Julia, 136, 33
Thompson, Jessica, 17
Torphy, Robert, 2
Tran, Thuy, EHV4
Valero, Monica, 25
Varley, Patrick, 35, 81
Vidri, Roberto, 76
Voss, Rachel, 51
Votanopoulos, Konstantinos, 86
Vreeland, Timothy, V7
Webb, Christopher, 44
Weiser, Martin, V1
Weiss, Anna, 112
Williams, Richelle, 114
Woeste, Matthew, 125
Wong, Stephanie,9
Wright, G. Paul, 17, 18
Wu, Shan-san, 10, 25
Yamada, Shinichiro, 69
Yang, Yun, V2
Yoon, Sam, V6, 141
Zafar, Syed Nabeel, 47

AUTHOR INDEX

72nd Annual Cancer Symposium
Society of Surgical Oncology
March 27–30, 2019
San Diego, CA

C

D

E

F

I

J

K

L

M

N

O

P

Q

R

S

T

U

V