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Renal Sympathetic Vasomotion Monitoring as a Novel Method for Intraoperative Feedback for Renal Denervation

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A Comparative Analysis of Survival and Funding Discrepancies in Cancers with High Mortality

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Mentor: Chandrakanth Are

Program: General Surgery

Background & Objectives: Discrepancies in research funding may contribute to stagnant survival rates in pancreatic ductal adenocarcinoma (PDAC). Comparative analyses of survival and funding statistics in cancers with high mortality were performed to quantify discrepancies and identify areas for intervention.

Methods: The Surveillance, Epidemiology, and End Results database was queried for survival statistics. Funding data were obtained from the National Cancer Institute (NCI). Clinical trial data were obtained from www.

clinicaltrials.gov. Cancers with high mortality were included for analyses.

Results: Since 1997, PDAC has received lesser funding (\$1.13 billion) than other cancers such as breast (\$9.46 billion), prostate (\$4.46 billion), lung (\$4.26 billion), and colorectal (\$4.08 billion). Similarly, fewer clinical trials have been completed in PDAC (n=680) compared to breast (n=2,077), lung (n=2,046), prostate (n=1,134) and colorectal (n=1,196) cancer. Despite this, since 1997, NCI dollars invested in PDAC research produced a greater return on investment with regards to 5-year overall survival (5Y-OS) compared to breast, prostate, uterine, melanoma, and ovarian cancer. Incremental cost effectiveness analysis demonstrates that

millions (liver, non-Hodgkin's lymphoma) and billions (colorectal, lung) of dollars were required for each additional 1% increase in 5Y-OS compared to PDAC. Funding of research towards early detection and diagnosis of PDAC has decreased by 50% since 2007. For nearly all cancers, treatment-related research receives the highest percentage of NCI funding.

Conclusions: Funding of PDAC research is significantly less than other cancers despite its higher mortality and greater potential to improve 5Y-OS. Increased awareness and lobbying are required to increase funding, promote research and improve survival. ■

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Synthetic Resorbable vs. Cellulose Bandage for Minor Hemorrhage in a Porcine Model

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Mentor: Mark Carlson

Program: General Surgery

Introduction: Commercially-available topical hemostats for minor hemorrhage incurred during elective surgical procedures are relatively expensive. We believe that more economical synthetic hemostats could be produced. Our objective here was to compare the efficacy and toxicity of a synthetic resorbable hemostatic bandage vs. an analogous commercial product in a porcine model of minor hemorrhage.

Methods: For the nonsurvival efficacy study, anesthetized domestic swine (boars, 3 months, 29-40 kg) underwent arterial/venous line placement and splenectomy. A 1 x 8cm section of liver was resected from the

edge of the left lateral lobe, and test bandage (macroporous polycaprolactone mesh, PCL; N = 10) or oxidized regenerated cellulose (ORC; Surgicel®, Ethicon®; N = 10) was applied with manual pressure for 5 minutes. Resuscitation then was performed with warm LR (target MAP = 80% of preinjury), and blood loss was measured 60 min after injury. For the survival toxicity study, a similar resection technique was employed (N = 6 for each material), and necropsy was performed at 30 days to evaluate for bandage toxicity (subject growth, serum chemistry, histology).

Results: Pre-injury weight, VS, and laboratory testing did not differ among groups. Resection mortality was zero. In the efficacy study, there were no differences between the PCL vs. ORC groups in blood

loss or other post-injury variables (Table), except that the resuscitation fluid volume in the ORC group was greater. Other results from the efficacy study not shown in the Table include platelet counts and coagulation testing (no significant differences). Other than minor granuloma formation at the implantation site with both PCL and ORC, the survival study did not reveal any measurable toxicity.

Conclusion: The efficacy and toxicity of the PCL test bandage vs. the ORC comparator were not different in a porcine model of minor hepatic hemorrhage. Based on projected costs of production (not shown), the PCL bandage could represent a lower-cost alternative to ORC for the treatment of minor surgical bleeding. ■

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Renal Sympathetic Vasomotion Monitoring as a Novel Method for Intraoperative Feedback for Renal Denervation

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Mentor: Irving H. Zucker

Program: Anesthesiology

Background & Objectives: The sympathetic nervous system is a master regulator of homeostasis, and sympathetic dysfunction is implicated in the pathophysiology of cardiovascular, renal, and neurological disease. Despite its widespread importance, sympathetic nervous system outflow cannot be assessed in a clinically useful way, negatively impacting the assessment and treatment of prevalent diseases. One such example is the controversial pivotal trial failure of renal denervation, a promising intervention-

based therapy for hypertension in which the renal sympathetic nerves are ablated by an endovascular approach. The inability to assess the sympathetic nervous system, and thus adequate renal sympathetic nerve ablation, remains an existential problem facing the field of renal denervation.

Methods: Based on the fact that renal sympathetic nerve activity exerts rhythmic, baroreflex-driven, and vasoconstrictive control of the renal vasculature, we developed a novel technique for identifying rhythmic sympathetic vascular control using a time-varying, two-component Windkessel model

of the renal circulation. This technology was tested in two different animal models of renal denervation; ten rabbits underwent chronic, surgical renal denervation, and nine pigs underwent acute, functional renal denervation via intrathecal administration of ropivacaine.

Results: Both methods of renal denervation reduced low-admittance gain, negative-phase shift renal vascular control at known sympathetic vasomotor frequencies, consistent with a reduction in vasoconstrictive, baroreflex-driven renal sympathetic vasomotion, but did not affect mean renal blood flow.

Conclusions: Renal sympathetic vasomotion monitoring could provide intraoperative feedback for interventionists performing renal denervation and serve more broadly as a platform technology for the evaluation and treatment of diseases affecting the sympathetic nervous system. ■

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Different Strokes for Different Folks: Trends in Elective Surgery for Diverticular Disease

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Mentor: Sean Langenfeld

Program: General Surgery

The approach to patients with sigmoid diverticulitis has evolved towards more conservative management regardless of initial presentation or number of episodes. Despite this trend, approximately 20% of patients with diverticulitis will still require surgical intervention. It is unknown how the approach for diverticular disease has changed with the increasing popularity of new operative platforms.

The purpose of this study was to evaluate recent trends in elective surgery for diverticulitis, patient demographics, and outcomes.

The American College of Surgeons National Surgical Quality Improvement Program Colectomy Procedure-Targeted Database was queried from 2012 to 2016. This clinical

database allows for direct identification of different minimally invasive techniques (laparoscopic/LAP, laparoscopic hand-assist/LHA, robotic/RC, single-incision/SILS). Patients with ICD-9/ICD-10 diagnoses codes for diverticular disease of the large intestine were identified and stratified by operative approach (12,697 cases).

Patients undergoing open colectomy were older, had higher ASA class, and had higher rates of comorbidities. BMI and race were similar except for SILS. Robotic colectomies increased yearly from 2012–2016 ($P < 0.0001$), while LAP cases declined. However, there was not an increase in the overall use of minimally invasive techniques LAP/LHA/RC/SILS). Robotic-assisted operations took significantly more time as compared to all other approaches ($P < 0.001$), but had a lower conversion rate when compared to LAP/LHA. Anastomotic complications were highest in

converted group. Patients undergoing open operations (planned or converted) stayed significantly longer compared to other approaches ($P < 0.001$), had higher rates of 30-day readmission ($P < 0.001$), and were less likely to be discharged directly to home ($P < 0.001$). Minimally invasive techniques have remained the preferred method for elective diverticular disease; however, a growing percentage of cases are being performed with a robotic approach. Robotic-assisted surgery had a lower conversion rate at the expense of longer operative times. ■

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Delirium Assessment for Acute Ischemic Stroke Patients at UNMC

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Mentor: Daniel L. Murman

Program: Neurology

Background & Objectives: To investigate incidence of delirium in acute ischemic stroke patients at the University of Nebraska Medical Center (UNMC) and identify associated factors with development of delirium in acute ischemic stroke.

Methods: This is a prospective observational study. We screened delirium daily for patients aged 18 or older admitted with acute ischemic stroke using Confusion Assessment Method for the ICU and 3-minute Diagnostic Confusion Assessment Method starting within 48 hours after recognition of stroke until post-stroke day 7 or discharge. Data on patient characteristics were collected through chart review and analyzed using multivariate logistic regression.

Results: Of 74 patients included in the study, 29 (39.1%) developed delirium. The mean age and NIH stroke scale (NIHSS) at presentation were higher in delirium group than non-delirium group (69.4 ± 2.76 vs 65.1 ± 2.00 , 13.0 ± 1.30 vs 7.1 ± 1.00). Also, delirium group showed higher rates of prolonged ICU stay, presence of aphasia, embolic stroke, bilateral cerebral involvement, history of previous stroke and cognitive decline compared with non-delirium group. In contrast, more patients in non-delirium group received intravenous antithrombotic therapy. However, only the associations with NIHSS (OR=1.26, 95% CI 1.10 to 1.44, $P < 0.01$) and intravenous antithrombotic therapy (OR=0.04, 95% CI 0.00 to 0.35, $P < 0.01$) were statistically significant.

Conclusions: This pilot study demonstrated high incidence of delirium among acute

ischemic stroke patients at UNMC. Further studies with a larger sample size are required to identify risk factors of delirium in this patient population and proactively manage it for better outcomes. ■

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