5 GROWTH SUPPRESSION BY ALTERATION IN KEAP1/NRF2-NOTCH-STAT3 SIGNALING IN CHOLANGIOCARCINOMA
S. Kunnimalaiyaan, T. C. Gamblin and M. Kunnimalaiyaan
*Corresponding author. Muthusamy Kunnimalaiyaan, Medical College of Wisconsin, USA

Background: Recently, we have reported that xanthohumol, a prenylated chalcone showed anti-proliferative effect in CCA cell lines both in vitro and in vivo. However, the exact mechanism of action remains unclear. Our objective is to test the hypothesis that xanthohumol will effectively inhibit CCA proliferation by altering keap1/Nrf2-Notch-STAT3 axis.

Methods: Human CCA cell lines were used for the treatment with increasing concentrations of xanthohumol for three days. Western analysis was carried out for the levels of keap1/Nrf2-Notch-STAT3 axis proteins as well as apoptotic markers. Notch1, Keap1, and Nrf2 loss-of gene function by shRNAs and their effects were analyzed.

Results: Dose dependent reduction of Keap1 with corresponding level of Notch1 reduction with XN treatment was observed. Importantly, this is associated with a reduction in phosphorylated STAT3 without affecting the levels of total STAT3 proteins. Notch1 depletion significantly reduced the levels of STAT3 phosphorylation. Growth suppression due to apoptosis was evidenced by an increase in the pro-apoptotic marker, cleaved PARP and caspase-3.

Conclusion: Xanthohumol treatment reduced keap1, Notch1 and phosphorylated STAT3 proteins. Notch1 specific depletion showed reduction in STAT3 phosphorylation suggested that Notch1 affects STAT3 pathway. This provides evidence to the role of keap1/Nrf2-Notch-STAT3 signaling pathway in CCA. Importantly, this study provides insight into dual targeted therapies such as Notch and STAT3 inhibitors in combination. This is the first study to show the regulation of keap1/Nrf2-Notch-STAT3 by xanthohumol in cholangiocarcinoma.

6 LONG-TERM OUTCOMES OF PATIENTS WITH INTRADUCTAL GROWTH SUB-TYPE OF INTRAHEPATIC CHOLANGIOCARCINOMA
Ozgür Akgül, Fabio Bagante, Matthew Weiss, Katiuscha Merath, Sorin Alexandrescu, Hugo P. Marques, Luca Aldrighetti, Shishir K. Maithel, Carlo Pulitano, Todd W. Bauer, Feng Shen, George Poultsides, Olivier Soubrane, Guillaume Martel, Bas G. Koerkamp, Guglielmi Endo, Alfredo Itaru and Timothy M. Pawlik
*Corresponding author. Fabio Bagante, The Ohio State University, USA

Background: Intrahepatic cholangiocarcinoma (ICC) is morphologically classified as mass forming (MF), periductal infiltrating (PI) or intraductal growth (IG) type. IG tumors typically present as papillary lesions and may be associated with a different prognosis. We sought to define the characteristics of patients with IG ICC and characterize long-term outcomes of IG patients relative to patients with MF and PI tumors

Methods: 1,083 patients who underwent curative-intent liver resection for ICC between 1990 and 2015 were identified using an international database. Data on clinicopathological characteristics, operative details, and morphological status, were recorded and analyzed

Results: ICC morphology consisted of MF (n = 911, 84%), PI (n = 142, 13%), or IG (n = 30, 3%) subtypes. Among patients with IG ICC, 63% has a T1a/T1b tumor and the majority of patients (67%) were node negative. In contrast, most patients with MF (52%) or PI (78%) tumors had more advanced T2/T3/T4 disease; the incidence of lymph node metastasis among MF (34%) or PI (59%) was comparable (both p > 0.05). On final pathology, the incidence of R0 margins was also similar among IG (93%) and MF tumors (89%)(p = 0.46), yet lower among patients with PI ICC (77%)(p = 0.04). Lympho-vascular invasion (IG, 13% vs. MF, 29% vs. PI, 46%) was lower among patients with IG ICC (p < 0.001). In addition, the incidence of perineural invasion was also lower among IG patients (IG, 17% vs. MF, 18% vs. PI, 38%; p = 0.03). While 5-year overall survival was comparable among patients with IG (41%) and MF ICC (42%), long-term outcome was lower among patients with PI ICC (25%)(p = 0.04)

Conclusion: Patients with IG ICC tended to present with earlier T-stage disease, yet had the same overall incidence of nodal metastasis. Long-term outcomes were comparable to the most common MF morphological ICC subtype, yet was better than PI ICC

7 DOES ADDITIONAL RE-RESECTION OF A POSITIVE PROXIMAL MARGIN IN HILAR CHOLANGIOCARCINOMA AFFECT SURVIVAL? MAYO EXPERIENCE
L. Yohanathan, K. P. Croome, C. A. Puig, M. Traynor and D. M. Nagorney
*Corresponding author. Lavanya Yohanathan, Mayo Clinic, USA

Background: The impact of additional resection for positive proximal bile duct margins during hepatic resection of
hilar cholangiocarcinoma (HCCA) on survival and disease progression remains unclear. We sought to determine whether additional resection of positive proximal bile duct margins during resection of HCCA affected outcomes.

Methods: Single institution, retrospective review of all patients undergoing HCCA resection between 1993 and 2017 was undertaken. Both frozen section and final margin status for all patients was reviewed. Patients were categorized based on margin status on frozen section and final pathology as: Group A (margin – to margin –), Group B (margin + to margin –) and group C (margin + to margin +). Overall survival and disease progression were primary outcomes.

Complication rates and need for adjuvant therapy were secondary outcomes.

Results: 154 patients underwent hepatic and bile duct resection with regional lymphadenectomy and Roux Y hepaticojejunostomy for HCCA. Median survival (months) for Group A, Group B, and Group C was 45, 33, and 30. There was no significant difference in overall survival.

Conclusion: Current evidence fails to support survival advantage for re-resection for initially margin positive HCCA.

9 LAPAROSCOPIC PARENCHYMA-SAVING LIVER RESECTION FOR COLORECTAL METASTASES

Davit L. Aghayan, Egidijus Pelanis, Ásmund A. Fretland, Airazat M. Kazaryan, Mushegh A. Sahakyan, Bård I. Røsok, Leonid Barkhatov, Bjørn A. Bjørnbeth, Ole J. Elle and Bjørn Edwin

*Corresponding author. Davit Aghayan, Oslo University Hospital, Norway

Background: Laparoscopic liver resection (LLR) of colorectal liver metastases (CLM) is increasingly performed in specialized centers. While there is a trend toward a parenchyma-sparing strategy in multimodal treatment for CLM, its role is yet unclear. In this study we present short- and long-term outcomes of laparoscopic parenchyma-sparing liver resection (LPSLR) at a single center.

Methods: LLRs were performed in 951 procedures between August 1998 and March 2017 at Oslo University Hospital, Oslo, Norway. Patients who primarily underwent LPSLR for CLM between August 1998 and March 2016 were included in the study. LPSLR was defined as non-anatomic LLRs, i.e. the patients, who underwent hemihepatectomy and sectionectomy were excluded. Perioperative and oncologic outcomes were analyzed. The Accordion
Methods: Two hundred ninety patients were included in this retrospective study. Clinical effect of chemoradiotherapy for positive hepatic margin on survival and recurrence was not fully evaluated.

Results: Hilar margin was negative (hm−) in 257 and positive (hm+) in 38. Of 38 patients with positive hepatic margin, 20 patients received postoperative chemoradiotherapy and 18 did not. Hepatic stump recurrence was occurred in 13 patients. The incidence was significantly higher in patients with positive hepatic margins (16%) than those with negative hepatic margins (3%) (p = 0.003). Among patients with positive hepatic margins, the incidence was almost identical between patients with and without chemoradiotherapy; 17% (3/18) in hm+/CRT− and 15% (3/20) in hm+/CRT+ patients (p = 0.616). Median survival time was 48 months in hm−, 38 months in hm+/CRT−, and 50 months in hm+/CRT+ patients, respectively. The differences were not significant between each group. Multivariate analysis revealed that presence of lymph node metastasis, histologic grade of G2/G3, and combined portal vein resection as the significant prognostic factors. However, performance of postoperative adjuvant chemoradiotherapy did not contribute the prolongation of survival.

Conclusion: Chemoradiotherapy for positive hepatic ductal margin was not effective in survival and stump recurrence.

11 SURVIVAL AFTER RESECTION OF MULTIPLE TUMOR FOCS OF INTRAHEPATIC CHOLANGIOCARCINOMA
*Corresponding author. Stefan Buettner, The Ohio State University, USA

Background: Bilobar lesions and multiple tumor foci of intrahepatic cholangiocarcinoma (ICC) are often considered a contra-indication for resection. We sought to define long-term outcomes in this subset of patients.

Methods: Patients who underwent resection for ICC between 1990 and 2015 were identified from 12 major HPB centers. Outcomes of patients with solitary and multiple tumors were compared.

Satellite lesions, small lesions within 1 cm from the index tumor or within the same segment of a larger lesion, were not defined as multiple tumors. Multivariable regression analysis was used to assess survival.

Results: 1,023 patients underwent a curative-intent resection of ICC. On final pathology, 235 patients (23.0%) had multiple tumors. Patients with multiple tumors had a median of 2 tumors (interquartile range [IQR]: 2–3). Recurrence occurred in 416 (52.8%) patients with a solitary tumor versus 135 (57.4%) patients with multiple tumors (p = 0.209). Median survival of patients with a solitary tumor was 42.6 months (95%CI: 35.9–49.4), while the median survival of patients with multiple tumors was 26.9 months (p < 0.001) One-, 3-, and 5-year survival of patients with multiple tumors were 75.1%, 40.4% and 25.6% respectively. In multivariable analysis, positive resection margin (Hazard Ratio [HR]: 1.57; p = 0.001), lymph node metastasis (HR:1.84; p < 0.001), invasion of adjacent organs (HR: 2.02; p < 0.001), and tumor size (per centimeter increase) (HR: 1.06, p < 0.001) were each associated with an increased hazard of death. In contrast, presence of multiple tumors was not an independent prognostic factor of survival (HR: 0.943, 95%CI: 0.87–1.32; p = 0.506).

Conclusion: Five-year survival after complete resection of patients with multiple ICC was 25.6%. Multi-focal ICC should not be considered an absolute surgical contra-indication and may provide a benefit in a subset patients.
THE CONUNDRUM OF <2 CM PANCREATIC NEUROENDOCRINE TUMORS: A PREOPERATIVE RISK SCORE TO PREDICT LYMPH NODE METASTASES AND GUIDE SURGICAL MANAGEMENT


*Corresponding author. Alexandra Lopez-Aguiar, Emory University, USA

Background: Management of <2 cm pancreatic neuroendocrine tumors (PanNETs) is controversial. Although often indolent, the oncologic heterogeneity of these tumors, particularly related to lymph node (LN) metastases, poses challenges when deciding between resection vs surveillance.

Methods: All pts who underwent curative-intent resection of primary non-functional <2 cm PanNETs at 8 institutions of the US Neuroendocrine Tumor Study Group from 2000 to 2016 were analyzed. Tumors with poor-differentiation and Ki-67 > 20% were excluded. Primary tumour location and Ki-67 were assigned a value weighted by their odds ratio: (proximal: 4, Ki-67 > 20%: 1, Ki-67 < 20%: 2, distal: 1, Ki-67 < 20%: 2, Ki-67 > 20%: 3). Scores were categorized into low(1–2), intermediate(3–4), and high(5–7) risk groups.

Results: Of 695 pts with resected PanNETs, 309 were <2 cm. 25% of tumors were proximal (head/uncinate), 23% had a Ki-67 < 20%, and only 8% were moderately-differentiated. 9% of all <2 cm tumors were LN(+), which was associated with worse 5-yr recurrence-free survival compared to LN(-) disease (80% vs 96%; p = 0.007). Preoperatively known factors associated with LN metastases were proximal location (OR4.0; p = 0.002) and Ki-67 < 20% (OR2.7; p = 0.05). Moderate-diff was not associated with LN(+). Location and Ki-67 were assigned a value weighted by their odds ratio: (distal: 1, proximal: 4; Ki-67 < 3%: 1, Ki-673%: 3), which formed a LNRS ranging from 1 to 7. Scores were categorized into low(1–2), intermediate(3–4), and high(5–7) risk groups.

Incidence of LN metastases progressively increased based on risk group: Low: 3.2%; Intermediate: 13.8%; High: 20.5%(Table). Only 3.4% of Ki-67 < 3% tumors in the distal pancreas were LN(+) compared to 21.4% of Ki-673% tumors in the head/uncinate.

Conclusion: This simple and novel LN risk score utilizes readily available preoperative factors (tumor location and Ki-67) to accurately stratify risk of LN metastases for <2 cm PanNETs and may help guide management strategy.

<table>
<thead>
<tr>
<th>Lymph Node Risk Score</th>
<th>Percent</th>
<th>p-value</th>
<th>OR (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (Score 1–2)</td>
<td>3.2%</td>
<td>Ref</td>
<td>–</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intermediate (Score 3–4)</td>
<td>13.8%</td>
<td>4.9</td>
<td>(1.5–15.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>High (Score 5–7)</td>
<td>20.5%</td>
<td>7.9</td>
<td>(2.5–24.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

EVALUATION OF THE SAFETY AND EFFICACY OF STING AGONISTS FOR DOWNSTAGING AND MARGIN ACCENTUATION STRATEGIES IN A MURINE MODEL OF LOCALLY ADVANCED PANCREATIC CANCER


*Corresponding author. Ephraim Tang, Providence Cancer Center, USA

Background: Of patients presenting with LAPC (locally advanced pancreatic cancer), less than a quarter will be down-staged to resectability. STING (Stimulator of interferon genes) ligands induce potent inflammation, and hemorrhagic necrosis in murine tumors. Our group has also previously shown that intra-tumoral injection is effective in murine models of pancreatic cancer. We sought to generate and test their application in a pre-clinical model of LAPC.

Methods: PAN-02 cells were used to establish tumors in C57BL/6 mice. Tumors were established in the femoral triangle with encasement of the femoral vessels, and within the distal pancreas. Mice were evaluated by CECT (contrast enhanced CT) at 14–21 days, and injected intra-tumorally with 50-100 µg of the STING ligand CDA (Cyclic Di-adenosine). Mice were re-examined at 3 days post by CECT and gross examination. In an R2 resection model, subcutaneous flank tumors were established with SCC7, and after partial resection, 25 µg of CDA or PBS in Matrigel were applied to the resection bed.

Results: PAN-02 cells readily established tumors in the femoral triangle, and in the pancreatic tail. These tumors were noted to encase the femoral and splenic vessels with preserved patency. After intra-tumoral injection of CDA, patency was preserved with no hemorrhagic or thrombotic complications noted on CT or at the time of gross evaluation. In the R2 resection model, CDA treated mice had no evidence of recurrence at 30 days, while PBS treated mice readily recurred.

Conclusion: STING ligands represent a novel class of agents that could be used in neoadjuvant, or margin accentuation strategies for LAPC. In an R2 resection model, CDA can prevent recurrence, and in a model of
LAPC, initial results suggest CDA is safe. Evaluation of the safety and efficacy of CDA in this setting is ongoing.

**MONITORING GASTRIC MYOELECTRIC AFTER PANCREATECODUODENECTOMY FOR DIET "READINESS"**


*Corresponding author. Brendan Visser, Stanford University, USA

Background: Delayed gastric emptying (DGE) is a frustrating complication of pancreatecoduodenectomy (PD). Limited clinical indicators immediately after PD allow for prediction of DGE. This study is to assess whether monitoring of postoperative gastric motor activity after PD can identify patients at risk for DGE.

Methods: Sixty-five patients were studied since April 2016. After PD, battery-operated wireless patches (GutCheck, G-Tech Medical) that acquire gastric myoelectrical signals are placed on the anterior abdomen and transmit data by Bluetooth. Patients were divided into EARLY and LATE groups, by regular diet tolerance as of 7 and 9 days postop. Patients who did not meet target ERAS goals (in the LATE group. Tolerance of solid food was noted by 6 and 9 days in the EARLY vs LATE group (p < 0.05). Nasogastric insertion was required in 50% of patients included after initiation of the ERAS protocol in May 2017.

Results: The EARLY and LATE groups had 41 and 24 patients, respectively, with length of stay 7 and 11 days (p < 0.05). Gastric activity was notably higher in the EARLY vs LATE group (Figure); this stomach signal continued to be predictive in the ERAS cohort despite earlier initiation of oral intake. Gastric myoelectrical activity within the first 48 h of surgery was inversely correlated with time to tolerance of regular diet (r = −0.50, p < 0.05).

Conclusion: Measurement of gastric activity after PD can distinguish between patients with shorter or longer times to regular diet. Patients in the LATE group had more clinically relevant DGE and weaker stomach signal as early as 2 days postop. Patients who did not meet target ERAS goals also had weaker stomach signals. This technology provides objective data that identifies patients at risk for DGE and may guide timing of oral intake by gastric "readiness.”

**DECODING GRADE B PANCREATIC FISTULA: A CLINICAL AND ECONOMICAL ANALYSIS AND SUBCLASSIFICATION PROPOSAL**


*Corresponding author. Laura Maggino, University of Pennsylvania, USA

Background: The 2016 ISGPS refined definition of grade B fistula (B-POPF) is predicated on various post-operative management approaches, ranging from prolonged drainage to interventional procedures. However, the spectrum of clinical severity within this entity is yet undefined.

Methods: Pancreatectomies performed at two institutions from 2007 to 2016 were reviewed to identify B-POPFs and their treatment strategies. Sub-classification of B-POPFs into three groups was modeled after the Fistula Accordion Severity Grading System (B1: prolonged drainage only; B2: antibiotics/artificial nutrition/somatostatin analogues/antifusions; B3: percutaneous/endoscopic/angiographic procedure). Clinical and economic outcomes, unique from the ISGPS definition qualifiers, were analyzed across subgroups.

Results: B-POPF developed in 320/1949 patients (16.4%), commonly required prolonged drainage (67.8%), antibiotics (70.3%) and artificial nutrition (54.7%). Percutaneous drainage occurred in 79 patients (24.7%) — always in combination with other strategies. Median number of strategies/patient was 2 (range 1–6). Subclasses B1-3 comprised 19.1%, 52.2% and 28.8% of B-POPFs, respectively, and were associated with progressively worse clinical and economic outcomes (Table 1). These results hold true when analyzing pancreatecoduodenectomies and distal pancreatectomies separately, and were confirmed by multivariable analysis adjusted for clinical and operative factors. Notably, distribution of the B-POPF subclasses was influenced by institution and type of resection (p < 0.001), while clinical/demographic predictors proved elusive.

Conclusion: B-POPF is a heterogeneous entity, where three distinct classes with increasing clinical and economic burden can be identified. This classification framework has potential implications for accurate reporting, comparative research and performance evaluation.
ENHANCEMENT OF ANTI-TUMOR IMMUNITY AND SURVIVAL PROLONGATION BY NEOADJUVANT 5-FU, OXALIPLATIN AND IRINOTECAN (FOLFIRINOX) IN PANCREATIC DUCTAL ADENOCARCINOMA PATIENTS


*Corresponding author. Lei Cai, Massachusetts General Hospital, Harvard Medical School, USA

**Background:** Due to the encouraging results in the metastatic setting, patients with locally advanced PDAC (LA PDAC) have been treated with FOLFIRINOX, often followed by radiation, with the hope of getting them to resection. Our aim was to characterize the immunological profile of the tumor microenvironment, by analyzing: i) the expression of HLA antigens by PDAC cells, since these molecules play a crucial role in the interactions of tumor cells with host’s immune system and ii) the infiltration of tumors by immune cells which has been shown to reflect patients’ antitumor immune response in the tumor microenvironment.

**Methods:** Clinicopathologic data were collected from 63 FOLFIRINOX treated patients between 2012 and 2014, 18 photon patients (50.4Gy) between 1998 and 2010 and 154 no neoadjuvant patients between 1998 and 2012. Immunohistochemical staining was performed for HLA-A, HLA-B, HLA-C, CD8, CD4, and FoxP3.

**Results:** Of the 235 patients the median age was 66 yo and 50% were women. Immunohistochemical staining demonstrated defects in both HLA-A and HLA-B and C expression in more than 60% of the PDACs analyzed the frequency of HLA-A defects in PDACs from FOLFIRINOX patients was significantly lower than in tumors from the other two cohorts (p = 0.001). Both CD8 + and CD4 + T cell density in tumors from FOLFIRINOX patients was significantly higher than that in tumors from photon and no neoadjuvant patients. FoxP3 + cell density in PDACs from FOLFIRINOX patients was significantly lower than that in tumors from photon and no neoadjuvant patients (p = 0.001). In the FOLFIRINOX cohort CD8 + T cell density, but not CD4 +, correlated with HLA-A expression (p < 0.001).

**Conclusion:** FOLFIRINOX increases the expression of HLA class I and the immune infiltrate. The altered immune microenvironment may make FOLFIRINOX an attractive therapy to combine with an immune modulator in PDAC.

---

Table 1 Clinical and economic outcome measures stratified by subtype of grade B fistula

<table>
<thead>
<tr>
<th>Outcome measure n(%)</th>
<th>Total Grade B 320 (100)</th>
<th>B1 61 (19.1)</th>
<th>B2 167 (52.2)</th>
<th>B3 92 (28.8)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total strategies used to treat the fistula; median (IQR)</td>
<td>2 (1–3)</td>
<td>1</td>
<td>2 (2–3)</td>
<td>3 (3–4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Occurrence of non-fistulous complications</td>
<td>244 (76.3)</td>
<td>29 (47.5)</td>
<td>135 (80.8)</td>
<td>80 (87.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of non-fistulous complications; median (IQR)</td>
<td>1 (0–2)</td>
<td>0 (0–1)</td>
<td>1 (0–2)</td>
<td>1 (1–3)</td>
<td>0.008</td>
</tr>
<tr>
<td>Total drain duration, days median (IQR)</td>
<td>29 (22–39)</td>
<td>26 (23–31)</td>
<td>26 (19–36)</td>
<td>36 (28–58)</td>
<td>0.733</td>
</tr>
<tr>
<td>ICU transfer</td>
<td>38 (11.9)</td>
<td>6 (9.8)</td>
<td>14 (8.4)</td>
<td>18 (19.6)</td>
<td>0.025</td>
</tr>
<tr>
<td>Duration of index stay, days median (IQR)</td>
<td>18 (10–28)</td>
<td>9 (7–13)</td>
<td>21 (15–30)</td>
<td>20 (9–33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Readmission</td>
<td>84 (26.3)</td>
<td>12 (19.7)</td>
<td>31 (18.6)</td>
<td>41 (44.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multiple readmissions</td>
<td>15 (4.7)</td>
<td>4 (6.6)</td>
<td>1 (0.6)</td>
<td>10 (10.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Fistula-related readmission</td>
<td>67 (20.9)</td>
<td>0</td>
<td>28 (16.8)</td>
<td>39 (42.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of total stay, days median (IQR)</td>
<td>21 (14–31)</td>
<td>11 (8–14)</td>
<td>24 (16–32)</td>
<td>25 (19–38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PMI, mean ± SD</td>
<td>0.325 ± 0.157</td>
<td>0.221 ± 0.163</td>
<td>0.313 ± 0.139</td>
<td>0.417 ± 0.130</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fistula ACB mean, ±SD</td>
<td>0.274 ± 0.081</td>
<td>0.110 ± 0</td>
<td>0.260 ± 0</td>
<td>0.370 ± 0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fistula as the highest graded complication</td>
<td>254 (79.4)</td>
<td>34 (55.7)</td>
<td>141 (84.4)</td>
<td>79 (85.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Costs* median (IQR)</td>
<td>2.3452</td>
<td>1.363</td>
<td>2.460</td>
<td>2.892</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cost variation**</td>
<td>+135%</td>
<td>+36%</td>
<td>+146%</td>
<td>+189%</td>
<td>–</td>
</tr>
</tbody>
</table>

PMI, post-operative morbidity index; ACB, average complication burden.

*Costs data arc inflation-adjusted and expressed as a proportion to the cost of a non-complicated resection.

**As compared to the patients experiencing no complications.
### Results

Between Eras 1 and 3, the CR-POPF rate of CR-POPF were calculated utilizing a multi-institutional derivation set (5,316 PDs). Observed-to-expected (O/E) data-driven adjustments of anastomotic stent use (n = 94), development/codification of practice (n = 27), and recognition learning curve for PD (i.e., change from resectable to locally-advanced to metastatic disease, p = 0.593).

**Conclusion:** Patient outcomes for pancreatoduodenectomy can be optimized by risk-adjusted evaluation and deliberate modification of practice.
Only two (8.0%) patients had less disease than initially anticipated i.e. resectable disease at JHH after OSH evaluation showing more advanced disease. Blinded radiologist review revealed the causes of mistaging were: poor contrast timing (N = 11, 44.0%), low contrast enhancement (N = 8, 32.0%), lack of MPR/3D sections (N = 2, 8.0%), slice thickness (N = 2, 8.0%), image noise (N = 4, 16.0%), disease progression (N = 2, 8.0%) and presumed radiologist experience (N = 6, 24.0%).

**Conclusion:** Approximately a quarter of PDAC patients in the study were mistagged on imaging due to multiple radiological factors. Attention to these factors can significantly reduce mistaging.

---

**RISK OF TRANSPLANT WAITLIST PROGRESSION IN HEPATOCELLULAR CARCINOMA USING BIOMARKERS OF TUMOR IMMUNE TOLERANCE PRIOR TO TRANSARTERIAL CHEMOEMBOLIZATION**

P. Thevenot, K. Nunez, T. Sandow, J. Gimenez, J. Gonzalez-Rosario, M. Patel, A. Alfadhli, D. Wyczewskas and A. Cohen
*Corresponding author. Paul Thevenot, Ochsner Health System, USA*

**Background:** Lymphopenia in treatment-naïve waitlist HCC patients is predictive of embolization response and recurrence risk. In this prospective cohort, we correlate pre-HCC patients is predictive of embolization response and recurrence risk.

**Methods:** Waitlist HCC patients undergoing TACE (100–300 micron particles, 100 mg doxorubicin) were recruited. Blood was collected before and 30 days following the procedure. Leukocytes were analyzed by flow cytometry. Study endpoint was transplantation or waitlist progression defined as AFP > 1000 ng/mL, progression beyond Milan, or extrahepatic involvement.

**Results:** Analyzed were 56 patients, 75% Hepatitis C, median MELD score of 11, 80% within Milan and 77% treatment naïve. Lymphopenia stratification (count < 1.2 k/\(\mu\)L) revealed no change in demographic, etiology, or tumor radiographic parameters. Lymphopenia was associated with non-objective primary treatment response, defined as stable or progressive mRECIST (62% vs. 20%, \(p = .005\)). In the transplanted cohort, viable explant lesions were present in 6/6 transplanted lymphopenic patients compared to 1/6 normopenic patients. Lymphopenia was associated with leukopenia (\(p = .002\)), thrombopenia (\(p < .001\)), hypoalbuminemia (\(p < .001\)), and elevated indirect bilirubin (\(p = .011\)). An immunoregulatory shift in lymphopenia was confirmed by dramatic decrease in monocytes (\(p = .002\)) with a compensatory increase in myeloid-derived suppressor cells MDSCs (\(p = .007\)) accompanying elevated CD4:CD8 T cell ratio (\(p = .005\)). MDSC and CD4:CD8 profiles remained stable 30 days after treatment. MDSC elevation (>5% of leukocytes) was present in (6/8) cases of waitlist progression.

**Conclusion:** Biomarkers of immune tolerance, including lymphopenia, MDSC expansion and CD4:CD8 imbalance may be valuable indicators of tumor aggressiveness and HCC recurrence risk early in the transplant process.

---

**HALTHCC AS A NOVEL TUMOR RESPONSE METRIC IN PATIENTS WITH HEPATOCELLULAR CARCINOMA UNDERGOING LOCOREGIONAL THERAPY WHILE AWAITING LIVER TRANSPLANTATION**

K. Sasaki, D. J. Firl, S. Kimura, J. McVey, F. Fontan, K. Hashimoto, H. Yeh, C. M. Miller, J. F. Markmann and N. F. Aucejo
*Corresponding author. Kazunari Sasaki, Cleveland Clinic Foundation, USA*

**Background:** Pre-transplant locoregional therapy (LRT) has been established as a standard treatment approach in liver transplantation (LT) for hepatocellular carcinoma (HCC). The current LRT response evaluation frameworks are not ideal because they were not originally designed to evaluate repetitive LRTs. Our group recently established a simple continuous risk equation (HALTHCC score, Sasaki et al. Lancet GastroHep 2017) which can be calculated using only preoperatively accessible data and which outperformed all previous metrics in a US nationwide experience. This study aimed to test the hypothesis that HALTHCC score can serve as a more accurate LRT response evaluation metric than the current gold standard.

**Methods:** Data for 271 patients undergoing pre-LT LRT between 2002 and 2014 were analyzed for this retrospective multicenter study. Overall, 1452 imaging reports with MELD-NA and AFP value at the same time point were evaluated showing more advanced disease. Blinded radiologist review revealed the causes of mistaging were: poor contrast timing (N = 11, 44.0%), low contrast enhancement (N = 8, 32.0%), lack of MPR/3D sections (N = 2, 8.0%), slice thickness (N = 2, 8.0%), image noise (N = 4, 16.0%), disease progression (N = 2, 8.0%) and presumed radiologist experience (N = 6, 24.0%).

**Conclusion:** Approximately a quarter of PDAC patients in the study were mistagged on imaging due to multiple radiological factors. Attention to these factors can significantly reduce mistaging.
collated. The pre-specified primary endpoint was overall survival (OS). The prognostic utility for HALTHCC was examined with specific reference to changes associated with LRT and was compared to mRECIST.

**Results:** Both mRECIST and delta-HALTHCC identify a cohort of progressive disease patients following LRT. However, the delta-HALTHCC had higher sensitivity at all levels. Relative change in HALTHCC also outperforms mRECIST in terms of stratifying risk of mortality after LT. Specifically, delta-HALTHCC could identify 26 patients of 77 (34%) who had mRECIST nonresponse but had good prognosis and 43 of 194 patients (22%) who had mRECIST response but had demonstrably poor prognosis after LT.

**Conclusion:** Relative change in HALTHCC outperforms mRECIST in terms of stratifying risk of mortality after LT.

---

**21 OUTCOMES OF TRANSPLANTATION FOR BIPHENOTYPIC LIVER TUMORS ARE SIMILAR TO OUTCOMES OF TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA**


**Background:** Biphenotypic liver tumors have features of both hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (CCA). Similar to CCA, biphenotypic tumors are not normally considered for liver transplant due to a perceived high risk of recurrence.

**Methods:** Patients with HCC, CCA, and biphenotypic tumors treated surgically at a single center January 2009—August 2017 were retrospectively reviewed. Using Kaplan—Meier survival curves and the log-rank test, disease-free (DFS) and overall survival (OS) rates were compared among tumor groups for patients with surgical resection and transplant. Comparisons were also made for each tumor type between resection and transplant.

**Results:** 483 patients were surgically treated: 167 resection (85 HCC, 35 biphenotypic, 47 CCA) and 316 transplant (293 HCC, 20 biphenotypic, 3 CCA). Although HCC resection compared to biphenotypic and CCA had better OS (p = 0.03), DFS and 5-year recurrence rates were comparable based on tumor type (both p > 0.72). When comparing biphenotypic and HCC after transplant, there was no difference in outcomes (all p > 0.13). Transplantation for HCC and biphenotypic had better OS and DFS as well as lower recurrence rates than resection for both tumor types (all p < 0.05). 75% of biphenotypic and 82.6% of HCC were treated with liver-directed therapy pre-transplant (p = 0.37) as opposed to resection where 8.6% of biphenotypic tumors and 21.2% of HCC were pre-treated (p = 0.12). Five (25%) biphenotypic and 17.4% of HCC were downstaged to within Milan criteria (p = 0.37).

**Conclusion:** Patients transplanted for either biphenotypic or HCC have better outcomes than those undergoing resection. Transplantation for biphenotypic tumors has DFS, OS and 5-year recurrence similar to transplantation for HCC. Transplantation is an excellent treatment for biphenotypic tumors, even with downstaging to within Milan criteria.
time was higher for STSCC (39 minutes vs. 30, p < 0.01). There was no difference in total graft ischemia time (345 min vs. 345, p = 0.933) and operative time was significantly reduced (246 min vs. 303, p < 0.01). STCC was associated with significantly reduced intraoperative blood loss (3 vs. 6 liters), red blood cell transfusions (2 units vs. 4), fresh frozen plasma (6 units vs. 9), cell saver (0.8 L vs. 2), and rates of temporary abdominal closure (4% vs. 22%) compared to TP (all p < 0.05).

Postoperative intensive care unit transfusions were also significantly lower for STSCC, with 82% requiring no red blood cell transfusions.

Conclusion: STSCC is superior to TP implantation with regard to technical ease, operative time, blood loss, and transfusion requirements during LT. Future studies evaluating long-term outcomes including graft and patient survival following STSCC are warranted.

23 REDUCING READMISSIONS AFTER LIVER TRANSPLANTATION


*Corresponding author. David Levi, Carolinas HealthCare System, USA

Background: Early readmissions after liver transplantation (LT) are a source of significant resource expenditure. Our goal was to reduce readmissions without adversely affecting patient outcomes.

Methods: We devised a protocol to address readmissions that set readmission guidelines, expanded outpatient services, and refined peritransplant teaching. Data collected included patient demographics, length of stay (LOS), readmission events and reason, inpatient charges, and patient survival. Data were compared for the time periods before and after protocol implementation.

Results: From Jan 2012 to Mar 2017, 304 adult primary LTs were performed. The protocol was initiated Oct 2013. Before the protocol (n = 121), 40% and 53.7% of patients were readmitted at 30 and 90 days, respectively. After the protocol (n = 183), 15.8% and 25.6% of patients were readmitted at 30 and 90 days, respectively (p < 0.001). The reduction in readmissions at 90 days resulted in a 33.5% reduction in inpatient hospital cost reduction. Median LOS for the protocol (n = 183), 15.8% and 25.6% of patients were readmitted at 30 and 90 days, respectively. After the protocol implementation.

Conclusion: Our protocol significantly reduced early hospital readmissions after LT, resulting in substantial cost savings, without negatively affecting LOS or patient survival.

24 UNDERSTANDING FIBRINOLYSIS SHUTDOWN IN LIVER TRANSPLANTATION


*Corresponding author. Vikrom Dhar, University of Cincinnati, USA

Background: Fibrinolysis shutdown (FS), the pathologic cessation of fibrin clot breakdown, has been associated with increased morbidity and mortality in coagulopathic trauma patients. Patients undergoing liver transplantation (LT) have a similarly complex coagulation profile that is not well understood. We aim to evaluate the prevalence and impact of FS on outcomes for patients undergoing LT.

Methods: Thromboelastography data were obtained for LTs performed from 2013 to 2017 during the preoperative, anhepatic, neohepatic, and initial postoperative phases. The percentage of fibrinolysis at 30 min, LY30, was used to stratify patients into hyperfibrinolytic (≥3%), physiologic (0.8–2.9%), and FS (0–0.8%) groups. Perioperative outcomes including transfusion requirements and rates of reoperation for bleeding were evaluated.

Results: Of 119 patients undergoing LT, 70.6% were in a state of FS, 20.2% were physiologic, and 9.2% were hyperfibrinolytic at the start of the operation. Prevalence of FS increased over the course of LT, found in 59.7% of patients during the anhepatic phase, 79.8% during the neohepatic phase, and 99.2% postoperatively. No significant differences in patient, disease, or donor characteristics were noted between groups (all p > 0.05). Presence of FS at induction was not associated with adverse perioperative outcomes including increased transfusion requirements, respiratory failure, hepatic artery thrombosis, need for reoperation, or ICU length of stay (all p > 0.05).

Conclusion: A significant majority of LT patients (99.2%) were found to be in a state of FS in the immediate postoperative period. Presence of FS at induction was not associated with adverse perioperative outcomes. Further understanding of this clinical state and its impact on long-term outcomes following LT is needed.

25 EFFECTS OF SEVOFLURANE METABOLITE HEXAFLUORO-2-PROPA NOL PRECONDITIONING IN EXPERIMENTAL LIVER ISCHEMIA REPERFUSION INJURY


*Corresponding author. Joel Rocha Filho, Hospital das Clínicas of University of Sao Paulo, Brazil

Background: Volatile anaesthetics (VA) promote protection against liver ischemia reperfusion (IR) injury. Hexafluoro-2-propanol (HFIP) is a primary metabolite of VA sevoflurane that has been associated with beneficial immunomodulatory effects in different models of inflammation. The aim of this study was to investigate if HFIP preconditioning decreases liver normothermic IR injury.

Methods: Rats anaesthetised with ketamine-xylazine and mechanical ventilation were submitted to 30 min of partial normothermic liver ischemia (Control group; n = 8), or preconditioned with intravenous HFIP 67 mg/kg, 10 min prior to liver ischemia (HFIP group; n = 8).

Immediately after reperfusion non-ischemic liver right and caudate lobes were resected, allowing evaluation global IR liver injury. Blood samples were acquired 4 h after reperfusion.

Results: HFIP group showed significantly decreased AST (2,336 ± 809 U/L) and ALT (2,251 ± 768 U/L) levels compared to Control (4,859 ± 3,053 U/L) and

HPB 2018, 11 (1), 1–31
mainly in situations where volatile anaesthetics cannot be used. HFIP can emerge as a new strategy to liver protection due to its mechanism of preconditioning liver protection effect. Intravenous release of both electrolytes involved in the main mechanism of preconditioning liver protection effect. The imbalance of serum K and iCa may be related to increased intracellular K and iCa levels in HFIP group. The ionic imbalance of K and iCa may be related to increased intracellular K and iCa levels in HFIP group. 

Conclusion: In experimental normothermic liver IR injury, HFIP protects the liver demonstrated by marked decrease in liver transaminases. The ionic imbalance of K and iCa may be related to increased intracellular K and iCa levels in HFIP group. The ionic imbalance of K and iCa may be related to increased intracellular K and iCa levels in HFIP group. Intravenous HFIP can emerge as a new strategy to liver protection mainly in situations where volatile anaesthetics cannot be applied.

![Graphs showing electrolyte levels in HFIP group compared to Control](image)

26 CAN HIGH-VOLUME ANESTHESIOLOGISTS DECREASE PERIOPERATIVE COSTS FOR PANCREATIC SURGERY?

A. Uppal, B. Voung, A. Dehal, P. Hansen, J. Mejia, A. Ong, S. Stern and A. Bilchik

*Corresponding author. Abhinheet Uppal, John Wayne Cancer Institute, USA

Background: Pancreatic surgery outcomes are associated with surgeon and center experience. Anesthesiologists as value drivers have not been explored. We sought to evaluate whether anesthesiologists impact perioperative costs for pancreatic surgery.

Methods: Within an integrated health care system, 428 pancreaticoduodenectomies (PD) and 208 distal pancreatectomies (DP) were performed from 1/2014 to 1/2017. 198 anesthesiologists participated in PDs and 156 in DPs. Operative and anesthesia costs driven by anesthesiologists (OR time, billing and procedures), transfusions, vasopressor use and ICU admissions were determined for each case. Anesthesiologists with volumes greater than 75th percentile (8 for PDs, 4 for DPs) were considered high-volume anesthesiologists (HVAs) vs. $4,70 per minute, p < 0.001), and OR time were not different for either operation. By multivariable analysis of OR/anesthesia costs adjusting for anesthesiologist and surgeon volume, OR time, ASA class, BMI and age was performed.

Results: Of 981 patients included in the study, 18% had calci
cations and 17% were cystic. Median tumor size was larger for tumors with than without calci
cations (3.2 cm vs. 2.0 cm, p = 0.001), but not for cystic vs. solid tumors (2.3 cm vs. 2.2 cm, p = 0.144). Tumors with calci
cations were more commonly associated with Ki-67 3% (47% vs. 33%, p = 0.029) and lymph node metastasis (36% vs. 24%, p = 0.011). Cystic tumors were less commonly associated with lymph node metastasis (12% vs. 30%, p < 0.001). Calci
cations and cystic morphology were associated with lower and higher RFS, respectively (Figure 1a,b), with cystic tumors without calci
cations representing the most favorable group (Figure 1c).

Conclusion: Easily detectable radiographic features, such as calci
cations and cystic morphology, can be used preoperatively to stratify prognosis in patients with PNETs, possibly guiding the extent of resection or utilization of neoadjuvant therapy strategies.
conjunction with surgeons may further improve the value of care provided.

TUMOR LOCATION PREDICTS PRESENCE OF HIGH GRADE DYSPLASIA AND INVASIVE CARCINOMA IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS


*Corresponding author. Stephanie Kerlakian, University of Cincinnati, USA

**Background:** Traditionally, intraductal papillary mucinous neoplasms (IPMNs) of the pancreas with certain high-risk stigmata or worrisome features are referred for surgical management. We aim to assess if tumor location is associated with increased cancer risk in patients with IPMN.

**Methods:** Perioperative data of patients that underwent resection for IPMN from seven institutions between 2000 and 2015 (n = 275) were collected. High-risk stigmata and worrisome features were defined by the 2012 Fukuoka international consensus guidelines. Logistic regression was used to identify predictors of HGD or invasive carcinoma.

**Results:** The majority of patients, 168 (61%), were found to have head/uncinate tumors, while 107 (39%) had tumors located in the pancreas neck/body/tail. No differences were noted with regard to patient age, tumor histology and size, or presence of worrisome features between these groups. Patients with tumors confined to the head/uncinate were more often male (55% vs. 39%), had high-risk stigmata (24% vs. 11%), and more often harbored HGD or invasive carcinoma (62% vs. 33%) [all p < 0.05]. On multivariate analysis, only tumor location remained associated with presence of HGD or invasive carcinoma, with having a tumor in the head/uncinate significantly increasing odds of harboring malignancy (OR 4.76, p = 0.02).

**Conclusion:** Tumor location is predictive of HGD or invasive carcinoma in patients with IPMNs, with tumors of the head/uncinate significantly more likely to harbor malignancy compared to those of the neck/body/tail. Evaluating tumor location is an important consideration when determining which IPMN patients should be recommended to undergo surgical resection.

ROBOTIC PANCREATODUODENECTOMY WITH VASCULAR RESECTION: HOW STEEP IS THE LEARNING CURVE?


*Corresponding author. Joal Beane, University of Pittsburgh Medical Center, USA

**Background:** The safety, efficacy, and learning curve for robotic pancreateoduodenectomy (PD) has been previously reported, however no studies have evaluated the learning curve and outcomes of robotic PD with vascular resections (PD-VR). Our aim was to evaluate the outcomes of robotic PD-VR compared to PD without vascular resection (PD) and to identify the learning curve and benchmarks for improved performance during for PD-VR.

**Methods:** A retrospective review was performed of patients who underwent robotic PD and robotic PD+VR (venous and/or arterial). Patients were analyzed consecutively and cumulative sum (Cusum) analysis was performed to detect improvements in performance over time.

**Results:** Of 380 patients, 50 (13%) had a vascular resection at the time of PD. Compared to PD, PD-VR were more likely to have pancreatic adenocarcinoma (84% vs 42%) and receive neoadjuvant therapy (35% vs 65%, p < 0.01). Cusum analysis of PD+VR operative time revealed a steady significant decrease over time (Rho = −0.38 p = 0.006) with marked initial improvement after the first 8 cases and maturation of the learning curve after 35 cases. A significant reduction in length of stay was observed over the entire experience (Rho = −0.528, p < 0.0001), while margin status, pancreatic fistula, maximum Clavien grade-complication, and mortality remained constant and were comparable to robotic PD alone.

**Conclusion:** Robotic PD-VR is feasible and has comparable morbidity and mortality to robotic PD alone. For surgeons who have surpassed the learning curve of robotic PD, improvements in performance of PD-VR can be seen in as early as 35 cases.
stratification as well as assess for significant decrease in PEP using selective prophylaxis.

**Methods:** A prospectively-maintained ERCP database was used to identify all stratified patients who underwent biliary and/or pancreatic sphincterotomy at our institution between October 2012 and June 2017 (N = 905). At the time of intervention, patients were placed into two cohorts according to risk for development of PEP. One group included those at normal risk (n = 626) and the other included patients at increased risk (n = 269). Selective use of prophylaxis in the increased risk group was ultimately determined by the surgeon at the time of ERCP.

**Results:** As summarized in Table 1; with no prophylaxis, the PEP rate was significantly higher in the group of patients at increased risk (normal risk, 6.02% vs. increased risk, 22.2%; p < 0.001). With prophylaxis, the PEP rate was comparable between patient groups (8.5% vs. 11.7%; p = 0.350).

**Conclusion:** Based on these data, our criteria for prospectively identifying patients at increased risk for PEP are accurate. Moreover, use of selective PEP prophylaxis can result in a significant decrease in acute pancreatitis following ERCP.

### Table 1

<table>
<thead>
<tr>
<th>Criteria for increased risk</th>
<th>Normal Risk</th>
<th>Increased Risk</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>626</td>
<td>269</td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>40 (6.39)</td>
<td>40 (14.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>498 (79.55)</td>
<td>81 (30.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pancreatic stent</td>
<td>49 (7.83)</td>
<td>104 (38.66)</td>
<td></td>
</tr>
<tr>
<td>Indomethacin</td>
<td>65 (10.38)</td>
<td>31 (11.52)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>14 (2.24)</td>
<td>53 (19.7)</td>
<td></td>
</tr>
</tbody>
</table>

**Criteria for increased risk**

| None                        | 475 (75.88) | 13 (4.83)  |
| Balloon dilatation of ampulla| 25 (3.99)   | 26 (9.67)  |
| Deep pancreatic cannulation with guidewire | 25 (3.99) | 5 (1.86)  |
| Heavy injection of pancreatic duct | 16 (2.56) | 27 (10.04) |
| Mild injection of pancreatic duct | 53 (0.47) | 51 (18.96) |
| Sphincter of Oddi dysfunction | 3 (0.48)   | 19 (7.06)  |
| Ongoing acute pancreatitis   | 20 (3.19)   | 23 (8.55)  |
| Prolonged cannulation attempts | 6 (0.96)  | 74 (27.51) |
| Previous ERCP pancreatitis  | 2 (0.32)    | 3 (1.12)   |
| Traumatic cannulation        | 1 (0.16)    | 28 (10.41) |

**Low Risk**

| N without any prophylaxis | 498 | 81 |
| Pancreatitis             | 30 (6.02) | 18 (22.22) | <0.001 |
| N with any prophylaxis   | 118 | 188 |
| Pancreatitis             | 10 (8.47) | 22 (11.7) | 0.350 |

**IN PATIENTS UNDERGOING HEPATIC RESECTION, IS THE LIVER SURGERY COMPLEXITY SCORE A BETTER PREDICTOR OF CASE COMPLEXITY AND POSTOPERATIVE MORBIDITY THAN THE CONVENTIONAL MAJOR/MINOR CLASSIFICATION?**

M. H. Al-Temimi, I. F. Moussa and A. L. DiFronzo

*Corresponding author. Mohammed Al-Temimi, Kaiser Permanente, Los Angeles Medical Center, USA

**Background:** To validate the updated liver surgery complexity score (LSCS) (Strasberg, 2016) and compare it to the major/minor classification (MMC) in predicting major complications (Clavien-Dindo grade ≥ 3) and case complexity (CC).

**Methods:** Case complexity was assessed using estimated blood loss (EBL) and operative time (OT) as surrogates. Multivariate logistic regression models were developed for prediction of major morbidity and CC. EBL and OT were dichotomized using the medians of the variables (350 ml and 240 min respectively). The performance of MMC3 (≥3 vs. <3 segments), MMC4 (≥4 vs. <4 segments), LSCS (low, medium, and high complexity), and case-specific-LSCS (using each specific hepatectomy listed by expert survey) in predicting CC and serious postoperative morbidity was compared using the Receiver Operating Characteristics curve analysis

**Results:** Of 662 hepatic resections from 2005 to 2015, 485 were classified by LSCS and were included (single segment and multiple sub-segmental resections were excluded). Low (43%), medium (45%) and high (12%) complexity cases were associated with major morbidity of 16%, 32% and 57% respectively (p < 0.05). MMC4 (AUC = 0.813) and LSCS (AUC = 0.809) were comparable to MMC3 (AUC = 0.807) in predicting complications (p > 0.05). Case-specific-LSCS (0.826) has better predictive ability than MMC3 (p < 0.05), but not MMC4 (p = 0.117). LSCS and case-specific LSCS were superior to MM3 and MM4 in predicting case complexity, as reflected in more accurate prediction of EBL and OT as separate outcome variables in multivariate logistic regression models (p < 0.05)

**Conclusion:** The LSCS is significantly associated with case complexity and postoperative complications. In comparison to the conventional MMC, LSCS is a better predictor of CC; case specific-LSCS and MMC4 most accurately predict postoperative complications

**IMPROVED PERFORMANCE WITH MINIMALLY INVASIVE LIVER RESECTION: A SINGLE CENTER WESTERN EXPERIENCE WITH 1,062 CASES**


*Corresponding author. Forat Swaid, University of Pittsburgh Medical Center, USA

**Background:** We report our experience with minimally invasive liver resection (MILR) in 1,062 patients at a single western center.
Methods: A retrospective review of consecutive patients undergoing laparoscopic liver resection between 2001 and 2017 was performed.

Results: A total of 1,062 patients underwent MILR. There were 664 females (63%) and 398 males (37%), with a mean age of 58 years (range: 17–94), BMI of 29 kg/m² (range: 16–61), and ASA score of 2.6. The approach was pure laparoscopic in 724 (68%) patients, hand-assisted 134 (13%), hybrid 130 (12%), and robotic 74 (7%). Laparoscopic major hepatectomy (right or left lobectomy) was done in 91/1,062 (9%) cases. Indication for resection was malignancy in 413/1,062 (39%) of cases (HCC 38%, mCRC 37%, ICC 6%, NET 5%, Other 14%), or symptomatic benign lesions in the rest. OR time, pRBC transfusion, use of pure laparoscopic approach, and post-op complications all statistically improved over time (Table). Seventy-seven (7.2%) patients developed complications (cardiopulmonary in 22, bile leak in 6, post-op bleeding in 6, intra-abdominal abscess in 5, thromboembolism in 6, and ileus in 8). Unplanned open-conversion rate was 2.5% and did not change during periods. Average hospital length of stay was 2.8 days.

Ninety-day mortality rate was 4/1,062 patients (0.4%).

Conclusion: To our knowledge, this is the largest single-center series of laparoscopic liver resection reported worldwide. MILR results in excellent surgical outcomes and low overall complication rates. Surgical performance improved and peri-operative morbidity decreased with greater experience over time.

Table

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>OR time (min)</td>
<td>213</td>
<td>195</td>
<td>139</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Transfusions (%)</td>
<td>5</td>
<td>4.7</td>
<td>0.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Pure laparoscopic (%)</td>
<td>45</td>
<td>68</td>
<td>71</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Complications (%)</td>
<td>15.2</td>
<td>5.4</td>
<td>5.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Conversion to open (%)</td>
<td>2.4</td>
<td>2.3</td>
<td>2.7</td>
<td>0.82</td>
</tr>
</tbody>
</table>

33

A MULTI-INSTITUTIONAL ANALYSIS OF MINIMALLY INVASIVE LIVER RESECTIONS

A. A. Smith, I. Konstantinidis, Y. Fong, J. Martini, D. Iannitti and J. F. Buell

*Corresponding author. Alison Smith, Tulane University School of Medicine, Carolinas Medical Center, City of Hope, USA

Background: As minimally invasive liver resection (MILR) gains acceptance, techniques and outcomes must be analyzed in multi-institution series comparing both laparoscopic and robotic approaches to open liver resections. The objective of this study was to describe the experience with MILR at three high volume centers.

Methods: Retrospective tri-institutions analysis of minimally invasive liver resection from 2000 to 2016. Minimally invasive liver resection was defined as laparoscopic and robotic-assisted resections.

Patient demographics, tumor characteristics, and outcomes were analyzed for statistical significance compared to open liver resection (OLR).

Results: A total of 1,323 patients were included with 746 OLR (56.4%) and 577 MILR (50 laparoscopic, 40.0% and 47 robotic liver resections, 3.4%). The number of MILRs increased during the study period (0.5%, year 2000, vs. 5.5%, year 2016, p < 0.001). MILR had significantly decreased estimated blood loss (634.2±33.4 mL vs. 274.6±18.3 mL, p < 0.0001), incidence of post-operative complications (34.2% vs. 16.6%, p < 0.0001), hospital length of stay (8.7±0.3 vs. 4.2±0.2 days, p < 0.0001), and re-admissions (10.1% 4.0% vs. p < 0.0001). No difference in bile leak (p = 0.4185), post-operative infection (p = 0.2987), or take back to the operating room (p = 0.2912) was found between the techniques. Ninety day patient mortality was higher in the open liver resection group (1.7% vs. 0.3%, p = 0.0180).

Conclusion: The current study evaluates the steady adoption of minimally invasive liver resection in high volume centers. This data confirms MILR, whether performed laparoscopically or robotically, confers significant patient benefits including less blood loss, complications, length of stay, readmissions while no evidence of increased bile leak, need for takeback operation, or 90 day mortality.
STANDARDIZATION OF OPERATIVE TECHNIQUE IN LAPAROSCOPIC RIGHT HEPATECTOMY: IMPROVING COST-VALUE RELATIONSHIP THROUGH VALUE STREAM MAPPING


*Corresponding author. Mohammad Raheel Jajja, Emory University, USA

**Background:** With the current emphasis on improving quality and cost reduction in medicine, it is imperative to critically evaluate cost-value relationships for surgical procedures. Previously our group had demonstrated comparable clinical outcomes, reduced length of stay (LOS) and reduced operative time for Laparoscopic Right Hepatectomy (LRH) compared to open right hepatectomy (ORH). Though the two groups had similar overall costs, intraoperative cost in the LRH group was higher.

**Methods:** We decoded LRH into its component critical steps using value stream mapping (VSM), and analyzed the associated costs. We prospectively modified our surgical technique to target those steps that had high intraoperative costs (parenchymal transection, hemostasis) and measured the changes in outcomes. We reviewed medical records at our institution for patients who underwent elective LRH before (pre-LRH n = 22) and after (post-LRH n = 22) the intervention and those who had ORH (n = 65), between January 1, 2008 and November 30, 2016.

**Results:** Average overall cost for the procedure was significantly lower for the post-standardization LRH group (post-LRH $21,768, pre-LRH $28,066, ORH $33,020; p < 0.0001). Average intraoperative blood loss was significantly reduced with LRH (post-LRH 167 mL, pre-LRH 292 mL, ORH 509 mL; p < 0.001). Operative times were significantly shorter for LRH (post-LRH 147 mins, pre-LRH 190 mins, ORH 229 mins; p < 0.001). LOS was significantly reduced for LRH (post-LRH 3 days, pre-LRH n = 22) intervention and those who had ORH (n = 65), between January 1, 2008 and November 30, 2016.

**Conclusion:** Using a common quality improvement tool (VSM), we have established a model for cost effective clinical care in hepatobiliary surgery. These tools allow surgeons to overcome personal and traditional biases such as stapler choices, but most importantly eliminate nonvalue added interventions for patients.

---

MULTIDISCIPLINARY, PERIOPERATIVE CARE BUNDLE DECREASES SURGICAL SITE INFECTION IN PATIENTS UNDERGOING SYNCHRONOUS COLORECTAL/LIVER RESECTION


*Corresponding author. Lauren Tufts, Memorial Sloan Kettering Cancer Center, USA

**Background:** Surgical site infections (SSIs) are a major cause of morbidity, mortality, and healthcare costs. Patients undergoing synchronous colorectal/liver resection are at especially high risk. This study measures the effects of a multidisciplinary, SSI reduction project in metastatic colorectal cancer patients undergoing synchronous colorectal/liver resection.

**Methods:** Consecutive patients undergoing synchronous colorectal/liver resections at Memorial Sloan Kettering Cancer Center from 2011 to 2016 (n = 424) were included in the study. The intervention, implemented on Nov 1, 2013, included 13 total preoperative, intraoperative, and postoperative care components. The primary endpoint was SSI (both superficial/deep and organ space). Secondary endpoints were hospital length of stay (LOS) and 30-day readmission rate. Analysis was performed with Wilcoxon Rank Sum and Fisher’s Exact tests and multivariate logistic regression.

**Results:** Overall, superficial/deep, and organ space SSI decreased by 60.5% (34.2% v 13.5%, p < 0.001), 80.6% (13.4% v 2.6%, p < 0.001), and 47.6% (20.8% v 10.9%, p < 0.008) after implementing the intervention, respectively (Table). Median LOS decreased from 9 (IQR 4-60) to 8 days (4-48) (p < 0.001), and 30-day readmission rates did not change (18.6% v 20.7%, p = 0.6). Operative duration, smoking, wound classification and implementation of the care bundle (intervention) predicted SSI. Smoking, wound classification and implementation of the care bundle were independently associated with SSI.

**Conclusion:** In patients undergoing combined colorectal/liver resection, implementation of a multidisciplinary care bundle was associated with a 61% reduction in SSI and modest reduction in LOS. Rates of all types of SSI improved, but greatest advance was noted in superficial/deep SSI. Future multidisciplinary strategies should target deep organ space infection.

---

**Table** Summary of primary and secondary study endpoints

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention cohort</th>
<th>Post-intervention cohort</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>231</td>
<td>193</td>
<td>N/A</td>
</tr>
<tr>
<td>Overall SSI</td>
<td>79 (34.2%)</td>
<td>26 (13.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Superficial/deep</td>
<td>31 (13.4%)</td>
<td>5 (2.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Organ space infection</td>
<td>48 (20.8%)</td>
<td>21 (10.9%)</td>
<td>0.008</td>
</tr>
<tr>
<td>LOS (days, range)</td>
<td>9 (4-60)</td>
<td>8 (4-48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>30 day readmission rate</td>
<td>43 (18.6%)</td>
<td>40 (20.7%)</td>
<td>0.62</td>
</tr>
</tbody>
</table>
ANATOMICAL HEPATIC RESECTION VERSUS WEDGE RESECTION FOR GALLBLADDER CANCER: ANALYSIS OF MULTI-CENTER DATABASE

M. H. Al-Temimi, I. F. Mousa, V. O’connor and A. L. DiFronzo
*Corresponding author. Mohammed Al-Temimi, Kaiser Permanente, Los Angeles Medical Center, USA

Background: To compare anatomical hepatic resection (AHR) to wedge resection (WR) for gallbladder cancer.

Methods: Hepatic resections for GBCA at 13 medical centers (2002-2017) were included. WR was defined as non-anatomical resection of 2-3 cm of the gallbladder fossa. AHR was defined as identifying and dividing the vasculobiliary pedicle for hepatic segments 4b and 5. Overall postoperative morbidity (OM), 90-day major (Clavien ≥3) morbidity (MM), mortality, and hospital length of stay (LOS) were compared among bivariate and multivariate analysis.

Results: In 753 patients with GBCA, 341 (45%) underwent cholecystectomy only and 112 (15%) underwent hepatic resection. Four resection cases were excluded, because they involved extended right hepatectomy. Of the remaining 108 cases, 25 (23%) underwent AHR. OM, MM and mortality were 44%, 25% and 1.8% respectively. Patients undergoing AHR were more likely to have hepaticojejunostomy (28% vs. 6%, p < 0.001) and open surgery (76% vs. 53%, p = 0.041). There was an association of AHR with OM (60% vs. 40%, p = 0.082), but this difference was not statistically significant. There was no difference in mortality (4% vs. 1.2%, p = 0.363), MM (32% vs. 24%, p = 0.429), organ/space infection (24% vs. 19%, p = 0.587), bile leak (12% vs. 10%, p = 0.869), and LOS (7.8 ± 4.7 vs. 6.7 ± 4.7 days, p = 0.307) between groups. Patients undergoing AHR and WR had comparable 5-year overall survival (43% vs. 46%, p = 0.113), disease-free survival (44% vs. 54%, p = 0.510) and disease-specific survival (59% vs. 51%, p = 0.657).

Conclusion: AHR for GBCA is associated with more complex hepatic resection than WR without improved long-term oncologic outcomes. Further studies with larger sample size are needed to confirm these findings.


case study

WOUND PROTECTORS MITIGATE SUPERFICIAL SURGICAL SITE INFECTIONS AFTER PANCREATODUODENECTOMY

J. B. Liu, M. S. Baker, V. M. Thompson, E. M. Kilbane and H. A. Pitt
*Corresponding author. Jason Liu, Lewis Katz School of Medicine at Temple University, USA

Background: Potential strategies to decrease surgical site infections (SSIs) include the choice of antibiotic prophylaxis, the type of incision, and the use of wound protectors. Wound protection has been studied extensively, but randomized trials and meta-analyses remain underpowered. Thus, the objectives of this study were to examine a national database to determine which mitigation, patient and operative factors were associated with decreased SSIs after pancreatoduodenectomy.

Methods: The 2016 American College of Surgeons-National Surgical Quality Improvement Program pancreateoduodenectomy database was queried. Data on recommended antibiotic prophylaxis (1st and 2nd generation cephalosporins), incision (midline or subcostal) and wound protector use were gathered on 3,979 patients. Multivariable logistic regression models were constructed to determine the effect of antibiotic prophylaxis, incision type, and wound protector use as well as patient and operative factors on SSIs.

Results: The overall SSI rate was 19.9%. Superficial SSIs occurred in 6.9% of patients. Deep incisional SSIs developed in 0.9%, and organ space infections (OSIs) occurred in 13.9% of patients. On multivariable analyses, wound protector use was independently associated with decreased SSIs of any type (Table). This influence was mediated by a reduction in superficial SSIs but not organ space infections (OSIs). Neither antibiotic choice nor incision type influenced any category of SSI. Among multiple potential variables, being overweight or obese, contaminated/dirty wound class, soft pancreas and prolonged operative time were independently associated with OSIs.

Conclusion: Wound protectors reduced superficial, but not organ space, infections in patients undergoing pancreatoduodenectomy. Wound protectors should be routinely utilized in patients undergoing pancreatoduodenectomy.

Table Influence of Mitigation, Patient and Operative Variables on Any Surgical Site Infection (SSI), Organ Space Infection and Superficial SSI

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency</th>
<th>Any SSI*</th>
<th>Organ Space Infection*</th>
<th>Superficial SSI*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MITIGATION</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommended Antibiotic</td>
<td>63%</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Midline Incision</td>
<td>81%</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Wound Protector</td>
<td>17%</td>
<td>0.73 (0.57–0.94)</td>
<td>0.85 (0.65–1.11)</td>
<td>0.66 (0.44–0.97)</td>
</tr>
<tr>
<td><strong>PATIENT/OPERATIVE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM (&gt;25)</td>
<td>70%</td>
<td>1.54 (1.30–1.82)</td>
<td>1.47 (1.24–1.75)</td>
<td>NA</td>
</tr>
<tr>
<td>Contaminated/Dirtty</td>
<td>17%</td>
<td>1.96 (1.03–3.79)</td>
<td>1.99 (1.04–3.81)</td>
<td>NA</td>
</tr>
<tr>
<td>Soft Pancreas</td>
<td>62%</td>
<td>1.82 (1.35–2.45)</td>
<td>2.50 (1.40–3.50)</td>
<td>NA</td>
</tr>
<tr>
<td>Operation Time (&gt;6 hr)</td>
<td>22%</td>
<td>2.09 (1.30–3.37)</td>
<td>1.88 (1.10–3.23)</td>
<td>NA</td>
</tr>
</tbody>
</table>

NS = Not Significant, NA = Not Associated
*Adjusted Odds Ratios (95% Confidence Intervals)
DEFINING A LIVER TRANSPLANT BENEFIT THRESHOLD FOR MODEL FOR END STAGE LIVER DISEASE

E. W. Beal, C. Akateh, D. Tumin, S. M. Black, K. Washburn, D. Azoulay and T. M. Pawlik
*Corresponding author: Eliza W. Beal, The Ohio State University, USA.

Background: Priority on the liver transplant (LT) waiting list is largely determined by the Model for End-stage Liver Disease (MELD) score. Prior studies have explored variation in transplant benefit — the difference between post-transplant survival versus survival on the waiting list — based on MELD. Serum sodium was recently added to the MELD score to improve survival prediction. We sought to define the MELD-Na threshold that corresponded to survival benefit for liver transplantation.

Methods: Data on adult LT candidates listed 6/2013-12/2015 were identified from the UNOS registry. Patients with MELD ≥ 12 were included. Six-month survival after listing was analyzed using multivariable Cox proportional hazards regression. MELD and MELD-Na scores at listing were examined as piecewise-constant time-varying covariates for patients undergoing LT. Transplant benefit was defined as hazard ratio (HR) of death <1 with receipt of transplantation.

Results: 12,243 patients with a median age of 56 years were included; 7,800 (63%) were male and 8,747 were white (71%). The most common etiology of liver disease was alcoholic cirrhosis (3,906, 32%). Using the original MELD score, 73% of patients were expected to derive benefit from transplantation with a MELD threshold of >18. Similarly, assessing the transplant benefit according to MELD-Na, 72% of patients had an expected transplant benefit with a threshold MELD-Na > 20 (Figure). Of note, transplant benefit was not consistent between MELD and MELD-Na prediction for 14% of patients. Specifically, the MELD-Na score resulted in a higher estimation of survival benefit for transplantation versus MELD alone.

Conclusion: Transition from MELD to MELD-Na did not define a more precise range at which patients benefited from transplantation. The population for whom transplantation was predicted to improve survival did change, however.

LIFE EXPECTANCY AFTER Pancreatic Cancer Resection, According to Hospital Operative Mortality

Mustafa Raoof, Byrne Lee, Laleh Melstrom, Susanne G. Warner, Gagandeep Singh and Yuman Fong
*Corresponding author. Mustafa Raoof, City of Hope Cancer Center, USA.

Background: Quality improvement initiatives in pancreatic cancer have focused on improving hospital operative mortality. It is not known if this is associated with long-term survival of patient’s treated at that hospital.

Methods: Patients without distant metastases undergoing pancreatectomy for pancreatic adenocarcinoma from 2004–2012 were analyzed from the National Cancer Database. Expected 90-day mortality rates were determined using multi-level logistic regression adjusted for clustering. For each hospital (with >30 resections during study period), percent mortality rate deviation (PMRD) from expected was calculated as: [(Observed/ Expected 90-day mortality)-1]×100.

Hospital improvement/worsening was calculated as the difference in PMD of each hospital for the two time periods: B (2009–2012) − A (2004–2008).

Results: A total of 22,782 patients treated at 164 hospitals met inclusion criteria. Long-term conditional survival was significantly associated with a hospital’s PMRD (HR 1.19, 95% CI 1.16 – 1.22, p < 0.001) — Figure 1. This association persisted when survival model was adjusted for patient-, disease-, and treatment-specific characteristics (Adjusted HR 1.24, 95% CI 1.21 – 1.28, p < 0.001).

For hospitals that had observed mortality greater than expected (n = 84, 51%) in time period A (i.e. PMRD > 0), any improvement in risk-adjusted mortality from time period A to B was associated with a significant reduction in risk of long-term death vs. no change or worsening of risk-adjusted mortality rate (Adjusted HR 0.86, 95% CI 0.81 – 0.92, p < 0.001).

Conclusion: Risk-standardized operative mortality rates of a hospital are strongly associated with long-term survival for pancreatic cancer patients treated at that hospital. Quality improvement initiatives focused on improving operative mortality of a hospital are likely to impact long-term survival as well.

Figure 1. Kaplan-Meier survival estimates

Percent Operative Mortality Rate Deviation:
-<25% of Expected
-Within 25% of Expected
-25% or more of Expected

Log-rank P-value: <0.001
40 ANALYSIS OF OUTCOME OF OPEN AND MINIMAL INVASIVE PANCREATICODUODENECTOMY USING NSQIP

Corresponding author. Hassan Aziz, Banner University Medical Center, USA

**Background:** Several large volume centers have published positive outcomes with laparoscopic and robotic pancreaticoduodenectomy (PD). The purpose of this study was to compare postoperative outcomes between open, laparoscopic and robotic pancreaticoduodenectomies using ACS National Quality Improvement Program (ACS-NSQIP).

**Methods:** We performed a Retrospective review of 2014–2015 NSQIP targeted data for patients undergoing pancreaticoduodenectomies for pancreatic cancer. Patients who underwent conversion from robotic or laparoscopic approach to open were excluded. Outcome measures were: hospital length of stay, operative time, 30-day postoperative complications, and mortality.

**Results:** 11,219 patients who underwent pancreaticoduodenectomies were evaluated. Majority were performed in open fashion (n=8654) were open, followed by laparoscopic (n = 1508), and robotic approach (n = 591). Compared to open approach, laparoscopic PD had lower rates of SSI (11% vs 3%; p = 0.02), higher rates of DVT (2.8% vs 6.6%; p = 0.034) and longer operative time (341 vs 480 min; p<0.001). In comparison with OP, robotic PD had lower rates of pneumonia (6.7% vs 1%; p = 0.03) and longer operative time (341 vs 510 min; p < 0.001). There was no significant difference between the three groups with regards to post-operative LOS, overall morbidity or mortality.

**Conclusion:** Smaller incisions did not predict a small hospital length of stay; or a reduced mortality or morbidity benefit in patients undergoing PD.

41 PANCREATECTOMY AND BODY MASS INDEX: AN INTERNATIONAL EVALUATION OF CUMULATIVE POSTOPERATIVE COMPLICATIONS USING THE COMPREHENSIVE COMPLICATIONS INDEX

B. P. Lovasik, P. Kron, P. A. Clavien, H. Petrowsky and D. A. Koobby
Corresponding author. Brendan Lovasik, Emory University, USA

**Background:** We examined the relationship between body mass index (BMI) and complications after pancreatectomy using the novel Comprehensive Complications Index (CCI), which processes cumulative events rather than only the most severe.

**Methods:** We retrospectively reviewed 500 patients (250 from USA and 250 from Europe) who underwent pancreatectoduodenectomy (PD, N = 351) or distal pancreatectomy (DP, N = 123) for postoperative complications using CCI. Patient BMI was stratified as Normal (N = 256, 51.4%), Underweight (N = 14, 2.8%), Overweight (N = 140, 28.1%), and Obese (N = 88, 17.7%). Binomial and multivariable regression was performed for factors associated with complications.

**Results:** Patients with non-ideal BMI had more complications (p < 0.05 each underweight/overweight/obese category). Obese patients had higher CCI (24.2 vs. 20.9, p = 0.000), more severe Clavien-Dindo indices (p = 0.007), and pancreatic fistulae rates (17.0 vs. 8.2%, HR 1.308, p = 0.026). In multivariable analysis, factors independently associated with higher CCI were higher patient BMI (HR 1.13, p = 0.009) and Comorbidity Index (HR 1.79, p = 0.001). Overweight/obese patients undergoing PD demonstrated higher CCI (29.6 vs. 20.9, p = 0.000), postoperative drainage procedures (14.0 vs. 3.9%, HR 2.173, p = 0.002), and 30-day readmissions (23.6 vs. 12.5%, HR 1.358, p = 0.027), with a trend toward more pancreatic fistulae (12.1 vs. 8.2%, HR 1.469, p = 0.06). Overweight/obese patients undergoing DP had a demonstrated a trend towards higher CCI (20.9 vs. 8.7, p = 0.062).

**Conclusion:** Overweight and obese patients are at significantly higher risk for postoperative complications and hospital readmission following pancreatic resection. Risk-prediction modeling and preoperative evaluation should include analysis of BMI. CCI is a powerful tool to assess post-pancreatectomy complications.

42 LOCAL REFERRAL OF PANCREATECTOMY PATIENTS TO IMPROVE SURGICAL QUALITY

M. E. Smith, U. Nuliyalu, C. J. Sonnenday, J. B. Dimick and H. Nathan
Corresponding author. Margaret Smith, University of Michigan, USA

**Background:** Referral of patients to high-quality hospitals (HQH) for complex procedures may improve outcomes. This is most feasible within small geographic areas, but access to specialized surgical procedures may be an implementation barrier. We sought to determine the availability of HQH performing pancreatectomy and the potential benefit of referral within small geographic areas.

**Methods:** We identified pancreatectomy patients age ≥65 years in 2012–2013 Medicare claims data. Hospitals were grouped by risk-adjusted complication rates (HQH: best 2 quintiles; low- quality hospitals, LQH: worst 2 quintiles), and patients were risk-stratified by clinical factors. The geographic units of analysis were Metropolitan Statistical Areas (MSAs), each consisting of a population center.
Results: We analyzed data on 5579 patients treated at 646 hospitals. Of the 2402 patients (43%) who received care at 258 LQH, 74% had a HQH in their MSA. Patients treated at LQH were a median of 24 miles from a HQH. Patients treated in MSAs with only LQH were a median of 60 miles from a HQH in an adjacent MSA (Fig 1). A similar pattern was seen among high-risk patients; 71% were treated at LQH despite the presence of HQH in their MSA. High-risk patients treated at LQH were a median of 25 miles from a HQH. If high-risk patients traveled 25 miles to a HQH, post-pancreatectomy mortality would decrease from 7% to 4% (p = 0.0013) and morbidity would decrease by 48% (38% v 20%, p < 0.001).

Conclusion: In small geographic areas pancreatectomy patients are often treated at LQH despite availability of HQH in the area or within an acceptable distance. Referral of patients, especially high-risk patients, to HQH within small geographic areas is a potentially effective strategy to improve outcomes of pancreatic surgery.

CD73 AS A NOVEL IMMUNE TARGET AND BIOMARKER IN PANCREATIC ADENOCARCINOMA


Background: Within the tumor microenvironment, the cell surface enzyme CD73 can mediate tumor immune escape by degrading extra-cellular adenosine triphosphate into immune suppressive adenosine. Although CD73 is emerging as a promising target for cancer immunotherapy, its relevance in pancreatic ductal adenocarcinoma (PDAC) has not been determined. Our goal was to investigate CD73 expression in resected PDAC and its prognostic value.

Methods: Using tissue microarrays, automated quantification (Visiomorph) of CD73 (Abcam), cytokeratins (CK8/18, Dako) and DAPI expression was measured by multiplex immunofluorescence on 108 tumors and paired peritumoral pancreatic tissue resected between 2000 and 2008. We tested associations between immune and clinicopathological features.

Results: CD73 expression (mean fluorescence intensity) was 1.8 fold higher on cancer cells compared to peritumoral pancreatic cells (P < 0.001). The mean CD73 expression on cancer cells was higher in stage IIb vs. I-IIa tumors (P=0.049), moderate/poor vs. well differentiated tumors (P = 0.008), T3 vs. T1-T2 tumors (P = 0.043) and N+ vs. N0 tumors (P = 0.049). The median time to recurrence and overall survival in patients with CD73high tumors (11.1 and 11.5 months, respectively) was significantly shorter than those with CD73low tumors (23.4 and 26.5 months, respectively, see Fig. 1). By multivariate analysis, high CD73 expression by pancreatic cancer cells was associated with poor patient prognosis independently of clinicopathological factors.

Conclusion: Our results suggest that CD73 may be a relevant immunotherapeutic target in PDAC and a promising immune prognostic biomarker. Further validation on independent cohorts and in metastases appears warranted.

COLLAGEN TARGETED MRI ACCURATELY MEASURES THE DESMOPLASTIC RESPONSE TO FOLFIRINOX TREATMENT IN A MURINE MODEL OF PANCREATIC CANCER

Derek J. Erstad, Mozhdeh Sojoodi, Christian T. Farar, Nicholas J. Rotile, Chloe Jones, Katherine Graham-O’Regan, Diego S. Ferreira, Shen Li, Sarani Ghoshal, Cristina R. Ferrone, Michael Lanuti, Peter Caravan, Kenneth K. Tanabe and Bryan C. Fuchs

Background: Neoadjuvant chemoradiotherapy for pancreatic ductal adenocarcinoma (PDAC) induces intense
fibrosis in the tumor field, known as the desmoplastic reaction. Conventional radiographic techniques have limited ability to distinguish desmoplasia from residual tumor, complicating surgical management. We show that molecular MRI using CM-101, a novel Type I collagen-binding probe, provides superior imaging resolution of tumor desmoplasia compared to standard MR contrast agents.

Methods: C57B/6 mice (n = 10 per group) were orthotopically implanted with 10 4 syngeneic Hy15549 PDAC cells (Ptf1-Cre; LSL-KRAS-G12D; p53 Lox/+). FOLFIRINOX was administered by intraperitoneal injection 2x/week starting on postoperative day 4. Mice were imaged on a 4.7T MRI with Gd-DOTA (180 nmol/g) and Gd-CM101 (30 nmol/g) 24h apart.

Results: CM-101 provided superior tumor enhancement compared to surrounding pancreas and retroperitoneum at all time points (p < 0.01), which was not observed with DOTA. CM-101 probe uptake was increased in collagen-dense, fibrotic tumor tissue compared to DOTA at 20 minutes post equimolar injection (41.3 ± 15.5 nmol/g vs. 23.9 ± 8.1 nmol/g, p < 0.01). FOLFIRINOX treatment increased tumor collagen proportional area (33. ± 6.1% vs. 20.7 ± 3.5%, p < 0.01), which correlated with decreased CM-101 MR signal attenuation (% of max) over 25 minutes compared to untreated tumors (82.9 ± 12.4% vs. 69.8 ± 14.4%, p < 0.05). CM-101 probe uptake was increased in FOLFIRINOX treated tumors (7.2 ± 2.6 vs. 4.9 ± 1.6, p < 0.05), consistent with imaging findings. There was no difference in DOTA signal attenuation between treatment groups.

Conclusion: Molecular MRI with CM-101 provides a novel imaging technique that could be used to monitor the desmoplastic response to neoadjuvant therapy in order to assist with patient selection for pancreatic resection.

45

INDUCTION OF PD-L1 EXPRESSION IN PANCREATIC TUMOR MICROENVIRONMENT BY IFN-Y: RATIONALE FOR PD-L1 THERAPY COMBINATION WITH IRREVERSIBLE ELECTROPORATION THERAPY

Y. Hong, H. Pandit, Z. Pulliam, N. Galbraith, S. Li, Y. Li and R. C. G. Martin
*Corresponding author. Young Hong, University of Louisville School of Medicine, USA

Background: PD-L1 inhibitors have shown recent optimism for treatment of various solid organs tumors with high expression of PD-L1 in their tumor. Irreversible electroporation can modulate the immune response and release variable amounts of IFN-y in the tumor microenvironment. We aim to demonstrate that PD-L1 expression can be induced by soluble IFN-y and propose a rationale for PD-L1 inhibitor to be used in combination to irreversible electroporation treatments for baseline low expressing PD-L1 pancreatic cancer cell lines.

Methods: MiaPaca and S20-13 pancreatic cell lines were treated in vitro with low-dose IFN-y (10 ng/ml) for 24 hours and analyzed for PD-L1 expression by quantitative RT-PCR, immunoblot, and flow cytometry. We analyzed the level of induction of PD-L1 expression from baseline after treatment and have been repeated in independent experiments.

Results: PD-L1 expression was significantly upregulated by qRT-PCR in both cell lines from low baseline expression in MiaPaca (15.2 rel. fold ±0.54; p < 0.01) and S20-13 (31.0 rel. fold ±4.36; p < 0.01) after 24-hour treatment of low-dose IFN-y (10 ng/ml). Confirmation of significant upregulation of PD-L1 protein expression was confirmed by both immunoblot and flow cytometry.

Conclusion: PD-L1 expression is significantly induced after stimulation with low-dose IFN-y exposure in pancreatic cancer cell lines. It is a rational treatment strategy to combine PD-L1 inhibitor with concurrent irreversible electroporation therapy for pancreatic cancer to further enhance the immune response to the tumor microenvironment.

46

LOCAL VERSUS CIRCULATING IMMUNE CELL POPULATIONS IN PANCREATIC DUCTAL ADENOCARCINOMA PATIENTS

*Corresponding author. Michael Gerber, University of Florida, USA

Background: Pancreatic ductal adenocarcinoma (PDAC) escapes both innate and adaptive immune responses via poorly understood mechanisms. We hypothesized that activation of mononuclear cell populations in regional lymph nodes (rLNs) would not correlate to the induction of a systemic, adaptive immune response in PDAC patients.

Methods: Patients undergoing pancreatic resection for PDAC had mononuclear cells isolated from peripheral blood and rLNs. Cells were immunostained and subjected to flow cytometer analysis to determine population frequencies of myeloid derived suppressor cells (MDSCs), dendritic cells (DCs), and various T-cell lineages.

Results: Ten patients that were therapy naïve at time of resection were analyzed. MDSC and DC populations as well as their activation marker (CD80) and inhibitory marker (PD-L1) were not different between the peripheral blood and rLN samples. The peripheral blood did differ from the rLN in five different T-cell populations: both CD8+ Tc1.17 and CD8+ effector memory (EM) were higher in the rLN whereas Tc0, CD8+ effector memory (EMRA), and CD4+ central memory (CM) were higher in the peripheral blood (p-values <0.05). No difference was detected in the MHC class II binding CD4+ Th0, Th1, Th1.17, Th17, memory naïve, EM, and EMRA populations. No difference was detected in the MHC class I binding CD8+ Tc1, Tc17, Tc2, memory naïve, and CM populations.
Conclusion: These data support the presence of a regional immune response to PDAC that fails to induce a systemic, adaptive immune response to the neoplasm.

47 CHANGE IN CIRCULATING TUMOR DNA AFTER HEPATIC RESECTION FOR METASTATIC COLORECTAL CANCER

Background: Hepatic resection can be curative in well-selected, metastatic colorectal cancer (mCRC) patients. Circulating tumor DNA (ctDNA) has shown promise in predicting response and early recurrence. This prospective study assessed the prognostic ability of ctDNA from blood drawn pre and post-resection.

Methods: Between November 2014 and November 2015, patients with radiologically detected, biopsy-confirmed mCRC were enrolled. Blood was obtained intraoperatively from the hepatic vein (HV), portal vein (PV), and a peripheral vein pre-resection and postoperatively from a peripheral vein within 2–4 weeks. The presence of commonly mutated, targetable genes in ctDNA was analyzed and the agreement was assessed with Cohen’s kappa and percent agreement (PA). Disease-specific survival (DSS) in all patients and disease-free survival (DFS) after complete resection was assessed from surgery with Kaplan-Meier methods.

Results: Fifty-nine patients were enrolled and 23 had their primary tumor removed at hepatic resection. Agreement was high between preoperative peripheral vein and HV and PV ctDNA containing mutated APC (n = 4, k = 0.78–0.88, PA = 95.9–98.0%) or TP53 (n = 7–8, k = 0.73–0.80, PA = 91.8–93.9%) pre-resection. No difference was seen between pre and postoperative mutated APC (P = 0.45), but postoperative mutated TP53 was significantly less common than before resection (P = 0.008), as was ctDNA overall (P = 0.002). DSS and DFS at 1 year were 97% (95% CI: 87–99%) and 53% (95% CI: 38–66%), respectively. In patients with ctDNA with an APC mutation, 1 year DFS was 80% (95% CI: 20–97%) compared to 50% (95% CI: 35–64%) in APC-absent patients (P = 0.06).

Conclusion: ctDNA detected before and after hepatic resection varied significantly but was not prognostic of DFS or DSS. APC mutations in patients with mCRC showed a possible trend toward better DFS.

48 NOVEL CELL MEMBRANE CATION TRANSPORTER ASSOCIATED WITH PLATINUM THERAPY RESISTANCE IN PANCREATIC ADENOCARCINOMA IDENTIFIED THROUGH CRISPR/CAS9 LOSS-OF- FUNCTION SCREEN
E. Dogeas, B. Chen, Y. Xie, J. T. Mendell and M. M. Augustine

Background: Platinum agents form the backbone of chemotherapy regimens for pancreatic cancer. However, the biologic mechanisms of platinum resistance remain poorly understood. Utilizing a new biologic approach, we performed a loss of function, unbiased, genome-wide screen to identify genes associated with platinum resistance.

Methods: The novel CRISPR/Cas9 technology was used to inactivate 20,000 genes in the MiaPaCa2 pancreatic cancer cell line. Each gene was targeted with 6 guide RNAs (sgRNA) delivered by lentiviral transduction. After puromycin selection, 2 replicates of cells were intermittently treated with 5uM cisplatin for 24 hours over 4 weeks. A second set of replicates served as non-treatment control. Finally, genomic DNA was extracted from surviving cells, guide sequences amplified and sequenced. MAGeCK analysis identified significantly enriched guides in the treated cells.

Results: Multiple genes were identified that, when lost, confer resistance to platinum agents (p-value <0.05). Amongst known mediators of chemoresistance such as Keap1 and 4 members of the STAGA chromatin modifying complex: USP22, TADA1, TAF5L and TAF6L, the loss of the cation transporter MAGT1 was associated with platinum resistance. sgRNA knock-out of these genes when compared to cisplatin treated non-target controls validated the screening results.

Conclusion: Our chemotherapy investigation platform identified a novel role for the membrane magnesium cation transporter, MAGT1, which has been associated with X-linked immunodeficiency, but never implicated in platinum resistance hitherto. Our findings nominate MAGT1 as a candidate biomarker for response to platinum therapy and open new avenues of mechanistic investigation into platinum action, including the cellular mechanisms of platinum drugs uptake and the interplay between intracellular magnesium level and platinum cytotoxicity.

49 THE EFFECTS OF P-NAK-TIDE AND SW033299 ON NASH ASSOCIATED CIRRHOSIS IN THE RODENT
M. Schade, J. A. Sanabria, R. Aguilar, M. Andryka, A. Mallick, J. Fannin and J. Sanabria

Background: NASH and its complications ESLD and HCC have become the second most common cause for liver cirrhosis in the rodent.
transplantation in US. The purpose of the present studies was to test the efficacy of two compounds developed by our group, “pNa/K-tide” and “SW033299” in reversing the liver disturbances produced by NASH.

Methods: C57Bl/6j mice (n = 7) were exposed to normal chow (Control-) or high fat diet + fructose (HFD). The mice on HFD was non treated (Control+) or treated with i) p-Na/K-tide, ii) with SW033299 or iii) exposed to an exercise protocol. Livers/plasma were collected “at weeks 7, 12, 16, 20, 24”. Body composition was determined by MRI spectroscopy. The proportion of cells undergoing mitosis or in cell arrest was determined against liver apoptotic index and collagen deposition by standard stains using morphometric techniques. Quantitative protein expression of genes p53, p21, mTOR1, STAT33, SIRT7, FOX01, Grb2 were determined by Western Blots. Metabolic profiles were measured on treated plasma by LC/MS-MS.

Results: The total body weight corrected by aging increased significantly in the HFD (HFD vs normal chow, p < 0.05 by ANOVA). The amount of liver fat accumulation, the number of cells in senescence and the apoptotic index were significantly decreased in both the pNaK and SW groups when compared to the HFD (p < 0.5 by ANOVA). In addition, the deposition of collagen was significantly lower in the pNaK and SW groups when compared to the HFD group.

Glutathione ratio, mitochondrial β-lipid oxidation function and Na/K-exchange pump activity after censored for aging followed similar trends among groups (p < 0.05 by ANOVA). Metabolic prints were significantly different among groups.

Conclusion: pNaK-tide and SW033299 not only prevent but reverse NASH due to high fat diet in the rodent model.

50
PERIOPERATIVE BLOOD TRANSFUSIONS FOLLOWING HEPATIC LOBECTOMY: A NATIONAL ANALYSIS OF ACADEMIC MEDICAL CENTERS IN THE MODERN ERA

V. K. Dhar, K. Wima, A. D. Jung, Y. Kim, S. A. Ahmad, S. H. Patel and S. A. Shah *Corresponding author. Vikrom Dhar, University of Cincinnati, USA

Background: We aim to characterize the prevalence and impact of perioperative blood use for patients undergoing hepatic lobectomy at academic medical centers on the national level.

Methods: The University HealthSystems Consortium database was queried for hepatic lobectomies performed between 2011-2014 (n = 6476). Patients were grouped according to base was queried for hepatic lobectomies performed between 2011-2014 (n = 6476). Patients were grouped according to models. The addition of genetic markers to risk models may improve prognostic stratification. We sought to develop a prognostic nomogram which incorporates both “BRAF” and “KRAS” mutational status for the first time.

Methods: We analysed an international cohort of 853 patients with a known “BRAF” status, treated at 7 tertiary-care centres. Independent predictors of OS were determined through multivariable Cox regression; the identified variables were then incorporated into the nomogram and assigned points according to their respective linear predictors.

Results: The nomogram (figure) incorporated the following variables: patient age, primary lymph node metastasis, extrahepatic disease, synchronous CRLM, carcinoembryonic antigen levels, tumor size and number, R1 resection, “BRAF” and “KRAS” mutational status. Importantly, the presence of “BRAF” V600E mutation was awarded the most points [score (s) = 76] and significantly improved the nomogram’s accuracy (p = 0.003). The resulting OS model achieved good prognostic discrimination [C-statistic = 0.66 (0.62–0.69)] and divided patients into 3 tertiles with distinct survival. Patients in tertile 3 (s > 131) exhibited substantially worse survival (5-year OS: 26%) than patients in tertile 2 (s: 112–131; 5-year OS: 46%; p = 0.001); in turn, patients in tertile 1 had significantly better prognosis (s < 112; 5-year OS: 66%; p = 0.021).

Conclusion: The proposed genetic risk nomogram demonstrated very good prognostic discrimination in an international multi-institutional cohort. Importantly, “BRAF”
V600E mutational status substantially improved prognostic accuracy and should be considered for inclusion in future risk models.

53
OPEN VERSUS LAPAROSCOPIC LIVER RESECTION FOR COLORECTAL LIVER METASTASES LOCATED IN THE POSTERO-SUPERIOR SEGMENTS: A SUB-GROUP ANALYSIS FROM THE OSLO-COMET TRIAL

D. L. Aghayan, Á. A. Freitaland, A. M. Kazaryan, M. A. Sahakyan, B. I. Rassok, B. A. Bjørnbeth and B. Edwin
*Corresponding author. Davit Aghayan, Oslo University Hospital, Norway

Background: Laparoscopic liver resection of tumors located in the postero-superior segments is considered to be technically challenging. This study aimed to compare the perioperative outcomes for laparoscopic versus open resection of colorectal liver metastases located in the PS segments.

Methods: This is a sub-study of the Oslo-CoMet trial. In this trial, 280 patients were randomly assigned to open or laparoscopic parenchyma-sparing liver resections of colorectal metastases. Inclusion was from February 2012 to February 2016. For the current study, patients with metastases in postero-superior segments were identified, and perioperative and short-term oncological outcomes were collected from the prospective trial database. The Accordion system and the Comprehensive Complication Index were used for grading of postoperative complications.

Results: 62 patients underwent laparoscopic and 74 patients underwent open liver resections. A total of 257 lesions were removed. A total of 23 patients(31%) in open group and 16 patients(26%) in the laparoscopic group developed postoperative complications (P = 0.49). The mean comprehensive complication index was 32 in the open group and 26 in the laparoscopic group (P = 0.19). Median postoperative hospital stay was 2 days in the laparoscopic and 4 days in the open group (P < 0.001). Blood loss was slightly higher in patients assigned to laparoscopic surgery (500 vs. 250 ml, P = 0.001), whereas the operative time (median, 145 vs. 143 min) was similar between the two groups.

Conclusion: In this subgroup-analysis of patients in the Oslo-CoMet trial, we found similar postoperative complications rate and shorter hospital stay following laparoscopic resection of posterior-superior segments.

52
DOUBLE LIGATION OF PORTAL AND HEPATIC VEINS ACHIEVES HYPERTROPHY COMPARABLE TO ALPPS - A STUDY IN PIGS

*Corresponding author. Erik Schadde, Rush University Medical Center, USA

Background: Liver hypertrophy induced by partial portal vein ligation (PVL) is accelerated by adding parenchymal transection (“ALPPS procedure”). Previous experiments suggested that transection abrogates portal neocollateral formation between lobes. This preclinical experimental study in pigs tests the hypothesis that simultaneous ligation of portal and hepatic veins (PVL + HVL) of the liver functionally abrogates collateral formation as well and thereby also accelerates hypertrophy.

Methods: Simultaneous PVL + HVL was performed in landrace pigs by simultaneously ligating portal veins and major hepatic veins with the help of intraoperative ultrasound and ligated using pledgeted transparenchymal sutures. Kinetic growth was compared to a model of PVL. The anatomy of the portal vein system was studied after 7 days using epoxy casts of the portal circulation. Portal vein flow and portal pressure were measured and Ki-67 staining was used to evaluate the proliferative response.

Results: Pigs were randomized to PVL (n = 8) and PVL + HVL (n = 6). PVL + HVL was well tolerated, led to mild cytolysis and no necrosis in the portal vein deprived lobe. The portal vein supplied sector increases by 90 ± 22% after PVL + HVL compared to 29 ± 18% after PVL (p < 0.001). Collaterals to the deportalized liver developed after 7 days in both procedures, but were markedly reduced in PVL + HVL. Ki-67 staining at 7 days was comparable. Volume increase after PVL + HVL appeared comparable to a pig model of ALPPS established before.

Conclusion: This study shows that simultaneous PVL + HVL leads to accelerated hypertrophy comparable to ALPPS. The findings suggest that reduced collateral formation indeed is an important element of rapid hypertrophy. Simultaneous Bi-embolization of portal and hepatic veins may well replace ALPPS to increase the efficiency of regenerative liver surgery.
assess the role of plasmatic Factor V levels after LT as an predictor of mortality after LT.

**Methods:** This retrospective study has assessed patients that underwent LT between 2007 and 2017 at the Hospital de Clinicas de Porto Alegre, Brazil. All patients had measured plasmatic Factor V levels on the 2 nd post-operative day after LT. The Factor assay followed international standards. Early graft dysfunction (EGD) was defined by Olthoff et al. The primary outcome was overall mortality. The threshold for Factor V was established by ROC curve and Youden index. A multivariate analysis using Cox regression was performed to analyze the impact of Factor V in predicting death.

**Results:** 225 patients were included in the study. The area under the ROC curve was 0.8. The sensitivity was and specificity to predict EGD was 72.3% and 72.9%, respectively. Patients with Factor V >43.65% were classified as High Factor V and ≤43.65% as Low Factor V. The Low Factor V group had 89 patients and the High Factor V group had 136 patients. Table 1 shows the demographic and clinical characteristics of patients. The proportion of patients diagnosed of EGD in the lower factor V group was 48% while it was 12% in the high Factor V group (p < 0.001). The median overall survival was 7.2 years for the high Factor V group vs. 5.9 years for the low Factor V group (p = 0.02). Factor V was an independent predictor for 6-months mortality [HR 0.96 (95%CI 0.94 – 0.98) and overall mortality [HR 0.98 (95% CI 0.97 – 0.99) after LT.

**Conclusion:** Factor V may be an earlier predictor of mortality after LT. Further studies should be done to confirm these results and test Factor V relationship with other hepatic function markers.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low Factor V</th>
<th>High Factor V</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 89</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years (IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipients</td>
<td>58 (48–61)</td>
<td>57 (60–62)</td>
<td>.87</td>
</tr>
<tr>
<td>Donors</td>
<td>37 (22–51)</td>
<td>42 (23–55)</td>
<td>.38</td>
</tr>
<tr>
<td>BMI donor, Kg/m² (IQR)</td>
<td>24.4 (22.8–26.4)</td>
<td>25.4 (23.1–27.3)</td>
<td>.2</td>
</tr>
<tr>
<td>HCV, yes (%)</td>
<td>57 (64)</td>
<td>99 (72.8)</td>
<td>.12</td>
</tr>
<tr>
<td>HCC (%)</td>
<td>43 (48.3)</td>
<td>81 (69.5)</td>
<td>.06</td>
</tr>
<tr>
<td>MELD score (IQR)</td>
<td>14 (10–21)</td>
<td>13 (10–18)</td>
<td>.09</td>
</tr>
<tr>
<td>Donor cause of death</td>
<td></td>
<td></td>
<td>.24</td>
</tr>
<tr>
<td>Cerebrovascular accident (%)</td>
<td>41 (46.1)</td>
<td>76 (55.9)</td>
<td></td>
</tr>
<tr>
<td>Traumatic (%)</td>
<td>40 (44.9)</td>
<td>48 (35.3)</td>
<td></td>
</tr>
<tr>
<td>Other (%)</td>
<td>8 (9)</td>
<td>12 (8.8)</td>
<td></td>
</tr>
<tr>
<td>Cold ischemia time, min (IQR)</td>
<td>450 (430–470)</td>
<td>440 (424–480)</td>
<td>.33</td>
</tr>
<tr>
<td>Warm ischemia time, min (IQR)</td>
<td>35 (30–40)</td>
<td>35 (30–40)</td>
<td>.27</td>
</tr>
<tr>
<td>Surgical time, min (IQR)</td>
<td>360 (288–432)</td>
<td>315 (270–366)</td>
<td>.001</td>
</tr>
<tr>
<td>Hepatic artery thrombosis (%)</td>
<td>5 (5.6)</td>
<td>7 (5.1)</td>
<td>.55</td>
</tr>
<tr>
<td>EGD (%)</td>
<td>43 (48.3)</td>
<td>16 (11.8)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**55 POSITIVE CYSTIC DUCT STUMP AT INDEX CHOLOCYSTECTOMY IN INCIDENTAL GALLBLADDER CANCER IS A STRONG NEGATIVE PROGNOSTICATOR EVEN IN PATIENTS WITHOUT RESIDUAL DISEASE AT ONCOLOGIC RE-SECTION**


*Corresponding author. Eduardo Vega, The University of Texas MD Anderson Cancer Center and Hospital Sotero del Rio, USA

**Background:** The presence of residual cancer (RC) in patients undergoing oncologic extended resection (OER) for Incidental Gallbladder Cancer (IGBC) is associated with poor DSS. However, negative prognosticators at time of index cholecystectomy in patients with incidental gallbladder cancer who are not found to have RC at OER are poorly understood.

**Methods:** Pathologic features of incidental gallbladder cancer of patients who underwent OER for IGBC at two centers (USA & Chile) during 1999–2015 with curative intent and without RC were examined. Predictors of disease-specific survival (DSS) were analyzed.

**Results:** One-hundred-fourteen patients were included. Positive Cystic Duct Stump (PCDS) was found in 12 (11%) patients. Resection of the common bile duct was performed in 21 (18%) of those patients. DSS was significantly worse in the patients with PCDS at index cholecystectomy than without PCDS (DSS rate at 3 and 5 years, 58% vs 86% and 45% vs 80% with a p value <0.0001) (Figure 1) even when no RC was found at OER. Positive cystic duct stomp was predictive of worse DSS in the multivariate analysis (HR 10.6).

**Conclusion:** In patients without RC at OER, a positive cystic duct stomp at index cholecystectomy is a strong and singular predictive risk factor for worse DSS and should prompt consideration for additional multimodal therapy to achieve optimal oncologic outcome.
EVALUATION OF LIVER TRANSPLANT RESULTS WITH “LIVERS THAT NOBODY WANTS”

*Corresponding author. Emilio Quiñonez, Hospital el Cruce, Argentina

**Background:** The shortage of donors to meet the demand for transplants is a global problem. Several strategies have been implemented to ameliorate this situation, including the use of “livers that nobody wants” donors. Outcomes should be evaluated.

**Methods:** CRESL-SINTRA and retrospective data base were used to analyze transplant activity in Argentina and in the Hospital El Cruce (HEC), respectively during 2013–2016. 2 pre-specified groups: 1. patients receiving an organ beyond percentile 75 (p75) of the median of the rejected offers before graft acceptance. 2. rest of receptors. Percentages and median (with interquartile range/IQR), chi2 and Wilconxon Rank Sum test, Kaplan-Meier/log rank sum test were used. A p < 0.05 was considered statistically significant.

**Results:** 1325 liver transplants were performed nationally, 5 (IQR 3-11) as median of rejected offers before graft acceptance. 153 were performed in HEC, and its median was 7 (IQR 3-18), 55/36% of those grafts beyond p75; none used for acute liver failure. Comparing 1 vs 2 (55 vs 72), there were no differences in age, primary nonfunction, early extubation, dialysis, ICU and total length stay, graft and patient survival. Receptor’s MELD was the only difference (24 IQR 22-25 vs 28 IQR 25-33 p < 0.05).

**Conclusion:** One third of the population of our center received “livers that nobody wants” (grafts previously rejected 12 times), with similar results. Future research should determine the causes of such rejections.

IMPACT OF RECENT GUIDELINES ON OVERTREATMENT OF ASYMPTOMATIC PANCREATIC CYSTIC LESIONS

K. A. Baugh, H. S. Tran Cao, G. Van Buren, E. J. Silberfein, C. Hsu, O. Barakat, N. N. Massarweh and W. E. Fisher
*Corresponding author. Katherine Baugh, Baylor College of Medicine, USA

**Background:** Resection of pancreatic cystic lesions can prevent pancreas cancer but aggressive resection of benign cysts may cause harm. More conservative guidelines for cyst management have been proposed. We hypothesized that if conservative guidelines were applied to our patient population, pancreas resections for benign cystic lesions would decrease without failure to resect malignant lesions.

**Methods:** A retrospective review of a prospectively maintained database was performed from 2006–2017. Patients who underwent resection for asymptomatic cystic lesions were retrospectively categorized as candidates for resection or surveillance according to the Fukuoka and AGA guidelines. Final surgical pathology was reviewed.

**Results:** 264 patients underwent resection for pancreatic cysts. 212 were symptomatic and 7 were excluded because incomplete work-up precluded retrospective application of guidelines. Among 52 patients with asymptomatic cysts, 17 (38%) would have continued surveillance by Fukuoka guidelines and 24 (53%) by AGA guidelines. Guidelines were followed similarly regardless of cyst location (9 of 16 head (56%) / 18 of 28 tail (64%)) and compliance increased throughout the series. Final surgical pathologic diagnosis was of no malignant potential in 16 (36%), IPMN 23 (51%), PNET 1 (2%), other premalignant lesions 2 (4%), and IPMN with invasive cancer 3 (7%). No patient that would have been relegated to surveillance by the new guidelines harbored severe dysplasia or invasive cancer.

**Conclusion:** Consistent application of the Fukuoka or AGA guidelines in our practice may reduce the morbidity of unnecessary surgery without failing to resect malignant pathology.

EFFECT OF VESSEL PRESERVATION ON SPLENIC VOLUME AND FUNCTION IN PATIENTS WITH SPLEEN PERSERVING DISTAL PANCREATECTOMIES

Lavanya Yohanathan, Benjamin P. T. Loveday, Nishaan Brar, Paul D. Greig, Ian D. McGilvray, Carol-Anne Moulton, Steven Gallinger, Alice C. Wei and Sean P. Cleary
*Corresponding author. Lavanya Yohanathan, University of Toronto, Canada

**Background:** Spleen preserving distal pancreatectomy can be accomplished using vessel sparing (VSDP) or vessel ligating (Warshaw, WDP) techniques. The purpose of this study was to compare clinical and functional outcomes of the spleen between patients who underwent VSDP and WDP.

**Methods:** A retrospective cohort study was conducted at Toronto General Hospital from 2006–2015. Perioperative, hematologic and long-term outcomes were analyzed. Spleen volumes were calculated using volumetry software. Splenic infarction was assessed on contrast enhancement in the venous phase on postoperative CT scans.

**Results:** 82 patients were included (WDP n = 63, 77%; VSDP n = 19, 23%). In the WDP group there was more frequent laparoscopic approach (p = 0.043) and increased tumor diameter (p = 0.034). There was no difference in the operative duration, blood loss, length of stay, or Clavien (3) complication rate. Splenic infarction was more common in the WDP group (p = 0.032). No patient with splenic infarction required intervention. There was no significant difference in hemoglobin, red cell, white cell or platelet counts between the groups at postoperative day1,3,5 or at 3,6, and 12 months. Splenic volume did not change from baseline at any time point up to 12 months post-surgery, with no difference between the groups. Following WDP, there was decreased contrast enhancement in the upper pole, hilar region and lower pole (p < 0.05) in the first week which resolved after 3 months. Rates of long term complications were similar between the groups.

**Conclusion:** There were no significant differences between VSDP and WDP in hematologic parameters or splenic function and volume up to 12 months post-surgery, although CT evidence of splenic infarction was more
frequent after WDP. Both techniques maintain sufficient splenic perfusion to preserve its volume and function.

59 OUTCOMES AFTER PANCREATECTOMY WITH ROUTINE USAGE OF PASIREOTIDE

J. W. Kunstman, D. A. Goldman, M. Gönen, V. P. Balachandran, R. P. DeMatteo, M. I. D'Angelica, W. R. Jarnagin, T. P. Kingham and P. J. Allen *Corresponding author. John Kunstman, Memorial Sloan Kettering Cancer Center, USA

Background: The somatostatin analogue pasireotide lowered relative risk of clinically-relevant pancreatic leakage following pancreatectomy by over 50% in a double-blind randomized trial previously performed at our institution. Thus, we adopted routine usage of pasireotide following pancreatectomy. This study sought to assess the durability of the observed reduction in pancreatic leak with pasireotide in regular practice.

Methods: A prospective database was queried for all patients who underwent pancreatectomy after 10/2014 following completion of the above trial and received pasireotide (900 mcg SQ before incision, twice daily following completion of the above trial and received pasireotide (900 mcg SQ before incision, twice daily thereafter for 5–7 days of discharge). The primary outcome measure was identical to the prior randomized trial (pancreatic fistula [PF] or abscess requiring procedural intervention). Outcomes were recorded at 60 days and compared to the placebo arm of the above trial, and correlated with known PF risk factors.

Results: 653 of 662 patients during the 33-month study period (98.6%) received pasireotide and were evaluated (212 distal pancreatectomy [DP], 441 pancreaticoduodenectomy [PD]). The primary outcome occurred in 13.3% (n = 87) of patients in the current analysis, compared to the placebo arm of the above trial, and correlated with known PF risk factors. Multivariate Cox regression showed that age, pCR and NCT-S interval per 29 weeks were significantly predictive of OS, the rate of pCR and its predictors have not been elucidated yet. Our aim was to study factors predicting rate of pCR in a large data set and the impact on OS.

Methods: Patients listed in the National Cancer Data Base from 1998 to 2011 were studied. We included patients with NCT followed by surgery. Demographics, cancer characteristics, and treatment modalities including NCT to surgery (NCT-S) interval were studied.

Results: A total of 2093 patients were included. Mean age was 62, 51% were male, and 71% had neoadjuvant radiotherapy (NRT). NCT-S was divided into time quintiles in weeks: 8–11, 12–14, 15–19, 20–29 and ≥29 weeks; as well as a continuous variable. Median follow up was 74 months.

Rate of pCR was 2.1% (44/2093). OS in pCR vs non-pCR: 61 vs. 31 months, HR 0.3, 95% CI 0.1–0.9, p = 0.03. There was a significant increase in pCR with longer NCT-S interval (quintiles: 5/510 = 1.0%, 9/551 = 1.6%, 8/462 = 1.7%, 12/403 = 3.0% and 10/167 = 6.0%, p < 0.001). In logistic regression: NRT (OR 2.5, 95% CI: 1.1–6.1, p = 0.03) and NCT-S interval per week increase (OR 1.1, 95% CI 1.03–1.09, p < 0.001) as well as NCT-S >29 weeks (OR 6.1, 95% CI: 2.02–18.50, p < 0.001) were predictive of increased pCR rate. Multivariate Cox regression showed that age, pCR and NCT-S >29 weeks were significantly predictive of OS, while gender, race, facility type, tumor grade, cT, cN stage, single vs. multiple chemotherapy agents and NRT were not.

Conclusion: NCT-S interval >29 weeks and pCR were independent predictors of better OS in pancreatic cancer patients. NRT predicted increased pCR but not OS in the multivariate analysis. Further studies are needed to optimize multimodality regimens that best improve OS.

60 PATHOLOGICAL COMPLETE RESPONSE TO CHEMOTHERAPY IN Pancreatic CANCER: FREQUENCY, PREDICTORS AND IMPACT ON OVERALL SURVIVAL

B. Azab, C. Ripat, J. Amundson, F. I. Macedo, O. Picado, A. S. Livingstone and D. Yakoub *Corresponding author. Basem Azab, University of Miami Miller School of Medicine, USA

Background: While Pathological complete response (pCR) after neoadjuvant chemotherapy (NCT) in pancreatic cancer has been associated with improved overall survival (OS), the rate of pCR and its predictors have not been elucidated yet. Our aim was to study factors predicting rate of pCR in a large data set and the impact on OS.

Methods: Patients listed in the National Cancer Data Base from 1998 to 2011 were studied. We included patients with NCT followed by surgery. Demographics, cancer characteristics, and treatment modalities including NCT to surgery (NCT-S) interval were studied.

Results: A total of 2093 patients were included. Mean age was 62, 51% were male, and 71% had neoadjuvant radiotherapy (NRT). NCT-S was divided into time quintiles in weeks: 8–11, 12–14, 15–19, 20–29 and ≥29 weeks; as well as a continuous variable. Median follow up was 74 months.

Rate of pCR was 2.1% (44/2093). OS in pCR vs non-pCR: 61 vs. 31 months, HR 0.3, 95% CI 0.1–0.9, p = 0.03. There was a significant increase in pCR with longer NCT-S interval (quintiles: 5/510 = 1.0%, 9/551 = 1.6%, 8/462 = 1.7%, 12/403 = 3.0% and 10/167 = 6.0%, p < 0.001). In logistic regression: NRT (OR 2.5, 95% CI: 1.1–6.1, p = 0.03) and NCT-S interval per week increase (OR 1.1, 95% CI 1.03–1.09, p < 0.001) as well as NCT-S >29 weeks (OR 6.1, 95% CI: 2.02–18.50, p < 0.001) were predictive of increased pCR rate. Multivariate Cox regression showed that age, pCR and NCT-S >29 weeks were significantly predictive of OS, while gender, race, facility type, tumor grade, cT, cN stage, single vs. multiple chemotherapy agents and NRT were not.

Conclusion: NCT-S interval >29 weeks and pCR were independent predictors of better OS in pancreatic cancer patients. NRT predicted increased pCR but not OS in the multivariate analysis. Further studies are needed to optimize multimodality regimens that best improve OS.
A PROSPECTIVE STUDY OF PASIREOTIDE IN PATIENTS UNDERGOING PANCREATICODUODENECTOMY: A PROPENSITY SCORE MATCHED ANALYSIS


Background: Pasireotide is a newer generation somatostatin analogue which led to a significant reduction in pancreatic fistula (PF) after pancreatectomy in a single-center randomized controlled trial. We sought to determine if pasireotide reduces the incidence of PF and other complications following pancreaticoduodenectomy (PD) at our center.

Methods: All patients between April 2011 and January 2017 undergoing PD were prospectively followed in our institutional complications database. For 18 months (April 2015 to September 2016), 5 pancreatic surgeons trialed pasireotide in all patients undergoing PD. Patients receiving pasireotide were then propensity score matched to patients before and after this trial period who did not receive pasireotide using age, sex, comorbidities (coronary artery disease, jaundice, diabetes, hypertension, COPD, alcohol use, smoking, and ASA), malignancy, vascular resection, gland firmness, duct size, intraoperative blood loss, intraoperative blood transfusion, preoperative hemoglobin, intraoperative drain placement, and surgeon experience, and their outcomes compared.

Results: 459 patients underwent PD, and 127 patients (28%) received pasireotide. Patients who received pasireotide were significantly more likely to have dilated pancreatic ducts and have a drain left at the time of surgery. Patients who received pasireotide had no difference in PF (any grade or severe), overall complications, 90-day readmission, or 90-day mortality. Among 112 propensity score matched pairs, patients who received pasireotide did not have significantly different rates of any grade PF (17.0% vs 12.5, p = 0.35), and the rates of severe PF were identical between low, medium, and high volume groups. Similarly, there were no differences in operative time, blood loss, intraoperative fluid administration, use of internal pancreatic stents, or postoperative lactate (all p > 0.05). Patients with high 72-hour net fluid balance had a significantly higher rate of POPF compared to medium and low volume groups (31.4% vs. 11.4% vs. 8.8%, p = 0.024). On multivariate analysis, increasing net fluid balance was significantly associated with POPF (OR 1.25, CI 1.02-1.54, p = 0.03).

Conclusion: Implementation of routine pasireotide after PD at our center did not reduce the incidence or severity of PF following pancreaticoduodenectomy.

DOES PERIOPERATIVE FLUID RESUSCITATION IMPACT PANCREATIC FISTULA RATES AFTER PANCREATICODUODENECTOMY?


Background: Postoperative pancreatic fistula (POPF) remains a common and dreaded complication after pancreaticoduodenectomy (PD). Previous literature on intestinal anastomosis suggests that liberal perioperative fluid administration may contribute to poor anastomotic healing.

We aim to evaluate the relationship between perioperative fluid resuscitation and development of POPF after PD.

Methods: In this single-institution retrospective study, we analyzed net fluid resuscitation over the first 72 hours of patients who underwent PD between 2013 and 2017. One hundred and four patients were categorized by tertile into low, medium, and high fluid volume groups. POPF was defined by the International Study Group of Pancreatic Surgeons’ 2016 update, and only Grade B and C POPF were included. Statistics were performed using Chi-square, ANOVA and multivariate analyses.

Results: POPF was identified in 17.3% of patients (n = 18). No significant differences in race, sex, ASA, smoking status, hemoglobin A1C, and prevalence of chronic pancreatitis were identified between low, medium and high volume groups. Similarly, there were no differences in operative time, blood loss, intraoperative fluid administration, use of internal pancreatic stents, or postoperative lactate (all p > 0.05). Patients with high 72-hour net fluid balance had a significantly higher rate of POPF compared to medium and low volume groups (31.4% vs. 11.4% vs. 8.8%, p = 0.024). On multivariate analysis, increasing net fluid balance was significantly associated with POPF (OR 1.25, CI 1.02-1.54, p = 0.03).

Conclusion: In patients undergoing PD, high net 72-hour fluid balance is significantly associated with development of POPF. Given increasing efforts to develop enhanced recovery pathways that minimize PD morbidity, net fluid balance may represent both a clinical predictor and modifiable target for prevention of POPF.

THE IMPACT OF FAILURE TO ACHIEVE SYMPTOM CONTROL AFTER RESECTION OF FUNCTIONAL NEUROENDOCRINE TUMORS: AN 8-INSTITUTION STUDY FROM THE US NEUROENDOCRINE TUMOR STUDY GROUP


Background: The goals of resection for pts with functional neuroendocrine tumors (F-NETs) are two-fold: oncologic benefit and symptom control. The interaction between the two, however, is not well understood.

Methods: All pts with F-NETs of the pancreas, liver, duodenum, and ampulla who underwent curative-intent resection between 2000 and 2016 were identified. Cox regression analysis was utilized to determine clinicopathologic factors associated with reduced recurrence-free survival (RFS). A multivariable model was created by incorporating all variables associated with RFS with p < 0.1.

Results: Of 260 pts with resected F-NETs, 230 underwent curative-intent resection. 53% were insulinomas, 35% gastrinomas, and 12% other. 21% had a known genetic syndrome (majority MEN-1), 23% had LN(+) disease, 80% underwent an R0 resection, and 14% had no postoperative
symptom improvement (SI). Pts who did have SI were more likely to have an insulinoma (p = .01), no genetic syndrome (p = .001), and an R0 resection (p = .007). LN(+) disease did not correlate with postoperative SI. Factors associated with reduced RFS included non-insulinoma histology, known genetic syndrome, LN(+) disease, R1 margin, and lack of SI. On MV analysis, only the failure to achieve SI following resection persisted as being associated with reduced RFS (Table).

Considering only those pts with an R0 resection, failure to achieve SI was still associated with worse 3-yr RFS compared to pts with SI (36% vs 80%; p = 0.006).

Conclusion: Failure to achieve symptomatic improvement after resection of functional NETs is associated with worse recurrence-free survival, even when accounting for histologic type, presence of genetic syndromes, R1 resection margin, and LN involvement. These patients may benefit from short-interval periodic imaging postoperatively to assess for earlier radiographic recurrence of disease.

## Association Between Clinicopathologic Variables and Decreased Recurrence-Free Survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable HR (95%CI)</th>
<th>Multivariable HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insulinoma</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrinoma (including glucagonoma, somatostatinoma, VIPoma)</td>
<td>2.7 (1.0–7.2)</td>
<td>0.042</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>2.7 (1.0–7.2)</td>
<td>0.077</td>
</tr>
<tr>
<td><strong>Known Genetic Syndrome</strong></td>
<td>1.8 (0.9–3.5)</td>
<td>0.080</td>
</tr>
<tr>
<td>Lymph Mode Positive</td>
<td>2 (1.0–3.9)</td>
<td>0.052</td>
</tr>
<tr>
<td>R1 Resection Margin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Failure of Symptom Improvement</td>
<td>3.1 (1.3–7.2)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

## 64

**COMPLETION, AND NOT JUST INITIATION, OF INTENDED ONCOLOGIC THERAPY IS ASSOCIATED WITH IMPROVED SURVIVAL AFTER PANCREATIC RESECTION FOR CANCER**

Danielle K. DePeralta, Takuya Ogami, Benjamin Powers, Yun Y. Chen, Michael Schell, Pamela Hodul, Mokeng Malafa and Jason Fleming

*Corresponding author. Danielle DePeralta, Moffitt Cancer Center, USA*

**Background:** Adjuvant therapy is the standard of care for resected pancreatic adenocarcinoma. The ability to return to intended oncologic therapy (RIOT) has been proposed as a quality metric. We hypothesize that the ability to RIOT predicts improved long-term outcomes and explore the associated variables.

**Methods:** An IRB approved, single-institution retrospective chart review of patients treated with pancreatic resection for pancreatic adenocarcinoma from 1/2008-12/2015 was conducted. Demographics, clinical-pathological factors, adjuvant treatment and follow-up data were collected with a focus on the rate of RIOT, risk factors associated with an inability to RIOT, and associated survival outcomes.

**Results:** After a median follow-up of 60 months, 302 patients underwent pancreatic resection (Whipple n = 220, distal n = 65, total n = 14, completion, n = 3). Following surgery, 246 (81.5%) initiated adjuvant therapy and 196 (64.9%) completed the intended course. 135 (44.7%) patients were treated with adjuvant chemotherapy alone and 111 (36.8%) underwent chemotherapy and chemoradiation. The median time to initiation of adjuvant therapy was 53 days (range 26–217). The most frequent reasons cited for inability to RIOT were surgical complications (n = 26), poor performance status (n = 18), patient refusal (n = 11), and early recurrence with transition to comfort-based care (n = 5). The ability to RIOT was associated with improved overall survival (OS, p < 0.0001) and recurrence-free survival (RFS, p < 0.0001). On Cox multiple regression models for OS and RFS, the failure to initiate and failure to complete intended adjuvant therapy were both associated with worse outcomes (see table).

**Conclusion:** Completion of intended oncologic therapy is associated with improved OS and RFS in patients that undergo resection for pancreatic adenocarcinoma.

### Association Between Clinicopathologic Variables and Decreased Recurrence-Free Survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable HR (95%CI)</th>
<th>Multivariable HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known Genetic Syndrome</td>
<td>1.8 (0.9–3.6)</td>
<td>0.080</td>
</tr>
<tr>
<td>Failure of Symptom Improvement</td>
<td>3.1 (1.3–7.2)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

### Comparison Groups (Reference = successful completion of all intended oncologic therapy)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Recurrence-Free Survival (RFS)</th>
<th>Overall Survival (OS)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to initiate intended oncologic therapy</td>
<td>HR 2.418 (95%CI: 1.704–3.430)</td>
<td>HR 2.810 (95%CI: 2.020–3.909)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Successful initiation, but failure to complete all intended adjuvant therapy</td>
<td>HR 2.282 (95%CI: 1.604–3.246)</td>
<td>HR 2.317 (95%CI: 1.600–3.356)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

## 65

**CLINICAL CRITERIA FOR INTEGRATED MOLECULAR PATHOLOGY IN IPMN: LESS IS MORE**


*Corresponding author. Rachel Simpson, Indiana University, USA*

**Background:** PancraGEN is a malignancy risk score for pancreatic cysts integrating cyst fluid DNA/molecular profile and clinical criteria (IMP). Aside from main pancreatic duct diameter (MPD), integrated clinical criteria (CEA,
growth rate, and cyst size) are not International Consensus Guidelines high-risk stigmata. We sought to determine if exclusion of all clinical criteria except MPD could simplify the IMP and better predict IPMN malignancy.

**Methods:** A retrospective review of a prospective database of 1100 patients with IPMN from a single institution was performed. Of these, 285 had PancreaGEN testing with non-malignant cytology. Following testing, 100 underwent surgery and 185 underwent surveillance for ≥23 months. IMP sensitivity (Sn), specificity (Sp), and accuracy for malignancy was compared to DNA/molecular profile including only MPD ≥10mm (IMP*). Malignant outcomes were invasive IPMN/adenocarcinoma on surgical pathology, biopsy-proven adenocarcinoma during surveillance, or radiographic mesenteric vascular invasion or metastatic disease.

**Results:** IMP* had higher Sp and accuracy for predicting malignancy compared to IMP in surgery + surveillance patients (Sp 90% vs 74%; Accuracy 90% vs 74%.) However, IMP was more sensitive for predicting malignancy compared to IMP* for the surgery + surveillance group (80% vs 70%). Malignant outcomes were invasive IPMN/adenocarcinoma on surgical pathology, biopsy-proven adenocarcinoma during surveillance, or radiographic mesenteric vascular invasion or metastatic disease.

**Conclusion:** Inclusion of multiple clinical criteria in IMP captures more malignant cases than IMP* but with less specificity and accuracy. Thus, more patients without malignancy are improperly identified and may be subject to unnecessary surgery. IMP* excludes clinical factors that are unreliable predictors of malignant risk resulting in greater accuracy in predicting malignancy and more selectivity in who is recommended for surgery.

<table>
<thead>
<tr>
<th></th>
<th>IMP*</th>
<th>IMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery + Surveillance</td>
<td>70%</td>
<td>80%</td>
</tr>
<tr>
<td>Surgery Alone</td>
<td>70%</td>
<td>80%</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery + Surveillance</td>
<td>90%</td>
<td>74%</td>
</tr>
<tr>
<td>Surgery Alone</td>
<td>82%</td>
<td>59%</td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery + Surveillance</td>
<td>90%</td>
<td>74%</td>
</tr>
<tr>
<td>Surgery Alone</td>
<td>81%</td>
<td>61%</td>
</tr>
</tbody>
</table>

67

**A COMPARISON OF MICROWAVE THERMOSPHERE VERSUS RADIOFREQUENCY THERMAL ABLATION IN THE TREATMENT OF COLORECTAL LIVER METASTASES**


*Corresponding author. Kazunari Sasaki, Cleveland Clinic Foundation, USA

**Background:** Microwave thermosphere ablation (MTA) is a new generation microwave technology approved by FDA in 2014 that allows for a faster and more homogeneous heating of tissues compared to radiofrequency ablation (RFA). The aim of this study is to compare the efficacy of MTA and RFA in achieving local tumor control in patients with colorectal liver metastasis (CRLM).

**Methods:** This was a retrospective study of a prospective ablation database. Fifty-four patients with 155 CRLM lesions underwent RFA and 51 patients with 121 lesions underwent MTA in two different time periods. All patients were seen at the Multidisciplinary Liver Tumor Clinic and were either reviewed by a multidisciplinary team in advance or presented at the tumor board.

Clinical, operative and oncologic data were analyzed. Kaplan-Meier and Cox Proportional Hazards model were used for statistical analysis.

**Results:** The both groups were similar regarding demographics and liver tumor burden. Total operative and ablation time were significantly shorter for the MTA group compared to the RFA (154 vs 202 min, p < 0.001; 19.2 vs 37.4 min, p < 0.001). The patients were followed for a median of 18 months (Interquartile range (IQR): 12-25) in the RFA group and 17 months (IQR: 11-20) in the MTA group (p = 0.12). 90-day morbidity was 8.3% in the how fibrotic tissue may modulate the response to IRE treatment. In this study, we aim to characterize the electrical properties of normal and fibrotic liver tissue and their response to IRE ablation.

**Methods:** C57BL/6 mice with liver fibrosis induced by 0.1% 3,5-diethylcarbonyl-1,4-dihydrocollidine (DDC) diet were compared to matched control mice with normal liver. The electrical impedance of normal and fibrotic mouse liver was measured “in vivo” at baseline. IRE treatment was then administered and “in vivo” impedance of the IRE-treated liver parenchyma measured over a time course. Histological analysis of normal and fibrotic liver after IRE treatment was also performed.

**Results:** The electrical impedance of normal and fibrotic liver was comparable at baseline. Immediately after IRE treatment, there was a significant decrease in impedance in normal liver but not in fibrotic liver. Upon histological analysis, the electric field strength that induced tissue injury in normal liver did not induce injury in the fibrotic liver.

**Conclusion:** Normal and fibrotic liver tissue respond to IRE treatment differently. Fibrotic liver may be more resistant to IRE ablation, which may be important to consider when designing IRE ablation regimens for hepatocellular carcinoma that most commonly occur in fibrotic liver.
Mortality and 9.7% in the RFA group (p = 0.85). There was no mortality. Median hospital stay was 1 day for both groups. For the RFA vs MTA groups, local recurrence (LR) rate per lesion was 20.3% and 8.5%, respectively (p = 0.01). On Cox Proportion Hazards model, ablation modality was an independent predictor of LR following risk adjustment.

**Conclusion:** To our knowledge, this is the first comparison of RFA and MTA in the treatment of CRLM. Our results demonstrates MTA achieves better local tumor control with shorter operative and ablation time.

**68**
**LOSS OF MUSCLE MASS DURING PREOPERATIVE CHEMOTHERAPY PREDICTS WORSE RECURRENCE-FREE SURVIVAL IN PATIENTS WITH RESECTABLE COLORECTAL LIVER METASTASES**


*Corresponding author. Masayuki Okuno, The University of Texas MD Anderson Cancer Center, USA*

**Background:** The survival impact of specific body composition changes (total weight, skeletal muscle mass, muscle density, and others) during preoperative chemotherapy in patients with resectable colorectal liver metastases (CRLM) remains unclear.

**Methods:** Patients with CRLM who underwent preoperative chemotherapy and curative hepatectomy during 2009—2013 were retrospectively analyzed using CT and automated muscle volume data (Fuji). Recurrence-free survival (RFS) and overall survival (OS) were examined according to muscle mass and -density and body weight before and after preoperative. Muscle mass was calculated by skeletal muscle index (SMI; area of muscle [cm²]/square of height [m²]).

**Results:** The study included 169 patients, and the median follow-up period was 47 months. Neither SMI nor muscle density before or after preoperative chemotherapy was associated with RFS or OS. SMI and body weight changed significantly during chemotherapy (SMI: 0.52 cm²/m², P = .03; median change in body weight: +1.1 kg, P = .002). Muscle mass change was not moderately or strongly correlated with body weight change, number of cycles of preoperative chemotherapy and chemo-resistance (assessed by tumor size, change of CEA, and pathological response). Patients with major muscle mass loss (≥7%) had significantly shorter median RFS than patients with no/minor muscle mass loss (<7%) (9.6 months vs 15.9 months; P = .02). On multivariate analysis, major muscle mass loss was independently associated with poorer RFS (hazard ratio, 1.76; P = .045).

**Conclusion:** Major loss of muscle mass but not body weight during preoperative chemotherapy is significantly associated with poor RFS after hepatectomy in patients with CRLM and, hence, should prompt consideration for prehabilitation.

**69**
**ONCOLOGICAL BENEFIT OF COMPLETE METASTASECTOMY FOR SIMULTANEOUS COLORECTAL LIVER AND LUNG METASTASES**

M. Masaru, Y. Suguru, Y. Ryuji, N. Yujiro, A. Junichi, A. Nobuhisa, K. Junichi, S. Yoshihiro, N. Jun, K. Norihito and H. Kiyoshi

*Corresponding author. Masaru Matsumura, University of Tokyo, Japan*

**Background:** The oncological benefit of complete metastectomy for simultaneous colorectal liver and lung metastases (SLLM) and the significance of the time to surgical failure (TSF) in such patients are unknown.

**Methods:** Patients undergoing hepatectomy from 2005 to 2016 as an initial treatment for colorectal liver metastases (CLM) in a single tertiary hospital were divided into three groups: patients with isolated CLM undergoing complete resection (Group 1, n = 317), SLLM undergoing complete metastasectomy (Group 2, n = 33), and SLLM undergoing complete hepatectomy but incomplete lung resection (Group 3, n = 20). Upfront surgery was performed for patients with initially resectable disease. A staged strategy (hepatectomy followed by lung resection) without interval chemotherapy was mainly applied for SLLM as long as the lung metastases were resectable. Clinical characteristics and prognoses were compared among the groups.

**Results:** The 5-year overall survival rate of Group 2 was significantly better than that of Group 3 (70.3% vs. 11.9%, P < .001) and similar to that of Group 1 (63.5%, “P” = .859). The 5-year disease-free survival rate was significantly worse in Group 2 than 1 (22.1% vs. 34.6%, = .048), while the 5-year TSF was similar (52.9% vs. 49.9%, = .991). On multivariable analysis, a carcinoembryonic antigen level of >200 ng/ml was the sole predictor of incomplete resection of lung metastases (odds ratio, 13.8; 95% confidence interval, 1.75—298; = .011).

**Conclusion:** The prognosis in patients with SLLM who achieve complete metastasectomy is acceptable and might be improved by a carcinoembryonic antigen level of ≥200 ng/ml, appropriate selection based on operative indications, and aggressive repeat resection.
DISPARITIES IN HEPATOPANCREATOBILIARY OPERATIVE EXPERIENCE AMONG GENERAL SURGERY RESIDENTS: A 27-YEAR ANALYSIS OF ACGME CASE LOGS


*Corresponding author. R. Cutler Quillin, Columbia University, USA

**Background:** The ACGME requires hepatopancreatobiliary (HPB) surgery as a part of general surgery training. In this study, we evaluate the trends in HPB operative experience of general surgery residents.

**Methods:** ACGME national operative log reports from 1990 to 2016 were examined. Trends were analyzed relative to the 2003 duty hour restrictions (DHR): pre-DHR (1990–1999), DHR transition (2000–2008) and post-DHR (2009–2016). Statistical analysis was performed using ANOVA and linear regression analysis. A p-value < 0.05 was statistically significant.

**Results:** Operative logs of 27,851 general surgery graduates were examined. Median biliary, liver and pancreatic operative volumes increased by 29.9%, 32.8% and 27.3%, respectively.

Operative volume variability, defined as the difference between the most and least prolific residents (90th–10th percentile), increased by 15.5%, 21.2% and 73.0% for these categories (Figure). Trends were then analyzed for specific HPB operations. Increases in operative volume from pre- to post-DHR were seen for laparoscopic cholecystectomy (71.7%), hepatic lobectomy (140.9%), liver transplant (161.9%), distal pancreatectomy (130.8%) and pancreatoduodenectomy (152.4%, p < 0.05 for each), while decreases were seen for open cholecystectomy (−61.9%), open common bile duct exploration (−76.7%), hepaticojejunostomy (−52.6%) and hepatic wedge resection (−31.4%, p < 0.05 for each). For each specific HPB operation that increased, linear regression analysis revealed an increase in operative volume variability (p < 0.05 for each).

**Conclusion:** While the total HPB operative experience of surgical residents has increased over the past 27-years, an increase in operative volume variability has also occurred, suggesting a dissimilar HPB experience amongst trainees. Educators should be aware of this disparity to ensure equitable training amongst all graduates.