Cleveland Clinic
General Surgery Resident Research Day

Wednesday
October 21st, 2020

Digestive Disease & Surgery Institute
Department of General Surgery
About

The 2020 Resident Research Day is the inaugural showcase of the impressive research endeavors completed by General Surgery residents in both the clinical and basic sciences.

In addition to the scholarly activities required for graduation, over half of our residents pursue dedicated research endeavors and advanced degrees during an additional 1-3 years of focused professional development. This year, twelve residents are working in nine different departments throughout the Cleveland Clinic enterprise as well as three additional outside institutions. Residents routinely present their work at numerous national conferences, including meetings of the American College of Surgeons (ACS), Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), Society of Thoracic Surgeons (STS), Americas Hernia Society (AHS), and the Americas Hepato-Pancreato-Biliary Association (AHPBA), among others.

The work presented during Research Day has been evaluated through a blinded mentor grading system and has received top scores in study design, abstract composition, and potential research impact.
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Dr. Carla Pugh is Professor of Surgery at Stanford University School of Medicine. She is also the Director of the Technology Enabled Clinical Improvement (T.E.C.I.) Center. Her clinical area of expertise is Acute Care Surgery. Dr. Pugh obtained her undergraduate degree at U.C. Berkeley in Neurobiology and her medical degree at Howard University School of Medicine. Upon completion of her surgical training at Howard University Hospital, she went to Stanford University and obtained a PhD in Education. She is the first surgeon in the United States to obtain a PhD in Education. Her goal is to use technology to change the face of medical and surgical education.
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High-Resolution Transcriptomic Analysis of Colitis Associated Cancer In Vitro Co-Cultures

Reece DeHaan, MD

Background: Colitis-associated cancer (CAC) is a feared consequence of ulcerative colitis. The inflammatory microenvironment, especially the stromal fibroblasts, is associated with increased development of neoplasia. Further, even in the absence of histological neoplasia, transcriptional inflammatory and neoplastic signatures exist. Patient-derived epithelial organoids and fibroblasts, with high-resolution single cell analysis, permit unprecedented dissection of transcriptional expression. Single cell nuclear analysis was used to discriminate cell identity and individual cell transcriptional expression. We hypothesize that co-cultures of CAC epithelial organoids with proximal colitic but histologically normal fibroblasts recapitulates a neoplastic profile when compared to CAC epithelial organoids alone.

Methods: Matched patient derived epithelial organoids were cultured alone, or co-cultured with fibroblasts from an area of CAC, or with an area of proximal colon that was histologically normal. After 7 days of culture, the diameter of individual colonies (N = 150/sample) were measured as an indication of proliferation. Single-nucleus RNA-seq (sn-RNA-Seq) was performed (10x Genomics). Data analysis was performed in R utilizing the Seurat package for clustering and differential expression analysis. Dimensionality reduction was performed using Uniform Manifold Approximation and Projection.

Results: Colony diameters were found to be significantly increased in both the epithelial/CAC fibroblast co-culture and epithelial/normal fibroblast co-culture vs epithelia alone (p<0.0001). SnRNA-Seq was performed on epithelial organoids alone and co-culture with matched proximal and cancerous fibroblasts. Cell clusters were annotated utilizing known marker genes and differential expression analysis was performed between the three samples (Fig. 1). The transcriptomic signature of the co-culture with proximal fibroblasts demonstrates an increased proportion of inflammatory fibroblast and immature epithelial populations compared to epithelia alone or epithelia plus CAC fibroblast co-cultures (p < 1 x 10^{-9}; Fig. 1C, box).

Conclusion: We demonstrate in vitro modeling of colitis-associated cancer epithelia with matched normal colon and CAC stromal fibroblasts. Consistent with neoplasia, co-cultures of epithelia with either type of fibroblast exhibited increased size. Further, we show, for the first time, use of snRNA-seq of patient-derived epithelial organoids in co-culture to deconvolute the transcriptomic changes. Despite the normal histology of the proximal colitic fibroblasts, our data showed enrichment of inflammatory fibroblast and oncogenic drivers in our co-cultures with proximal colon fibroblasts when compared to CAC-fibroblast co-cultures. Therefore, we conclude that these model systems may be used to discriminate patient populations at risk for colitic neoplasia.
Clinical Staging Accuracy and the Role of Neoadjuvant Chemoradiotherapy for cT3N0 Rectal Cancer: Propensity Score Matched National Cancer Database Analysis

Dominykas Burneikis, MD

Background: While neoadjuvant chemoradiation therapy (nCRT) is largely accepted as standard of care for locally advanced rectal cancer, the approach to treatment of patients with clinically staged T3N0 disease has been increasingly debated. The trials that established this standard of care did not address the fact that the T3N0 subset of patients is considered lower risk for local recurrence, and thus the concern remains that nCRT may be an unnecessary adjunct to proper total mesorectal excision (TME). This study examines the accuracy of clinical staging for cT3N0 rectal cancer as recorded in the National Cancer Data Base (NCDB) and evaluates the role of nCRT in treating these patients.

Methods: Clinically staged T3N0M0 rectal cancer patients who received nCRT or proceeded to surgery first between 2004 and 2015 were included in the analysis. Total of 15,843 patient records were identified in the NCDB meeting inclusion criteria. Propensity score matching using the greedy nearest neighbor method was employed to balance the nCRT and surgery-first groups, resulting in 3665 matched pairs. Adjusted overall survival, pathological nodal upstaging and resection margin status were compared.

Results: Accuracy of clinical staging was poor, with 23% of cT3N0 patients undergoing surgery-first having pathologically positive nodes. Another 16% turned out to have < stage II disease on surgical pathology. The Kaplan-Meier curves for overall survival in matched nCRT and surgery-first groups demonstrated a survival advantage for cT3N0 patients treated with nCRT. 5-year survival for cT3N0 patients receiving nCRT was 71% compared to 65% for patients who proceeded to surgery first. Median overall survival was 9 and 7.8 years (p < 0.001) for nCRT and surgery-first groups respectively.

Conclusions: Current clinical staging accuracy remains poor, and can result in both undertreatment and overtreatment of cT3N0 rectal cancer. While administering nCRT appears to confer a slight survival advantage over proceeding to surgery first, this strategy must be balanced with the fact that it likely results in overtreatment in ~16% of cases. Until clinical staging accuracy improves nationally, nCRT should remain the standard in treating cT3N0 rectal cancer.
Tumor-Associated Glycans are Diagnostic Predictors of High-Grade Dysplasia and Malignancy in Intraductal Papillary Mucinous Neoplasms of the Pancreas

Kathryn Stackhouse, MD, MS

**Background:** Intraductal papillary mucinous neoplasms (IPMN) of the pancreas are lesions often incidentally found on abdominal imaging in asymptomatic patients. The decision to perform pancreatic resection is based on the lesion’s perceived risk of malignancy. Current guidelines utilize imaging criteria and cyst fluid chemistry, but have limited accuracy. We have identified a panel of tumor-associated glycans, often expressed in pancreatic ductal adenocarcinoma, to distinguish patients who would benefit from pancreatic resection.

**Methods:** Immunohistochemistry was performed on glass slides of resected IPMN specimens using monoclonal antibodies to cancer-associated glycans (Tn, STn, SLeA (CA19-9), SLeX). Staining intensity and extent was assessed in the IPMN lesions and uninvolved pancreatic parenchyma, and a combined H score was calculated. Staining results were correlated with pathologic diagnosis, including presence of invasive malignancy and/or grade of dysplasia.

**Results:** Forty-two resected IPMNs from our institution were included. Eight samples (19%) had invasive malignancy present. 31.7% had high-grade dysplasia, 31.7% had moderate-grade dysplasia, 34.2% had low-grade dysplasia, and 2.4% had no malignancy or dysplasia present. Increased Tn and SLeX expression was significantly associated with the presence of malignancy (p<0.001). STn expression was significantly associated with HGD. SLeA (CA19-9) expression, interestingly, was not significantly associated with malignancy in IPMN (p=0.09).

**Conclusion:** Expression of tumor-associated glycans, particularly Tn, STn, and SLeX antigens, accurately identifies invasive malignancy and high-grade dysplasia in resected IPMNs. We propose testing this hypothesis in cyst fluid obtained during diagnostic endoscopic ultrasound, which can then be used clinically to improve surgical decision making.
Factors that Minimize Curative Resection for Gallbladder Adenocarcinoma: an Analysis of Clinical Decision-Making and Survival

Breanna Perlmutter, MD

Background: Despite expert guidelines recommending definitive surgery for ≥T1b gallbladder cancer, surgical management is inconsistent. This study evaluates the factors that affect the completion of radical resection with portal lymphadenectomy and its impact on survival.

Methods: A retrospective review of all patients diagnosed with gallbladder cancer from 2007-2018 at an academic institution was performed. Patients were analyzed based on whether they underwent definitive surgical resection. Patient factors and clinical decision-making were analyzed; overall survival was compared using Kaplan Meier analysis.

Results: Seventy-five patients were identified, of who 32 (42.7%) underwent definitive resection. Fifty-four patients (72%) had gallbladder cancer identified as an incidental diagnosis following laparoscopic cholecystectomy. Among patients who did not undergo definitive resection, the underlying factors were quite varied. Only 24 (55.8%) patients in the non-definitive resection group were seen by surgical oncology. Among patients who underwent re-operation for definitive resection, 12 (38.7%) were upstaged on final pathology. Of the 43 patients who did not undergo definitive resection, 4 (9.3%) were found to have metastatic disease during attempted re-resection. Patients who underwent definitive resection had a significantly longer median overall survival compared to those who did not (4.3 v. 1.9 years, p=0.02).

Conclusions: Patients undergoing definitive resection have a significantly improved survival, including as part of a re-operative strategy. Universal referral to a surgical specialist is a modifiable factor resulting in increased definitive resection rates. Patients with incidentally diagnosed cancer have a high risk for residual and occult metastatic disease, highlighting the importance of diagnostic laparoscopy in all patients.
Per-Oral Endoscopic Myotomy with Submucosal Dissection for Zenker’s Diverticulum

Michael Klingler, MD

Background: In per oral endoscopic myotomy for Zenker’s diverticulum (Z-POEM), the cricopharyngeus muscle is divided within a submucosal tunnel started in the hypopharynx. We aimed to evaluate the safety and preliminary outcomes in patients who underwent a modified version of the Z-POEM where the tunnel is made directly overlying the cricopharyngeus, the mucosal incision and muscular interruption (MIMI) approach, and to compare these with patients who underwent a non-tunneled flexible endoscopic approach.

Methods: All patients with ZD who were treated by flexible endoscopy at our institution between January 2015 and February 2020 were identified by a retrospective chart review. Dysphagia symptoms were assessed using a validated scoring system.

Results: Nineteen patients with ZD underwent MIMI (mean age 76.1 years, 68.1% male) and seven patients underwent non-tunneled flexible endoscopic approach (mean age 64.4 years, 85.7% male) during the study period. Mean ZD size was 2.8cm in the MIMI group and 1.9cm in the non-tunneled group (p=0.03). Clinical success was achieved in 17/19 (89.5%) MIMI patients and 7/7 (100%) of non-tunneled flexible endoscopic patients (p=0.101). Dysphagia scores improved in both groups, although this difference was only significant in the MIMI group (p=<0.001). Recurrence occurred in 2/17 (11.7%) MIMI patients and 3/7 (42.9%) non-tunneled flexible endoscopic patients (p=0.096). There were 4 complications, including one pharyngeal perforation requiring open surgical repair in a patient with a small ZD with an associated cricopharyngeal bar in the MIMI group. Median length of follow up was 290 [142;465] days in the MIMI group and 1056 [258;1206] days in the non-tunneled group (p=0.094).

Conclusions: MIMI is a technically feasible and effective treatment for ZD. Care should be taken in patients with a cricopharyngeal bar and small ZD, as this may increase the risk of perforation. Larger studies with long-term follow up are needed to determine if MIMI reduces the risk of symptom recurrence when compared to non-tunneled flexible endoscopic approaches.
**Endoscopic Per-Oral Pyloromyotomy (POP) Improves Glycemic Control in Gastroparesis Patients with Poorly-Controlled Diabetes Mellitus**

*Joshua Landreneau, MD*

**Background:** Unpredictable gastric emptying and inability to coordinate insulin administration with intestinal nutrient absorption makes glycemic control in patients with concomitant gastroparesis (GP) and diabetes mellitus (DM) challenging. We aimed to characterize the effect of endoscopic per-oral pyloromyotomy (POP) on glycemic control in patients with poorly-controlled DM.

**Methods:** All patients with DM who underwent POP between April 2016 and February 2018 with at least 12 months follow-up were identified from a prospectively maintained database. Patients with poor pre-procedure glycemic control (hemoglobin A1c (HbA1c) >7.0%) were included.

**Results:** Twenty patients with DM and inadequate glycemic control underwent POP during the study period. The cohort was 85.0% female with a mean age of 48.9 years. The etiology of GP included diabetes (n=18, 90.0%), post-surgical (n=1, 5.0%), and idiopathic (n=1, 5.0%). Nine patients (45.0%) had type 1 DM, and seventeen (85.0%) required insulin therapy. The mean preoperative HbA1c was 8.5%. The mean operative time was 33.8 minutes with no procedural complications and one day median length of stay. At three months post-procedure, symptoms as measured by the Gastroparesis Cardinal Symptom Index (GCSI) were improved (3.8 vs. 1.1, p<0.01), as was mean four-hour retention on gastric emptying scintigraphy (64.4% vs. 21.6%, p<0.01). Glycemic control at a median of 13 months post-POP was improved (HbA1c: 8.5% vs. 7.7%, p<0.01). At last follow-up, six patients (30.0%) achieved target goal of HbA1c≤7.0%.

**Conclusions:** In patients with gastroparesis and poorly controlled diabetes, per-oral pyloromyotomy may produce significant improvements in symptoms, gastric emptying, and glycemic control.
Impact of Standard Dual Antibiotic Prophylaxis on Circular Site Infection when A Circular Stapler is Used to Create Foregut Anastomoses

Andrew Strong, MD

Background: Circular end-to-end anastomosis (EEA) stapler is the most widely used technique to create a gastrojejunal anastomoses during roux-en-y gastric bypass (RYGB) or other foregut operations bypassing or removing part of the stomach. Polymicrobial surgical site infection (SSI) at the EEA withdrawal site are preventable, likely related to seeding of intestinal flora to the abdominal wall. As a quality improvement protocol, preoperative prophylaxis was changed to a two drug regimen to cover historically etiologic bacteria, and followed for 1 year to ascertain the impact on SSI rate.

Methods: All laparoscopic RYGB, and other foregut operations where EEA use was expected from July 1, 2014 to June 2017 were included. These included partial and subtotal gastrectomies, in addition to operative intended for metabolic effect. The primary exposure was prophylactic ceftriaxone/metronidazole combination therapy, instituted July 1, 2016 to June 30, 2017. All other antibiotic regimens served as controls.

Results: There were 227 patients that met criteria, including 60 patients who received ceftriaxone/metronidazole prophylaxis, and 167 with other antibiotic regimens. There was no difference in age, body-mass index. There were 26.7% and 31.7% of cases that were revisions of prior foregut operations in the study and control arms. Cefazolin (75.4%) and vancomycin (12.6%) monotherapy were the most common antibiotic regimens in the control arm. There were 19 (11.4%) total SSI in the control arm, and 3 (5%) in the study arm, giving an absolute risk reduction of 6.4%.

Conclusions: Changing to dual therapy prophylaxis with extended Gram-negative and anaerobic bacterial activity using ceftriaxone and metronidazole resulted in an absolute risk reduction in SSI rate compared other single and dual antibiotic regimens.
Patient-Reported Opioid Use after Abdominal Wall Reconstruction: How Low Can We Go?

Aldo Fafaj, MD

**Background:** Little data exists to inform discharge opioid prescribing for patients undergoing abdominal wall reconstruction (AWR). The aim of this study was to evaluate postoperative patient-reported opioid use after AWR. We hypothesized that the majority of patients undergoing AWR would require between 16 and 30 opioid tablets after discharge.

**Methods:** Postoperative patient-reported opioid use was collected prospectively for all patients undergoing elective, open AWR at a single high-volume center. All opioid medications were converted to an equivalent number of 5 mg oxycodone tablets. The primary outcome was the total number of opioid tablets taken within 30 days of hospital discharge after AWR.

**Results:** Ninety-eight patients were included. Median hernia width was 15 cm (IQR 12-19), 41.8% were recurrences, and all underwent transversus abdominis release. At the 30-day follow-up visit, 23.5% reported no post-discharge opioid use, and 75.5% reported taking 15 tablets or fewer. Of the 23 patients who used no opioids on the day before discharge, 16 (70%) reported taking no opioids after discharge.

**Conclusions:** Most patients reported taking fewer opioid tablets than prescribed, within 30 days of AWR. Opioid use on the day before discharge may allow for prognostication of outpatient opioid requirements to prevent overprescribing.
To view the Poster Presentations and join the discussion, an online forum will be posted

**Novel Use of Colorectal Organoids from Familial Adenomatous Polyposis Patients: A Model of Personalized Chemoprevention**
Alicia Adams, MD

**Breast Pleomorphic Lobular Carcinoma In Situ: Our Single Institution Experience of Demographic, Upgrade Rate and Pathological Review**
Kevin Brown, MD

**Academic Surgery, Leadership, and Diversity: Modern Workforce Analysis**
Talia Burneikis, MD

**Detection of Unknown Pregnancy with Universal Screening in Preoperative Patients is a Rare Event**
Bess Connors, MD

**Evolution of a Laparoscopic Liver Resection Program: An Analysis of 203 Cases**
Mohammed Elshamy, MD

**Comparing the Accuracy of Natural Language Processing and Manual Chart Review with a Prospective Surgeon-Entered Quality Improvement Registry**
Aldo Fafaj, MD

**Is There an Advantage to Laparoscopy Over Open Repair of Primary Umbilical Hernias in Obese Patients?: An Analysis of the Americas Hernia Society Quality Collaborative (AHSQC)**
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**Laparoscopic Pyloroplasty versus Endoscopic Per-Oral Pyloromyotomy for the Treatment of Gastroparesis**
Joshua Landreneau, MD
Poster Presentations

Personal Statements in General Surgery: An Unrecognized Role in the Ranking Process
Robert Naples, DO

Best Practices in Letters of Recommendation for General Surgery Residency: Results of Expert Stakeholder Focus Groups
Robert Naples, DO

Results of The Comparative Study of 200 Cases: One Anastomosis Gastric Bypass vs Roux-en-Y Gastric Bypass.
Salvador Navarrete, MD

Risk Factors for Postoperative Respiratory Failure in Elective Abdominal Surgery
Danny Orabi, MD

Does Incisional Hernia Repair with Mesh Worsen Disease Burden in Patients with Crohn’s Disease?
Breanna Perlmutter, MD

Effect of Autotransfusion on Survival Outcomes in Patients Undergoing Liver Resection for Colorectal Liver Metastases.
Breanna Perlmutter, MD

Endoscopic Pyloromyotomy is Extremely Effective in Improving Post-Lung Transplant Gastroparesis and GERD
Jesse Rappaport, MD

Effects of Laparoscopic vs Open Abdominal Surgery on Costs and Hospital Readmission Rate and its Effect Modification by Surgeons’ Case Volume
Thomas Shin, MD, PhD

Effect Modification of Resident Autonomy and Seniority on Perioperative Outcomes in Laparoscopic Cholecystectomy
Thomas Shin, MD, PhD
Quantifying the Eye-Ball Test: A Novel Vitality Index to Predict Recovery after Esophagectomy
   Andrew Tang, MD

Long-term Outcome of Patients Undergoing Liver Transplantation for Mixed Hepatocellular Carcinoma and Cholangiocarcinoma: An Analysis of the UNOS Database.
   Valery Vilchez, MD

Effect of Critical Care Complications on Perioperative Mortality and Hospital Length of Stay after Hepatectomy: A Multicenter Analysis of 21,443 Patients
   Valery Vilchez, MD

SICU Training Course Improves Surgery Interns’ Comfort, Knowledge and Ability to Manage Critical Care Conditions
   Noah Weingarten, MD, MA

A Description of Laparoscopic Repair on a Patient with Valentino’s Syndrome Caused by a Perforated Duodenal Diverticulum
   Yaning Zhang, MD

Outcomes of Redo Transversus Abdominis Release for Abdominal Wall Reconstruction
   Samuel Zolin, MD

A New Paradigm for Surgical Research: Leveraging Registries to Conduct Randomized Controlled Trials
   Samuel Zolin, MD
We would like to thank the following people for making the 2020 Resident Research Day possible:

Jeremy Lipman, MD
R. Matthew Walsh, MD
Conor Delaney, MD, PhD
Lisa Paciorek
Janine Keough
Toms Augustin, MD, MPH
Walter Cha, MD
James Church, MD
Stefan Holubar, MD, MS
Emina Huang, MD
Amy Lightner, MD
Ajita Prabhu, MD
Michael Rosen, MD
Robert Simon, MD
Joseph Trunzo, MD

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