Surgery Research Day 2023

21ST ANNUAL WILLIAM C. WOOD RESEARCH SYMPOSIUM

MAY 4, 2023 | 7 AM - 12 PM | IN PERSON & ZOOM EVENT

Keynote Lecture: **"The Peaks and Pitfalls of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in Pediatric and Adolescent Patients"**

presented by **Andrea Hayes Dixon, MC, FACS, FAAP**
Dean, Howard University College of Medicine
Vice President of Clinical Affairs
Chair of Surgery, HUH

EMORY UNIVERSITY SCHOOL OF MEDICINE | **Department of Surgery**

SCHEDULE OF EVENTS

7:00 – 8:00AM	**Introduction of keynote speaker by Dr. Randi Smith** Title: The Peaks and Pitfalls of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in Pediatric and Adolescent Patients *Andrea Hayes Dixon, MD, FACS, FAAP*
8:15AM	**Dean's Welcome by Dr. Carlos del Rio** **Welcome remarks by Dr. Luke Brewster** **Oral Presentations – Session I** *(in person & virtual)* **Zoom Link:** https://zoom.us/j/91282343766?pwd=d2xoc3BiU0w3ck9pVXdSMXNXeXVJdz09 **Passcode: sgr** *Moderators: Onkar Khullar, Alison Linden and Paul Ghareeb*
8:20AM	Risk Factors for Unscheduled Healthcare Contact after Outpatient Surgical Fixation of Distal Radius Fractures *Ambika Menon, Samuel H. Payne, Evan D. Woodard, Rachel E. Williams, Jesse I. Emefiele, William J. Knaus, Paul Ghareeb*
8:35AM	A nanoformulated inhibitor of NADPH oxidases improves therapeutic efficacy in colon cancer by enhancing the effect of radiation therapy and activating immune responses *Lumeng Zhang, Tongrui Liu, Weiping Qian, Lei Zhu, Lily Yang*
8:50AM	Does the ViSiGi 3D® reduce staple loads and operative time? A randomized controlled trial (RCT) comparing endoscopic vs. suction calibration device in laparoscopic sleeve gastrectomy *Danny Mou, Victoria Delgado, Zachary Grunewald, Katherine Fay, Carrie P Hall, Jahnavi Srinivasan, Jamil L Stetler, Federico J Serrot, Ankit Patel, Omobolanle Oyefule, Maggie Diller, Edward Lin, Scott Davis, Elizabeth M Hechenbleikner*
9:05AM	RIPK3 drives cytokine production and mortality during polymicrobial sepsis *Yang CS, Liang Z, Burd EM, Coopersmith CM, Balachandran S, Lyons JD*
9:20AM	Comparison of Non-Autologous Hemodialysis Grafts: Bovine Carotid Artery versus Synthetic *Richard A. Meena*

9:30AM	**Poster Presentations – Basic Sciences** *(in-person only)* *Moderators: John Lyons, John Calvert and Chrystal Paulos*
	Poster Presentations – Clinical Sciences *(in-person only)* *Moderators: Michael Lowe, Lauren Postlewait, and Kendra Grubb*
	Oral Presentations – Session II *(in-person & virtual)* **Zoom Link:** https://zoom.us/j/91282343766?pwd=d2xoc3BiU0w3ck9pVXdSMXNXeXVJdz09 **Passcode: sgr** *Moderators: Olamide Alabi, Kendra Grubb and Michael Lowe*
10:45AM	Neoadjuvant Chemoradiation Does Not Improve Outcomes for Patients Undergoing Resection for Upper Rectal Cancer: A US Rectal Cancer Consortium Analysis *Caroline Medin*
11:00AM	Inhibition of CD154/CD11b Interaction Using a Novel Nanotherapeutic Improves Allograft Survival *Bahn-Humphrey, A. Liu, D. Zhu, L. Yang, L. Ford, ML.*
11:15AM	Utilizing time-specific machine learning models to predict mortality in trauma-related ultra-massive transfusion *Courtney H. Meyer, Andrew ElHabr,, John Lyons, Jason D. Sciarretta, Jonathan H. Nguyen, Randi N. Smith*
11:30AM	A Transcatheter Beating Heart Neoleaflet Device to Treat Mitral Valve Prolapse *Stephanie K. Tom, Julia Toma, Muralidhar Padala*
11:45AM	Head and Neck Melanoma: An International Outcomes Analysis in the Post-MSLT-II Era *Baecher KM, Broman KK, Hughes T, Dossett LA, Carr M, Bartlett E, Sharma A, Thompson JF, Nijhuis A, Hieken TJ, Kottschade L, Gyorki DE, Downs J, vanAkkooi A, Stahlie E, Zuur C, Boere T, Ollila D, O'Shea K, Moncrieff M, Nobes J, Han D, Vetto J, Farma J, Karakousis G, Song Y, Deneve J, Fleming M, Delman KA, Perez M, Olofsson Bagge R, Mattsson J, Lee AY, Berman R, Chai H, Kroon H, Beasley G, Farrow N, Teras J, Teras RM, Hui J, Kruijff S, Been LB, Zager JS, and Lowe MC.*
12:00PM	**Closing remarks by Dr. William C. Wood, Craig Coopersmith & John Sweeney**
12:15PM	**Announcement of the symposium winners by Dr. Luke Brewster**
	Adjourn

KEYNOTE SPEAKER

Andrea Hayes Dixon, MD, FACS, FAAP

Dr. Andrea Hayes Dixon FACS is the Professor and Chair of Surgery at Howard University School of Medicine. She is also the Associate Director of the Cancer Center at Howard. In October of 2022, she was appointed to the position of Dean of Howard University's College of Medicine and Vice President of Clinical Affairs. Dr. Hayes Dixon has a basic science laboratory which focuses on rare sarcomas and she also maintains clinical research efforts. She specializes in refractory and resistant tumors in children and specifically soft tissue sarcomas in children. Her patient's request her services from around the world because she was the first to do hyperthermic intraperitoneal chemotherapy, HIPEC, and cytoreductive surgery in a child. She was previously the Section Chief of Pediatric Surgery at UT MD Anderson Cancer Center, and the Surgeon in Chief of the University of North Carolina Children's hospital and Division Chief at UNC.

Dr. Hayes Dixon is the first African American female pediatric surgeon in the United States of America. She is nationally and internationally known for her work pioneering the HIPEC operation for children. She has been featured on local TV and printed news on many occasions including being recognized in the 'Houston Woman' magazine. She continues to be active and involved in mentorship for young surgeons interested in an academic career. She is married and has one daughter, Jenelle (27) and one son, Jonah (26). She enjoys participating in church activities such as medical mission trips and supporting her United Methodist Church orphanage in Kenya.

ORAL PRESENTATIONS: SESSION I

Moderators/Judges: Onkar Khullar, Alison Linden and Paul Ghareeb
Location: EUH Auditorium

8:20AM

Category: Clinical Sciences

#C3 - Risk Factors for Unscheduled Healthcare Contact after Outpatient Surgical Fixation of Distal Radius Fractures

Ambika Menon, Samuel H. Payne MD, Evan D. Woodard BS, Rachel E. Williams BA, Jesse I. Emefiele BS, William J. Knaus MD, Paul Ghareeb, M.D.

Introduction:
Distal radius fractures (DRFs) commonly require surgical fixation. Unscheduled healthcare contact (UHC) after surgery represents a potential area of quality improvement in surgical care. We postulate that UHC after outpatient surgical fixation of DRFs is more common in patients who undergo treatment at a safety-net hospital versus those treated at a university-affiliated facility.

Methods:
An IRB-approved retrospective review studied all patients who underwent outpatient surgical treatment of DRFs at a university-based academic practice from 01/2017-05/2021. Surgeries were performed either at a local safety-net hospital or at a university-affiliated hospital. UHC was defined as telephone calls, emergency room visits, and/or readmissions to the hospital within thirty-days of surgery. Demographic factors, medical comorbidities, and details about the injury and surgery were gathered for analysis (Table 1).

Results:
442 patients met inclusion criteria. 257 patients (58.1%) were treated at a university-affiliated facility while 185 patients (41.9%) had surgery at the safety-net hospital. The overall rate of UHC within thirty-days of surgery was 14.0%. Rates of UHC were higher at the safety-net hospital compared with a university-affiliated facility (26.5% vs 5.1%, $p<0.05$). On subgroup analysis of the safety-net hospital population, UHC was associated with chronic pain, insured status, substance abuse and white race.

Conclusion:
There was greater than 5x chance of requiring UHC for patients undergoing surgery in a safety-net hospital setting compared to a university-setting. UHC after surgery is often related to inadequate postoperative pain control or inadequate patient education. Reducing UHC can improve quality of care while reducing unnecessary healthcare cost.

	Safety-Net Hospital	University Associated Hospital	
Total Number of Patients	185 (48.9%)	257 (58.1%)	
Gender			
Male	98 (52.97%)	67 (26.07%)	**p <0.00001**
Female	87 (47.03%)	190 (73.93%)	
Race:			**p <0.00001**
Black	126 (68.10%)	53 (20.62%)	
White	30 (16.21%)	178 (69.26%)	
Hispanic	17 (9.19%)	6 (2.33%)	
Other	10 (5.41%)	19 (7.39%)	
Age (mean)	41.77	53.46	**p <0.00001**
BMI (mean)	27.81	26.95	p >0.05
Insurance Type:			**p <0.00001**
Private	38 (20.54%)	165 (64.20%)	
Medicare	14 (7.57%)	38 (14.79%)	
Medicaid	19 (10.27%)	27 (10.50%)	
Worker's Comp	4 (2.16%)	0 (0%)	
Uninsured	108 (58.38%)	21 (8.17%)	

Table 1. Demographics of patient population

8:35AM

Category: Basic Sciences

#B1 - A nanoformulated inhibitor of NADPH oxidases improves therapeutic efficacy in colon cancer by enhancing the effect of radiation therapy and activating immune responses

Lumeng Zhang, Tongrui Liu, Weiping Qian, Lei Zhu, Lily Yang

Objective: Genetic and oxidative stresses in tumor cells lead to the production of reactive oxygen species (ROS) and upregulation of cell survival pathways. Such a redox imbalance reduces sensitivity of cancer cells to therapeutic agents and radiation. Herein, we aim to develop a nanoformulated NADPH Oxidases (NOX) inhibitor to block the critical NOXs-ROS signal pathway for overcoming radioresistance in colon cancer.

Methods: Biodegradable hyaluronic acid nanoparticles (HANPs) encapsulated with NOX1/4 inhibitor, GKT831 (HANP/GKT831) has been developed. Targeted delivery and therapeutic response were determined in a subcutaneous mouse colon cancer model. The effect of HANP/GKT831 on radiation therapy was evaluated in the colon cancer model following five intravenous administrations of HANP/GKT831 (5 mg/kg equivalent dose of GKT831), in combination with radiation (2 Gy). Histological and immunological analyses of colon tumor tissues were used to determine mechanism of NOX1/4 inhibition on improving therapeutic response in colon cancer.

Results: Optical imaging determined the selective accumulation of HANP/GKT831 in colon tumors following systemic delivery. The combination of systemic administrations of HANP/GKT831 with local radiation had stronger tumor growth inhibition (~ 83%) than that of conventional GKT831 combined with Radiation (<60%). Our results showed that HANP/GKT831 increased DNA damage after radiotherapy. Furthermore, the combination therapy activated tumor-specific cytotoxic T cell response with increased levels of CD8+/CD107a+ and CD8+/CD28+ in tumors, while reducing the level of myeloid-derived suppressive cells (CD11b+/GR1+) in tumors.

Conclusion: HANP/GKT831 sensitizes tumor cells to radiation and enhances immune responses. It is a promising nanotherapeutic agent for colon cancer therapy.

8:50AM

Category: Clinical Sciences

#C12 - Does the ViSiGi 3D® reduce staple loads and operative time? A randomized controlled trial (RCT) comparing endoscopic vs. suction calibration device in laparoscopic sleeve gastrectomy

Danny Mou, Victoria Delgado, Zachary Grunewald, Katherine Fay, Carrie P Hall, Jahnavi Srinivasan, Jamil L Stetler, Federico J Serrot, Ankit Patel, Omobolanle Oyefule, Maggie Diller, Edward Lin, Scott Davis, Elizabeth M Hechenbleikner

Introduction

When performing laparoscopic sleeve gastrectomies (LSG), one must ensure consistent sleeve size and orientation. Various devices assist with this, including weighted bougies, esophagogastroduodenoscopy (EGD), and suction calibration devices (SCDs) like the ViSiGi 3D® (Boehringer Labs, PA). Prior studies suggest that SCDs decrease staple load firings and operative time. However, they are limited to single-surgeon experience and retrospective data. We performed the first RCT comparing EGD against SCD.

Methods

This is a randomized, nonblinded study from an MBSAQIP-accredited academic center. LSG patients were randomized to SCD or EGD calibration. Inclusion criteria include ≥ 18 years of age and clinical indication for LSG. Exclusion criteria include prior weight loss surgery and intraoperative hiatal hernia repair. Seven surgeons followed a standardized operative technique, including powered mechanical staplers, staple line reinforcement, and intraoperative leak test. Staple load firings and operative duration were analyzed with t-test.

Results

Inclusion criteria were met by 106 LSG patients (88% female). Average age was 43 years and average BMI was 48 kg/m^2. Patients received EGD (n=56) or SCD (n=50) calibration. No significant difference in baseline characteristics was identified. Mean number of staple load firings for EGD and SCD calibration arms were 5.4 and 5.3, respectively (Table 1; p=0.417). Mean operative times for EGD and SCD calibration groups were 96.5 minutes and 94.6 minutes, respectively (p=0.776). There was no significant difference in 30-day post-operative complications.

Conclusions

Relative to EGD calibration, SCD calibration does not reduce the number of staple load firings or operative time for LSGs.

Table 1. Total number of staple load firings in the EGD and SCD groups.

Total Number of Staple Load Firings	EGD	SCD	Total	*p-value*
4	6	8	14	-
5	28	23	51	-
6	15	17	32	-
7	6	2	8	-
8	1	0	1	-
Total	**56**	**50**	**106**	-
Average Number of Staple Load Firings	**5.4**	**5.3**	**5.4**	***0.417***

9:05AM

Category: Basic Sciences

#B7 – RIPK3 drives cytokine production and mortality during polymicrobial sepsis

Yang CS, Liang Z, Burd EM, Coopersmith CM, Balachandran S, Lyons JD

Introduction: Receptor interacting protein kinase 3 (RIPK3) regulates inflammatory signaling in mammalian tissues and immune cells, triggering cell death by necroptosis when its kinase domain is active and supporting cytokine production through kinase-independent binding interactions. The degree to which these variable signaling outcomes contribute to the inflammatory dysregulation of bacterial sepsis remains incompletely described.

Methods: Wild-type (WT) mice and those with deletion or mutation of RIPK3 were subjected to cecal ligation and puncture (CLP), an established model of polymicrobial intraabdominal sepsis. Animals were either followed for survival or sacrificed at 24 hours for tissue assays. Survival curves were compared via log-rank analyses and means of experimental groups were compared using Mann-Whitney testing. All statistical analyses were performed using Prism software.

Results: Deletion of RIPK3 (*Ripk3*$^{-/-}$) conferred a significant survival advantage over WT controls during polymicrobial sepsis (76% survival vs 40%, p=0.04, n=15-17/group), whereas inactivation of the pro-necroptotic kinase domain (*Ripk3*$^{K51A/K51A}$) did not. Furthermore, treatment of animals with the necroptosis inhibitor UH15-38 had no impact on overall survival (treatment: 16% survival vs control: 16%, p=0.89, n=12/group). Blood levels of IL-1β were reduced in mice lacking RIPK3 (5.5± 7.2 ρg/ml vs. 16.0± 13.8, p=0.007, n=11-12/group), and blood from *Ripk3*$^{-/-}$ mice contained lower numbers of bacteria (4.1 ± 1.3 log(colony-forming units/ml) vs. 7.9 ± 1.0, p=0.02, n=3-7/group).

Conclusion: RIPK3 mediates septic mortality following CLP through a process that is independent of kinase-mediated necroptosis. Loss of RIPK3 suppresses septic inflammation and improves control of polymicrobial infection.

9:20AM

Category: Clinical Sciences

#C14 - Comparison of Non-Autologous Hemodialysis Grafts: Bovine Carotid Artery versus Synthetic

Richard A. Meena

BACKGROUND – An arteriovenous fistula is considered the ideal option for first-time hemodialysis arteriovenous access (AVA). For patients presenting with poor caliber upper extremity veins, is unclear which non-autologous conduit choice is superior. We aimed to compare outcomes between bovine carotid artery (BCA) and synthetic grafts for first-time upper extremity AVA.

METHODS – We performed a retrospective review of first-time upper extremity AVA at four hospitals between 2003 and 2022. Primary outcomes included stenosis and thrombosis rates at 6 and 12 months. Secondary outcomes included loss of primary patency, infection rates, and number of interventions per graft at 6 and 12 months.

RESULTS – Of the included 295 accesses, 219 (74.2%) were synthetic, while 76 (25.7%) were BCA. There were no significant differences in baseline demographics or comorbidities between the two cohorts. Synthetic grafts thrombosed at a higher rate than BCA, both at 6 months (37.8% versus 13.0%, $p=0.002$) and at 12 months (64.7% versus 15.4%, $p<0.001$). Further, the mean number of interventions per graft was higher for the synthetic cohort at 6 months (0.31 versus 0.18, $p<0.001$) and at 12 months (0.45 versus 0.28, $p<0.001$). Infection rates, stenosis rates, and loss of primary patency were not significantly different between the two cohorts (Table 1).

CONCLUSIONS – At 6 and 12 months, BCA grafts had a lower mean number of interventions per graft and were less prone to thrombosis. A large-scale prospective study is necessary to elucidate whether BCA grafts still hold these advantages over synthetic grafts among patients requiring first-time upper extremity AVA.

Table 1. Comparison of primary and secondary outcomes at 6 and 12 months for patients undergoing first-time upper extremity arteriovenous access using synthetic and bovine carotid artery (BCA) grafts.

	Synthetic Grafts	**BCA Grafts**	***p-value***
6 Months	n=119	n=46	
Number of Interventions per Graft (mean)	0.31	0.18	***<0.001***
Stenosis	10 (8.4%)	1 (2.17%)	*0.15*
Thrombosis	45 (37.8%)	6 (13.0%)	***0.002***
Infection	4 (3.4%)	2 (4.3%)	*0.761*
Loss of Primary Patency	48 (40.3%)	13 (28.3%)	*0.150*
12 Months	n=102	n=39	
Number of Interventions per Graft (mean)	0.45	0.28	***<0.001***
Stenosis	17 (16.6%)	3 (7.7%)	*0.172*
Thrombosis	66 (64.7%)	6 (15.4%)	***<0.001***
Infection	7 (6.9%)	2 (5.1%)	*0.706*
Loss of Primary Patency	70 (68.6%)	22 (56.4%)	*0.172*

POSTER/QUICK-SHOT PRESENTATIONS: BASIC SCIENCE

Moderators: John Calvert, John Lyons & Chrystal Paulos
Location: EUH Classroom A

9:40AM

#B2 - Claudin-4 Deletion Improves Gut Permeability and Survival in Murine Abdominal Sepsis

Takashi Shimazui

Introduction: Claudin-4 is a tight junction protein that plays a significant role in maintaining gut integrity. Gut barrier function is worsened following sepsis although the mechanisms underlying this are incompletely understood.

Methods: Wild-type (WT) and claudin-4 knockout (KO) mice were subjected to cecal ligation and puncture (CLP)-induced polymicrobial abdominal sepsis and sacrificed at pre-determined timepoints or followed 7 days for survival. The three pathways of gut permeability (pore, leak, unrestricted) were assayed following oral gavage of different-size dyes followed by measuring their appearance in the blood. Jejunal protein expressions and plasma cytokine levels were evaluated to determine local and distant impact of claudin-4 deletion.

Results: Concentrations of creatinine (6Å) were significantly decreased 24 and 48 hours after CLP in KO mice, as were concentrations of Fluorescein isothiocyanate–dextran (28Å) at 24 hours, indicating decreased permeability via the pore and leak pathways respectively. No difference was found in Rhodamine B isothiocyanate–dextran (120Å) demonstrating the unrestricted pathway of permeability was unaffected. There changes were associated with significant increases in Claudin-2 and 12 in KO mice as well as significantly decreased Junctional Adhesion Molecule A. Both pro-inflammatory interleukin-6 and anti-inflammatory interleukin-10 were significantly lower in KO mice. Notably, seven-day mortality was markedly improved in KO mice (64.7% vs 11.1%).

Conclusion: Claudin-4 KO mice had improved gut permeability following intra-abdominal sepsis, associated with a significant improvement in survival. Claudin-4 deletion may play a protective role in abdominal sepsis by decreasing systemic inflammation modulated by gut luminal contents.

9:45AM

#B3 - NK Cell are Implicated in Early Rejection in Pig-to-Nonhuman Primate Renal Xenotransplantation

Steven C Kim, David V Mathews, Jakob Habib, Cynthia L Breeden, Mandy L Ford, Christian P Larsen, Andrew B Adams

Purpose: Xenotransplantation has recently re-emerged as a feasible solution to address the growing organ shortage. While our group and others have made significant improvements in abrogating the hyperacute rejection response with pre-transplant screening in preclinical xenotransplant models, acute rejection remains a risk to the intermediate survival of xenografts. The mechanisms underlying these pathways of injury are an area of active investigation, and the role of NK cells in xenograft rejection is under studied in the setting of a clinically available immunosuppression protocol utilizing CD28 directed costimulation blockade (CoB).

Methods: *In vitro* mixed lymphocyte reactions (MLRs) were done using CFSE labeled NHP responders stimulated by porcine GalKO/hDAF PBMCs. NK cell (CD3-CD4-CD8+) expansion was measured with CFSE dilution in the presence and absence of CoB. This was then translated to a preclinical *in vivo* model of pig-to-NHP renal xenotransplantation (n=3) using an immunosuppression protocol of CD4/CD8 depletion, MMF, steroids, and CD28-directed CoB (MST 21). Graft-infiltrating cells at the time of rejection were processed and compared to historical allotransplant controls treated with the same immunosuppression regimen (MST 91).

Results: MLRs demonstrated that CD28-directed CoB significantly reduced the proliferation of NK cells in response to *in vitro* xenostimulation (p=0.029) (Figure 1). In our *in vivo* preclinical NHP xenotransplantation model, we identified a significantly higher frequency of NK cells trafficking to the xenograft at the time of rejection compared to rejecting allografts (p=0.007) (Figure 2).

Conclusion: NK cell infiltration to the xenografts in a preclinical translational pig-to-NHP renal xenotransplantation model is associated with early xenograft rejection. Previously published data have shown an increased proportion of CD4 T cells that traffic to and mediate xenograft rejection compared with allograft rejection. These data implicate NK cells as an additional possible mediator of xenograft rejection under clinically relevant CoB based protocols and highlight the need for further study.

Figure 1:

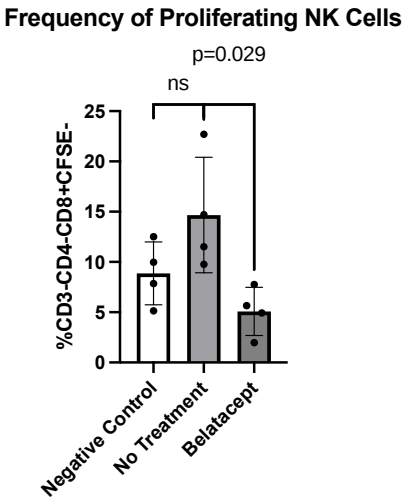
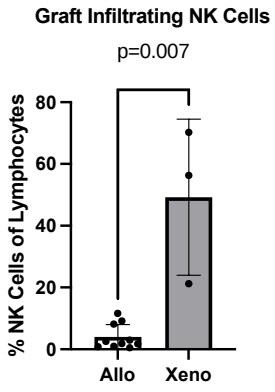


Figure 2:



9:50AM

#B5 - CD154:CD11b Blockade Increases MPEC Differentiation of Virus-specific CD8$^+$ T Cells

Katie Alexander

CD154 pathway blockade has been shown to significantly improve graft survival in transplantation. Recently, CD11b was identified as an alternate receptor for CD154. CD154:CD11b interactions promote rejection by increasing the recruitment of innate and adaptive immune cells into the allograft. However, the effects of CD154:CD11b blockade on the protective immune response to infection during immunosuppression has not been elucidated. To address this, MHV68, a murine homolog of EBV, was used to assess the antigen-specific CD8$^+$ T cell response. Naïve B6 mice were infected with MHV68 and treated on days 0, 2, 4, and 6 with a peptide inhibitor of CD154:CD11b binding (cM7). cM7 treatment resulted in an increase in tetramer$^+$ antigen-specific CD8$^+$ T cells 10 days post-infection that exhibited an increase in gene expression associated with activation and antigen processing. To determine if this increase was a result of enhanced proliferation, CTV-labeled OT-I T cells were stimulated in vitro. Results indicated that CD154:CD11b blockade did not impact proliferation. Instead, cM7 treatment in vitro resulted in an increase in the expression of CD69, CD25, and CD44, and in vivo resulted in an increase in CD127^{hi}KLRG1^{lo} MPECs. In conclusion, these data demonstrate that CD154:CD11b blockade enhances the quantity and quality of virus-specific CD8$^+$ T cells during protective immunity. We speculate that this could be due to the inhibition of terminal differentiation of antigen-specific T cells resulting in enhanced differentiation of high quality memory precursors, or could be due to altered balance of CD154:CD40 vs CD154:CD11b binding, promoting CD40-driven costimulation.

9:55AM

#B8 - Mitochondrial transcription is required for the enhanced anti-tumor activity of adoptively transferred stem-like memory T cells

Guillermo O. Rangel Rivera, Soundharya Kumaresan, Hannah M. Knochelmann, Aubrey S. Smith, Brandon B. Ware, Anna C. Cole, Megen Wittling, Megan M. Wyatt, and Chrystal M. Paulos

Background: Current clinical protocols for adoptive T cell therapy are not always effective against cancer. Therapeutic failure has been attributed to T cell exhaustion and poor mitochondrial quality, which can be driven by chronic PI3Kδ signaling. We hypothesized that PI3Kδ inhibition would generate stem-like memory T cells (T_{SCM}) that provide protection against melanoma by sustaining stemness and enhancing mitochondrial fitness.

Methods Melanoma specific T cells were expanded in the presence of Idelalisib, a PI3Kδ inhibitor, and infused into B16F10 tumor bearing mice. *In vitro* we tested T cell stemness by flow cytometry and RNA sequencing. We assessed mitochondrial qualities such as mass, membrane potential, reactive oxygen species, and respiratory capacity. We further tested the effect of ablating mitochondrial transcription by CRISPR knockout of *Rexo2*, an understudied regulator of mitochondrial transcription identifyed in our transcriptional analysis.

Results PI3Kδ inhibited T cells provided potent antitumor activity against melanoma, and resembled T_{SCM} denoted by high levels of Tcf-1 and Lef-1, while suppressing markers of exhaustion (Tim-3 and CD39). We

observed metrics of mitochondrial quality to be elevated in T_{SCM}. Furthermore, electron transport chain gene expression was selectively enhanced at the RNA and protein level. Ablation of *Rexo2* led to loss of mitochondrial transcription, perturbed cristae ultrastructure and vastly impaired the antitumor activity of T_{SCM}.

Conclusions. We discovered that enhanced mitochondrial transcription, regulated by REXO2 is required for T_{SCM} anti-tumor immunity. These findings suggest that mitochondrial transcription regulated by REXO2 is a potential target to bolster the activity of tumor specific T cells.

10:00AM

#B11 - CD103 Blockade Leads to a $CD8^+$ and Regulatory T Cell Mediated Increase in Mortality in a Murine Model of Sepsis

David A. Swift, Cameron W. Paterson, Zhe Liang, Craig M. Coopersmith, Mandy L. Ford

CD103 is an integrin involved in T cell trafficking to sites of epithelial injury and the suppressor function of regulatory $CD4^+$ $Foxp3^+$ T cells (Tregs). We evaluated whether CD103 blockade impacted morality in murine sepsis. C57BL/6 mice underwent cecal ligation and puncture with a CD103 blocking antibody or vehicle. Mice were sacrificed at 24h for flow cytometry or followed 7 days for survival. Anti-CD103 administration resulted in increased mortality (84.2 vs. 45.0% p=0.029) following sepsis. Anti-CD103 led to increased frequency (41.7% vs. 38.0% p<.001) and number of $CD8^+$s (relative count 1.52 vs. 1.00 p=0.029). Additionally, anti-CD103 led to increases in IFN-y producing $CD8^+$s (172,623 vs. 79,413 p=0.006) and Tregs (21,134 vs. 11,670 p=0.001). We then evaluated if the increased mortality seen with anti-CD103 was dependent on $CD8^+$s. Anti-CD103 in the context of $CD8^+$ depletion improved survival over anti-CD103 alone (85.0% vs. 35.3% p=.002), signaling that the effect of CD103 on mortality was $CD8^+$-dependent. Given the observed increase in IFN-y^+ Tregs, we next evaluated if Tregs were necessary for the decreased survival observed in the context of anti-CD103. In Treg depleted mice, anti-CD103 failed to alter mortality, exhibiting that Tregs were necessary for CD103's effect on survival. In the setting of Treg depletion, anti-CD103 also failed to alter the frequency or number of $CD8^+$s. Additionally, the increase in IFN-y^+ $CD8^+$s seen in CD103 blockade alone was absent following Treg depletion. These results demonstrate the ability of CD103 blockade to increase sepsis mortality is dependent on both $CD8^+$s and Tregs.

10:05AM

#B12 - Galectin-9 Favors the Generation of Effector and Terminal-Like T Cells While Thwarting Central Memory T Cells: A New Checkpoint Target for Biliary Tract Cancer Immunotherapy

Emilie A.K. Warren

INTRODUCTION

Galectin-9, a carbohydrate-binding protein, plays a role in immune cell homeostasis. Our prior retrospective analysis of plasma from metastatic biliary tract cancer (BTC) patients revealed that higher soluble galectin-9 associates with worse overall survival. We hypothesize that galectin-9 exerts inhibitory action on T cells, thereby impairing antitumor immune responses in BTC.

METHODS

CD3$^+$ T cells from buffy coats of healthy human donors were activated and expanded with IL-2 +/- exogenous galectin-9 (1 µg/mL). Longitudinal growth was measured daily by trypan blue. Five days after activation, cell phenotype and function were analyzed by flow cytometry.

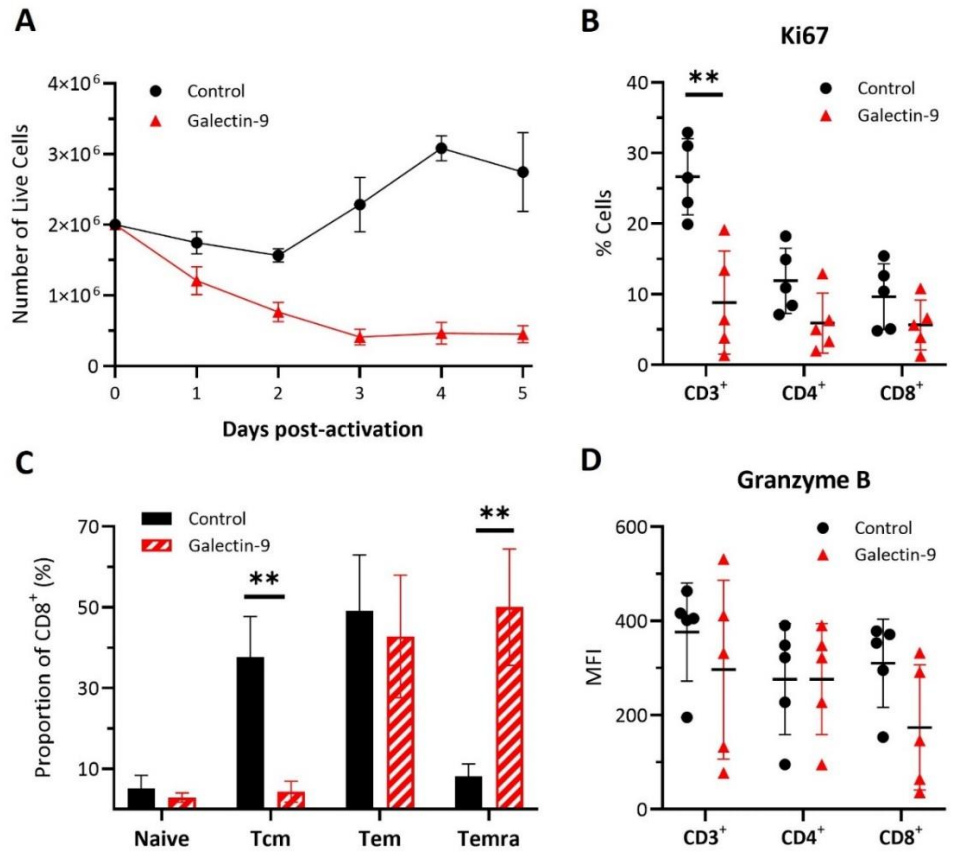
RESULTS

Galectin-9 significantly slowed T cell growth: while untreated T cells expanded in number, galectin-9 treated cell growth was stagnant (Figure 1A). Based on Ki67 expression, significantly fewer T cells were highly proliferative after galectin-9 treatment compared to untreated cells (p=0.008). In both CD4$^+$ and CD8$^+$ subsets, a striking reduction of central memory "Tcm" cells along with a pronounced increase of more terminally differentiated effector memory "Temra" cells manifested in cultures expanded with galectin-9 compared to the untreated cohort (p=0.008; Figure 1C). CD8$^+$ T cells trended in producing less granzyme B when cultured with galectin-9 versus control (p=0.056, Figure 1D).

CONCLUSIONS

We discovered that galectin-9 negatively regulates T cell growth *in vitro*. Moreover, the development of T cells with central memory phenotype, a crucial population for maintaining immunity, is restricted in the presence of galectin-9. These results identify galectin-9 as a potential target that could be leveraged to regulate the antitumor activity of T cells.

Figure 1



10:10AM

#B13 - T Cell Response to the Minor Antigen HY in Mice is Driven by Immunodominant Epitopes Generating Public and Conserved Response

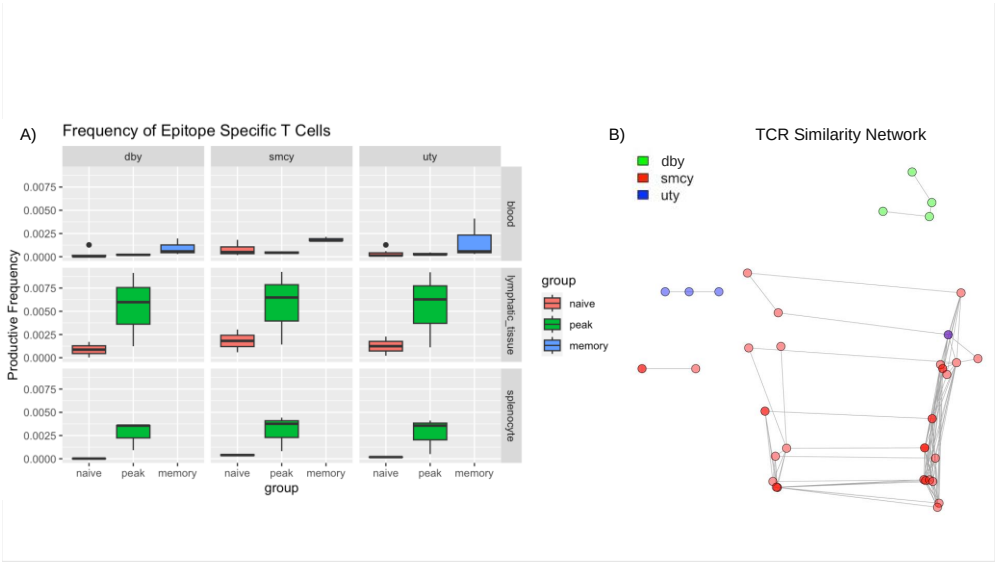
Aileen Johnson, Weiwen Zhang, Joan Zhang, Chris Larsen

Introduction: Allograft rejection occurs secondary to genetic polymorphisms between donor and recipient. The HY model, transplanting from male to female of an inbred mouse strain, minimizes this genetic difference, limiting immune response recognition to Y-chromosome proteins. Using the HY model, we aimed to map immunogenic peptides and characterize rejection-associated T cells.

Methods: Y-specific proteins expressed in C57BL/6 mice with corresponding X proteins were used to predict H-2b-restricted HY peptides. 100 peptides were screened by IFNy elispot against splenocytes from sensitized female C57BL/6. MHC tetramers specific to immunodominant peptides were used to isolate epitope-specific T cells. Tetramer-specific cells were captured by single cell and subjected to paired-chain TCR sequencing. Bulk repertoires from naïve, peak response, and memory mice were characterized by beta-chain TCR sequencing.

Results: Known peptides Smcy738, Uty246, and Dby608 were predicted strong binders and demonstrated immunodominance in functional response. Four additional public subdominant epitopes were identified. TCR sequence analysis demonstrated highest frequency of tetramer-specific clones in lymph nodes at the peak response timepoint, with Smcy738 dominating the response. However, the highest frequency of rejection-associated clones in peripheral blood, whether measured by public tetramer-isolated clones, metaclones, or public rejection-associated clones, was seen at the memory timepoint. Analysis of TCR sequence similarity identified distinct neighborhoods of response for each epitope.

Conclusions: Current immunosuppression in transplantation non-selectively suppresses T cells regardless of specificity, resulting in increased susceptibility to infection and malignancy. Using antigen specificity to target rejection-associated T cells could reduce complications associated with immunosuppression.



10:15AM

#B15 - Fcγr2B/Fgl2 AS A DRIVER OF MORTALITY IN SEPTIC MICE

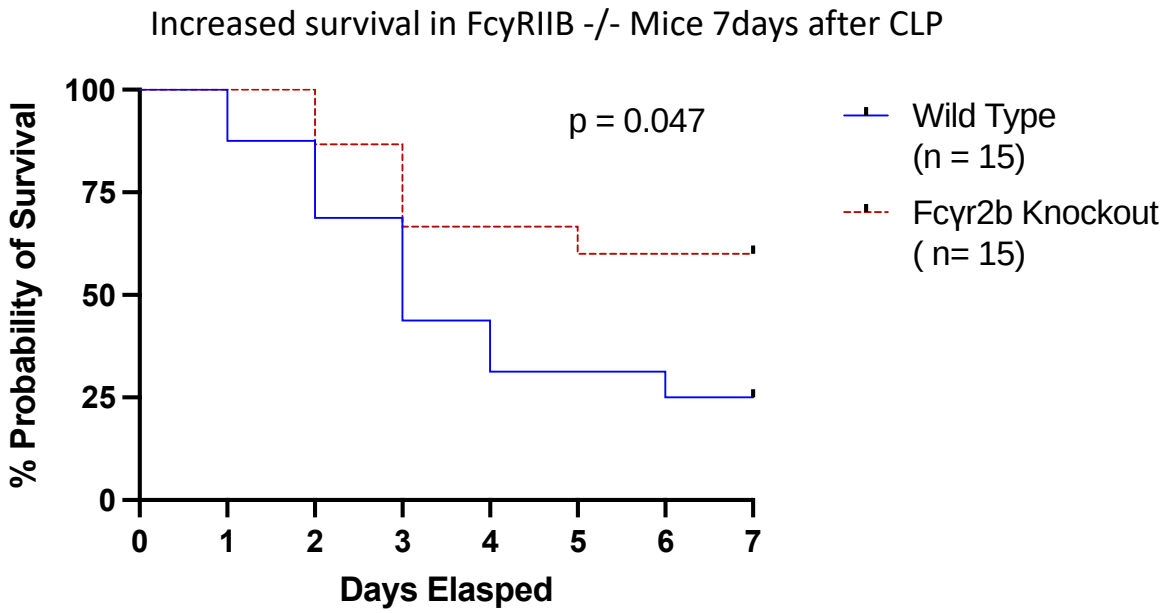
JC Williams, JC Anyalebechi, CM Coopersmith, ML Ford

Sepsis is a complex state of immune dysregulation characterized by an oscillation between hyperinflammatory and hypoinflammatory immune responses. Fibrinogen-like protein 2 (FGL2) is an inhibitory molecule that is elevated in both mice and humans during sepsis. FGL2 is a primary functional ligand of the anti-inflammatory Fc receptor, FcyRIIb. This FcyRIIB/FGL2 axis has been shown to result in a subdued immune cell response. This study aimed to determine the role and mechanism of the FcyRIIB/FGL2 axis in potentiating sepsis-related mortality.

Mice underwent cecal ligation and puncture (CLP). Splenocytes and serum were harvested at 24h for immunophenotyping and immunoassaying. 7-day survival was assessed.

The genetic knockout of FcyRIIB resulted in a significant improvement in sepsis mortality (25% vs 60%, p=0.047), a decrease in CTLA-4 on CD4+ and CD8+ T cells (p=0.006, p=0.005), and an increase in T cells, NK cells, macrophages, and B cells (p=0.03, p=0.004, p=0.016) as compared to WT controls. To address the role of FGL2 in sepsis pathophysiology, mice that constitutively express FGL2 were subjected to CLP. In the context of overexpression of FGL2 septic mouse mortality increased compared to wild type (p = .0199). Analysis of immune cells from human septic patients reveal that CD8+ T cells similarly express FcyRIIB, and early analyses have shown increased exhaustive phenotypes on FcyRIIB-positive subsets compared to FcyRIIB negative subsets (p = 0.028).

These data reveal the FcyRIIB/FGL2 axis is a potent mediator of immune reactivity during sepsis and suggest it could be a target of therapeutic intervention to improve sepsis outcomes.



10:20AM

#B19 - Efficacy of a New Interventional Cardiac Reshaping Device to Treat Post-Myocardial Infarction Heart Failure in Swine

Chase L. King, Michael Silverman, Stephanie K. Tom, Daisuke Onohara, Yuta Kikuchi, Brooks A Lane, Keawepono Wong, Julia Toma, Amanda Maddamma, Muralidhar Padala

Introduction:
Heart failure (HF) occurs in nearly 80% of patients surviving a myocardial infarction (MI). In HF, hearts are often dilated and spherical which leads to functional mitral regurgitation (FMR). Medical therapies have failed to yield a mortality benefit and thus new approaches are needed. We developed a new beating heart cardiac reshaping device that reduces the size and shape of the left ventricle and also eliminates FMR. Our hypothesis is that our approach reduces wall stresses on the left ventricle, which would halt progression of HF, reduce metabolic demand, and increase survival. This device and hypothesis were studied in a six-month swine model of post-MI heart failure.

Methods:
An MI was induced in ten Yorkshire swine and followed three months to develop HF, LV dilatation, spherical remodeling and FMR. The cardiac reshaping device was implanted in a beating heart through a sternotomy, and adjusted until LV end diastolic volume was reduced by 25-30% and FMR was eliminated, as confirmed using real time echocardiography imaging.

Results:
LV end diastolic volume was reduced by 26% (p=.007), sphericity index by 22% (p=<.001), and FMR was reduced. Mitral valve closure was significantly improved with an increased systolic coaptation 3.09±0.59mm to 5.21±1.32mm (p=0.0005), and decrease in tenting area from 147.0±38.73mm^2 to 118.8±30.89mm^2 (p=0.03). Stroke work reduced from 0.77±0.25mJ to 0.52±0.16mJ (p=0.06).

Conclusions:
In this preclinical study, our interventional approach to reduce and reshape the failing heart enabled better cardiac function, and may potentially provide a new avenue to treat a large patient population with a clear unmet need.

10:25AM

#B20 - Nicotine Exposure Impairs Mitochondrial Function of Patient Mesenchymal Stem Cells

McLaughlin D, Teichmann M, Brewster LP, Hekman KE

Introduction
Severe peripheral artery disease (PAD) is a significant cause of morbidity. There remains a need for improved therapies, especially for patients who are not candidates for surgical revascularization. Mesenchymal stem cells (MSCs) demonstrate promising preliminary results for restoring limb perfusion in animal models without surgery. Patient factors effect on MSC function and efficacy is unknown. Since mitochondrial function is a key driver of stem cell function, we evaluated patient smoking status effect on MSC mitochondrial function.

Methods

MSCs were harvested from tibia at time of major amputation for PAD. Samples were matched for age and diabetes. Metabolism was measured using the Seahorse analyzer. Reactive oxygen species (ROS) were measured with 2',7'–dichlorofluorescin diacetate. Treated cells were cultured with 250uM nicotine for 48 hours.

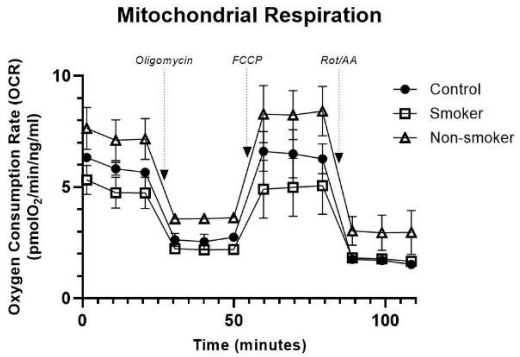
Results

MSCs from smokers displayed significantly more quiescent energy phenotype, seen as lower mitochondrial respiration and glycolytic capacity when compared with MSCs from non-smokers. ROS did not differ between samples at baseline or under physiologic oxygen conditions. Treating non-smoker MSCs with nicotine also suppressed respiration and glycolytic capacity. Recovery of respiration after withdrawal of nicotine treatment was variable between cell lines.

Conclusions

Our findings demonstrate suppression of MSC respiration resulting from chronic nicotine exposure in vivo and from acute nicotine exposure in vitro. Given the role of mitochondrial function in "stemness," further evaluation of the regenerative function and efficacy of MSCs from smokers will be necessary. Smoking status may need to be evaluated for efficacy as the field of cellular therapy moves forward for severe PAD.

A.



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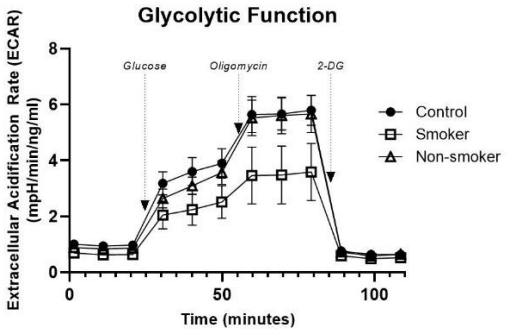

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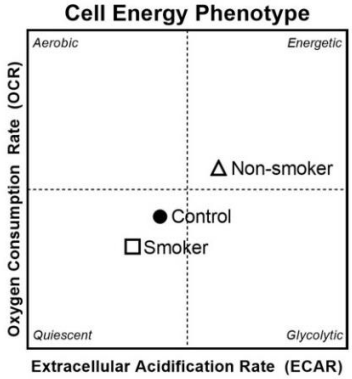


Figure 1. Chronic nicotine exposure suppresses mitochondrial function in patient obtained MSCs. Mitochondrial respiration (a) and glycolytic function (b) of MSCs from smokers (n=4) and non-smokers (n=4) were measured using the mitochondrial stress test and glycolytic stress test and measured using the Seahorse analyzer, respectively. A healthy MSC line was used as a control (n=1). Cell energy phenotype (c) was calculated based on the mitochondrial respiration and glycolytic function and was plotted. Error bars represent standard deviation.

POSTER/QUICK-SHOT PRESENTATIONS: CLINICAL SCIENCE

Moderators: Kendra Grubb, Michael Lowe & Lauren Postlewait
Location: EUH Classroom B/C

9:40AM

#C2 - Understanding Pre-operative Patient Body Image: Perception Is Not Reality

Ciara A. Brown, Troy Marxen, Barbara T. Biney, Makenna Ash, Albert Losken, Heather R. Faulkner

Introduction: A challenging role of plastic surgeons is managing patient expectations. Patients may have an unrealistic view of the possible surgical outcome, which may start with a pre-existing distorted self-perception. Understanding patient self-perception may aid plastic surgeons in providing improved pre-operative counseling and expectation-setting.

Patients and Methods: We performed a retrospective review of new patients who presented to 2 plastic surgeons from 2020 to 2022. The cohort consisted of patients that completed a pre-visit questionnaire which included patient-reported (PR) height and weight. PR height and weight were then compared to measured (MS) values (cm and kg) taken from the same visit. Our primary clinical outcome was to evaluate if PR and MS values differed.

Results: 355 patients were identified from the query, of which 184 patients completed the pre-visit questionnaire. The mean difference in PR weight and MS weight was 2.1 kg (range -4.8 to 46.9). There was a statistically significant difference between PR weight and MS weight in all visit types (Table 1). 83.2% of patients underestimated their weight. Patients with a measured BMI greater than 30 underestimated their weight more profoundly than patients with a measured BMI less than 30 (p=0.02) There was no significant difference between PR and MS height.

Conclusions: Patients seeking plastic surgery consultations may under-report their weight, which may indicate a distorted body image. Plastic surgeons should be aware of this potential discrepancy to determine appropriateness for surgery and ensure that accurate measurements are taken in their offices.

Table 1: Patient-Reported versus Measured Weight

	Pt reported weight Mean (SD)	Measured weight Mean (SD)	p
All patients	83.9 (22.0)	86.0 (22.5)	<0.001
Med necessary	87.6 (22.7)	89.8 (23.2)	0.0001
Cosmetic	77.8 (19.7)	79.4 (20.0)	<0.001
Blended (med nec + cosmetic)	81.4 (21.3)	83.3 (21.6)	<0.001

9:45AM

#C15 - Temporal Trends in Outcomes Following Surgical Aortic Valve Replacement in Men and Women

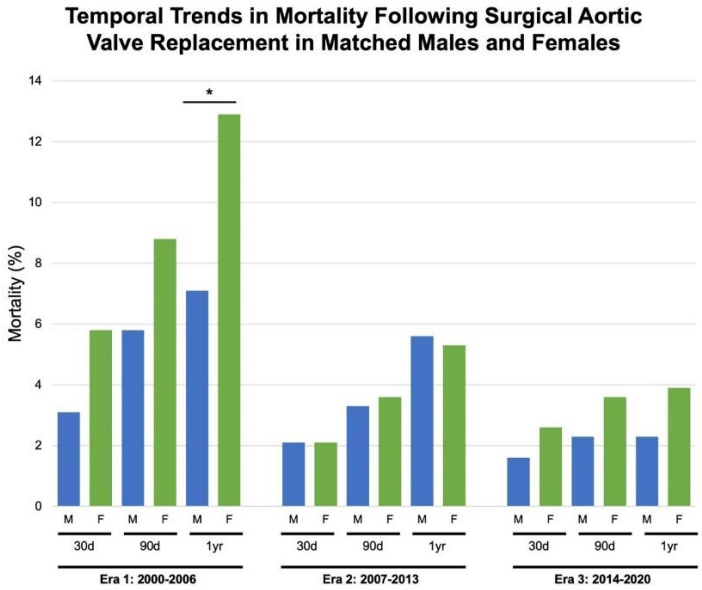
Lauren V. Huckaby, Elizabeth Norton, Kendra J. Grubb

Background
Women have demonstrated worse outcomes after surgical aortic valve replacement (SAVR) when compared to men. We sought to explore temporal trends in SAVR outcomes between the sexes.

Methods
A surgical database of adult patients (≥18 years) undergoing SAVR at a single institution between 2000-2020 was queried. Temporal trends (Era 1: 2000-2006; Era 2: 2007-2013; Era 3: 2014-2020) in outcomes including mortality and complications were compared between sexes. Propensity score matching of baseline characteristics was utilized to analyze males and females.

Results
A total of 3,861 patients were identified (61.8% male; mean age 63.1±14.1 years for males and 67.1±13.2 years for females). Post-operative stroke rates were significantly lower in men in Era 1 (7.5% vs 12.8%) though this disparity was not evident in Eras 2 and 3. Thirty-day all-cause mortality following SAVR in males and females was 3.4% versus 5.8% in Era 1, 2.7% versus 2.8% in Era 2, and 1.5% versus 2.7% in Era 3. Thirty- and 90-day mortality were similar in matched males and females across all eras. In the matched pairs, 1-year mortality was significantly lower in males compared to females in Era 1 (7.1% vs 12.9%, p=0.020) but not significantly different in the latter eras. Thirty-day, 90-day, and 1-year mortality rates improved significantly across the eras in both sexes.

Conclusions
Outcomes following SAVR have improved with resolution of sex-based mortality differences in the current era. Further work will be necessary to improve post-procedural morbidity and mortality in both sexes, including attention to patient selection for SAVR.



9:50AM

#C17 - A Deeper Dive into Racial Disparities in Coronary Artery Bypass Grafting Outcomes: Failure to Rescue and the Postoperative Phase of Care

William W. Qu, Jane W. Wei, Jose N. Binongo, and William B. Keeling

Introduction: African Americans experience greater morbidity and mortality compared to Caucasians after coronary artery bypass grafting (CABG). We examined failure-to-rescue (FTR) rates after CABG to better understand whether systems-level differences in postoperative care contribute to outcome disparities.

Methods: A retrospective review was completed on 22,324 patients undergoing isolated CABG between 2002 and 2022. FTR was defined as mortality within 30 days following postoperative stroke, prolonged ventilation, renal failure, or reoperation. Racial cohorts were balanced via propensity-score matching of variables included in the 2018 Society of Thoracic Surgeons predicted risk of mortality (STS-PROM) criteria.

Results: Univariate comparisons of black and white patients demonstrated significant differences in several preoperative characteristics, including New York Heart Association class III/IV symptoms (59.2% vs. 48.7%, $p < 0.0001$), history of stroke (12.5% vs. 8.1%, $p < 0.0001$), renal failure (10.9% vs. 3.0%, $p < 0.0001$), and STS-PROM (1.3% vs. 1.0%, $p < 0.0001$). 1,522 matched pairs were identified after propensity-score matching. African Americans had greater rates of postoperative renal failure (2.9% vs. 1.4%, $p = 0.01$). No significant differences were observed in rates of stroke (2.0% vs. 1.3%, $p = 0.15$), prolonged ventilation (10.3% vs. 8.4%, $p = 0.07$), reoperation (3.8% vs. 3.2%, $p = 0.32$), and 30-day mortality (2.1% vs. 1.6%, $p = 0.35$). There were no significant differences in FTR rates between black and white patients (Table 1).

Conclusion: African Americans who underwent CABG received similar systems-level postoperative management following major complications. Efforts to narrow the outcomes gap should focus on optimizing preoperative comorbidities.

Table 1. Propensity-score matched comparison between African American and Caucasian patients of failure-to-rescue rates after coronary artery bypass grafting.

Major Complication	African American	Caucasian	*p*-value
Stroke	2 / 30 (6.7%)	2 / 20 (10.0%)	0.99
Prolonged Ventilation	16 / 157 (10.2%)	14 / 128 (10.9%)	0.84
Renal Failure	6 / 44 (13.6%)	6 / 22 (27.3%)	0.18
Reoperation	9 / 58 (15.5%)	7 / 48 (14.6%)	0.89
Composite	19 / 225 (8.4%)	18/174 (10.3%)	0.52

9:55AM

#C19 - Patterns Of Completion Axillary Dissection For Patients With cT1-2N0 Breast Cancer Undergoing Total Mastectomy With Positive Sentinel Lymph Nodes

Lara Schwieger, Lauren McLendon Postlewait, Preeti Dilip Subhedar, Feifei Geng, Yuan Liu, Theresa Gillespie and Cletus A. Arciero

Introduction: The ACOSOGZ0011 trial (2011) found that 10-year overall survival (OS) for patients with 1-2 +nodes undergoing sentinel lymph node biopsy-alone (SLNB) was non-inferior to completion axillary lymph node dissection (ALND), but excluded patients undergoing mastectomy. This study examined patterns of ALND and its relationship with OS for SLNB+ patients undergoing mastectomy.

Methods: The National Cancer Database was queried (2010-2017) for patients with cT1-2N0 breast cancer undergoing mastectomy with +SLNs. Demographic and clinical data were compared. Cox proportional hazard models and propensity-score matched Kaplan-Meier tests were used to analyze OS.

Results: Of 20,001 patients, 8,427 (42.1%) underwent SLNB, and 11,574 (57.9%) had SLNB+ALND. The SLNB group had fewer +SLNs (median 1.3 vs. 2.6 p<0.001) and less frequently received nodal radiation (28.9% vs 33.4%, p<0.001). Patients in later years were less likely to undergo ALND (2010: reference; 2013: OR 0.46, 95%CI 0.4-0.52, p< 0.001; 2016: OR 0.33, 95%CI 0.29-0.33, p<0.001). Median follow-up was 74.8mo. Multivariable analysis showed that ALND (HR 0.98, 95%CI 0.90-1.07, p=0.63) and nodal radiation (HR 0.92, 95%CI 0.83-1.02, p=1.06) were not associated with improved OS (Table). Propensity-score matched 5-year OS was similar between patients who underwent SLNB and SLNB+ALND (90.3% vs 90.9%, p=0.65).

Conclusion: Following ACOSOGZ011, omission of ALND after +SLNB in patients with early-stage clinically node-negative breast cancer undergoing mastectomy is common and increased over time. Axillary radiation was not more common in the SLNB-alone group. For patients undergoing mastectomy for cT1-2N0 breast cancer with +SLNB, completion ALND and nodal radiation were not associated with improved survival.

Table: Multivariable Cox Proportional Hazard Model Evaluating Factors Associated with Overall Survival in Patients with Early-Stage Breast Cancer Undergoing Mastectomy with Positive Sentinel Lymph Node Biopsy

	Multivariate Analysis			
Variable	**Hazard Ratio**	**95%CI**	**Individual P-value**	**Overall P-value**
Race				
Black	0.99	0.85-1.14	0.859	**0.002**
Other/Unknown	0.65	0.52-0.83	**<0.001**	
White	Ref	Ref	Ref	
Age at diagnosis (years)				
>70	4.22	3.55-5.02	**<0.001**	**<0.001**
61-70	1.81	1.54-2.13	**<0.001**	
51-61	1.47	1.47-1.72	**<0.001**	
?50	Ref	Ref	Ref	

Regional population without high school degree*				
<7.0%	0.94	0.79-1.12	0.488	**0.010**
7.0-12.9%	1.13	0.97-1.31	0.108	
13.0-20.9%	1.13	0.98-1.30	0.099	
≥21.0%	Ref	Ref	Ref	
Insurance				
Not Insured/Unknown/Other	1.50	1.29-1.74	**<0.001**	**<0.001**
Medicare	1.48	1.29-1.68	**<0.001**	
Private	Ref	Ref	Ref	
Cancer Sequence				
Isolated malignancy	0.83	0.74-0.93	**0.001**	**0.001**
First of ≥2 malignancies	Ref	Ref	Ref	
Median income**				
≥$63,000	0.73	0.62-0.86	**<0.001**	**<0.001**
$48,000-$62,999	0.77	0.66-0.89	**<0.001**	
$38,000-$47,999	0.92	0.80-1.06	0.236	
<$38,000	Ref	Ref	Ref	
Charlson-Deyo Comorbidity Score				
≥2	2.27	1.95-2.64	**<0.001**	**<0.001**
1	1.43	1.28-1.59	**<0.001**	
0	Ref	Ref	Ref	
Grade / Differentiation				
Undetermined	1.25	0.97-1.60	0.083	**<0.001**
Poor / undifferentiated	1.82 1.23	1.57-2.11	**<0.001**	
Moderate	Ref	1.08-1.41	**0.003**	
Well		Ref	Ref	
Radiation				
Chest wall only	0.83	0.72-0.97	**0.021**	0.090
Chest wall and nodal	0.92	0.83-1.02	0.106	
Unknown	0.96	0.78-1.19	0.720	
None	Ref	Ref	Ref	
Adjuvant Systemic Therapy				
No	2.01	1.75-2.31	**<0.001**	**<0.001**
Yes	Ref	Ref	Ref	
Year of Diagnosis				
2017	0.69	0.53-0.88	**0.003**	**<0.001**
2016	0.79	0.64-0.97	**0.025**	
2015	0.79	0.66-0.96	**0.017**	
2014	0.92	0.78-1.09	0.344	
2013	0.82	0.70-0.96	**0.012**	
2012	1.08	0.94-1.25	0.278	
2011	1.01	0.88-1.16	0.904	
2010	Ref	Ref	Ref	
Molecular Subtype				
Her2+	0.92	0.81-1.06	0.248	**<.001**

Triple Negative	1.62	1.40-1.86	**<0.001**	
Unknown	0.97	0.76-1.25	0.840	
Hormone-Receptor+ / HER2-	Ref	Ref	Ref	
Lymphovascular invasion				
Negative	0.83	0.76-0.91	**<0.001**	**<0.001**
Unknown	1.00	0.87-1.14	0.960	
Present	Ref	Ref	Ref	
Tumor size, mean (cm)	1.26	1.20-1.32	**<0.001**	**<0.001**
SLNB and ALND	0.98	0.90-1.07	0.631	0.631
SLNB alone				

*Percentage of population within the patient's zip code not receiving a high school degree reported by quartile 2008-2012

** Median income of population within patient's zip code by quartile 2008-2012

ALND- axillary lymph node dissection; SLNB- sentinel lymph node biopsy

10:00AM

#C20 - Taking Back the Duct: Transcystic Laparoscopic Common Bile Duct Exploration for Pediatric Patients With Choledocholithiasis, A Multi-center study

Jessica L Raul, Goeto Dantes, Marshall Wallace, Amelia Collings, Gloria Sanin, Gabriel Cambronero, Maggie Bosley, Romeo Ignacio, Jennifer Leslie Knod, Bethany Slater, Michael H Livingston, Katerina Dukleska, Stefan Scholz, Matthew Santore, Irving J Zamora, Lucas P Neff

Background: Patients with choledocholithiasis are often treated with endoscopic retrograde cholangiopancreatography (ERCP) followed by laparoscopic cholecystectomy (LC). Initial LC, intraoperative cholangiogram (IOC), and transcystic laparoscopic common bile duct exploration (LCBDE) can avoid the need for subsequent ERCP. We hypothesized that upfront LC+IOC +/- LCBDE will decrease the length of stay (LOS) and the total number of interventions for children with suspected choledocholithiasis.

Methods: A multicenter, retrospective cohort study was performed on pediatric patients (<18 years) between 2018 to 2022 with suspected choledocholithiasis. Demographic and clinical data were compared for upfront LC with IOC +/- LCBDE and possible postoperative ERCP (OR1st) versus preoperative ERCP prior to LC (OR2nd). Primary outcomes were the length of stay (LOS) and complications. Complications were defined as postoperative pancreatitis, recurrent choledocholithiasis, bleeding, or abscess.

Results: Across five centers, 115 patients with suspected choledocholithiasis were treated with OR1st (n=78) or OR2nd (n=37). There were no differences in age, gender, or body mass index (p=0.13, p=0.06, p=0.91).

The incidence of complications was comparable in both groups (2% vs 8%, p=0.19). LOS was shorter in OR1st (3.5 vs 5.5 days, p<0.05). Of the LCBDE patients, 85% had definitive intraoperative management with the remaining 15% requiring postoperative ERCP. Fifty-five patients in the OR1st group (71%) underwent LCBDE, the remaining patients in the OR1st group did not have an LCBDE attempt due to either successful clearance with power flushing and glucagon, or hospital resources and surgeon preference.

Conclusion: Management of choledocholithiasis with upfront LC+IOC +/- LCBDE is a safe and effective management approach that is associated with decreased LOS and the need for a second procedure for the majority of patients. Postoperative ERCP remains an essential adjunct for patients who fail LCBDE. Further educational efforts are needed to increase the skills training for IOC and LCBDE in pediatric patients with suspected choledocholithiasis.

10:05AM

#C22 - Emory's Institutional Experience with Serial Transverse Enteroplasty in Adult Patients

Eli Mlaver, Abe Matar, Jahnavi Srinivasan, John Galloway

Introduction: Serial transverse enteroplasty (STEP) is used in the treatment of short bowel syndrome (SBS), in which a person does not have enough intestine to absorb nutrients and thus is susceptible to malnutrition. STEP utilizes a zigzag pattern of cuts in the intestine to lengthen the surface of bowel available to absorb nutrients.[1] Literature review yields small case series and one systematic review, almost exclusively focused on pediatric patients.[2–4] Our objective is to reflect on a master surgeon's 20 years of experience performing STEP on adult patients.

Methods: We retrospectively reviewed all STEP procedures performed at Emory University Hospital to describe the characteristics of patients that have undergone this procedure, the operative technique utilized, and outcomes.

Results: We identified 10 patients that underwent 11 STEP procedures (one patient had two STEP surgeries). Indications for STEP included SBS following multiple abdominal surgeries or intra-abdominal catastrophe and chronic partial bowel obstruction with evidence of dysmotility. The median bowel length was increased from 90 to 165 cm. After median length of stay of 21 days, 100% of patients were discharged home. All included patients remain alive after median follow-up of 24 months. Two patients have been fully weaned from TPN and two more have decreased frequency of TPN requirement.

Conclusion: This marks the largest case series reported of STEP in adult patients. The procedure nearly doubled the length of bowel in included patients, and it was well-tolerated with few complications. STEP should be more widely considered for patients with SBS.

Table: Patient characteristics, operative data, and outcomes for STEP

Patient demographics and comorbidities	**N = 10**
Age, years, mean (range)	49 (30-76)
Female, n (%)	7 (70%)
Race, n (%) Black White	 3 (30%) 7 (70%)
BMI [B], n (%) Underweight Normal Weight Overweight Obese	 2 (20%) 5 (50%) 3 (30%) 0 (0%)
Indication for STEP, n (%)	

SBS due to multiple abdominal surgeries	6 (60%)
SBS following intra-abdominal catastrophe	2 (20%)
Chronic partial bowel obstruction or dysmotility	2 (20%)
Pre-operative Teduglutide use, n (%)	4 (40%)
Pre-operative TPN use, n (%)	
Daily	8 (80%)
3-5 times/week	1 (10%)
None	1[D] (10%)
Smoking, n (%)	
Former	2 (20%)
Current	3 (30%)
Cardiac Disease [C], n (%)	4 (40%)
Operative Data	**N = 11[A]**
Pre-operative bowel length, cm, median (range)	90 (45-300)
Post-operative bowel length, cm, median (range)	165 (80-420)
Bowel length gained, cm, median (range)	75 (35-185)
Number of STEPs, median (range)	10 (7-39)
Also performed CAWR, n (%)	7 (63%)
Operative time, hours, mean (range)	9.5 (6.25-12.5)
Estimated blood loss, mL, mean (range)	313 (150-600)
Post-operative Outcomes	**N = 11[A]**
Hospital Length of Stay, days, median (range)	21 (15-36)
ICU Length of Stay, days, median (range)	3 (2-14)
Reoperation within 30 days, n (%)	0 (0%)
SSI, n (%)	1 (9%)
VTE, n (%)	0 (0%)
Pneumonia, n (%)	1 (9%)
Discharged to Home, n (%)	11 (100%)
Readmissions within 12 months, median (range)	1 (0-8)
Alive at Last Follow-Up, n (%)	10 [A] (100%)
TPN use at Last Follow-Up, n (%)	
Daily	4 (40%)
3-5 times/week	3 (30%)
None	3 (30%)
Follow-Up Time, months, median (range)	24 (3-128)

[A] One included patient underwent two separate STEP procedures
[B] BMI categories per CDC: <18.5 = Underweight, 18.5-25.0 = Normal, 25.0-30.0 = Overweight, >30.0 = Obese
[C] Includes Atrial Fibrillation (n=2) and Coronary Artery Disease / History of Myocardial Infarction (n=2)
[D] This patient had previously been TPN-dependent but had weaned pre-op and remains off TPN
[E] Abbreviations: STEP – Serial Transverse Enteroplasty, CAWR – Complex Abdominal Wall Reconstruction

10:10AM

#C30 - How to Maximize Long-Term Benefit from the Minimally Invasive Approach to Distal Pancreatectomy

Pranay S. Ajay, Hardik U. Shah, Sameer Sandhu, Caitlin P. Sok, Maria C Russell, Kenneth Cardona, Felipe B Maegawa, Shishir K. Maithel, Juan M. Sarmiento, David A Kooby, Mihir M. Shah

INTRODUCTION: Limited data exist regarding long-term benefits of Minimally Invasive Distal Pancreatectomy (MIDP) compared with Open Distal Pancreatectomy(ODP). We assessed the downstream development of incisional hernia in these populations.

METHOD: Records/imaging of patients who underwent distal pancreatectomy (DP) between 2017-2021 were analyzed. Patients without pre and postoperative imaging were excluded. Two radiologists blinded to the surgical technique and extraction site performed independent reviews. Specimen extraction sites were stratified as upper midline/umbilical (UMI) vs. Pfannenstiel. Patients were contacted directly and asked to complete an approved questionnaire regarding hernias. Chi-square and Multivariable Logistic regression analysis (MVA) were performed.

RESULTS: 250 patients were identified and 233 met selection criteria, of which 102(43.77%) patients responded to our call/questionnaire. There were 94(40%) ODP and 139(60%) MIDP, of which 70(30%) were laparoscopic with UMI/hand assist, 44(19%) robotic with Pfannenstiel incisions, 16(7%) were laparoscopic with Pfannenstiel incisions, and 9(4%) were MIDP converted to open. The median length of follow up was 12.68 months (interquartile range:3.71–30.28 months). Overall, 45(20.55%) patients were diagnosed with postoperative incisional hernia from extraction site (missing data=14patients)(Figure1). When rate of hernia was assessed based on specimen extraction site-UMI(n=172,74%) or Pfannenstiel(n=61,26%), the rate was significantly higher with UMI compared to Pfannenstiel incisions-26%vs5%, respectively($p<0.01$).

On MVA, overall odds of developing a hernia increased by 3% every month (OR-1.03,95%CI-1.01-1.05;p=0.001); while 7.89 times increase in odds of developing a hernia was noted with UMI compared to Pfannenstiel(OR-7.89,95%CI:2.27–27.42;p=0.001).

CONCLUSION: Minimally invasive distal pancreatectomy(laparoscopic/robotic) with Pfannenstiel extraction significantly decreases the odds of developing incisional hernias as compared with laparoscopic, hand-assist, or open procedures with upper midline incisions.

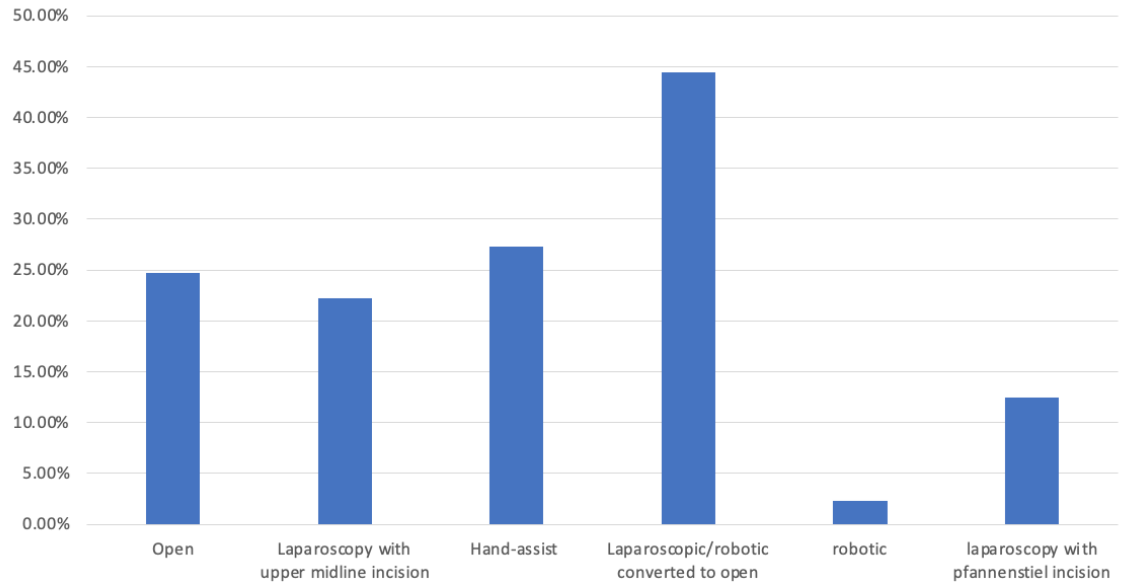


Figure 1 – Rates of extraction site hernia by operative technique

10:15AM

#C31 - Predictors of Autologous Fat Grafting in Immediate, Implant-Based Breast Reconstruction

Brown, O., Jean-Baptiste, O., Thompson, P.

Background: Autologous fat grafting (AFG) is a common adjunct to implant-based breast reconstruction (IBBR). Patients frequently need or desire fat grafting to improve common issues such as implant visibility and contour deformity, often done as a second, staged procedure following immediate reconstruction. This study aimed to identify which patient factors and reconstructive techniques predict the need for revision with AFG after IBBR.

Methods: Patients who underwent IBBR with either tissue expanders or implants following mastectomy from 2017 to 2021 were identified. Demographics, comorbidities, and the postoperative course were reviewed. The primary outcome variable was AFG after the initial reconstruction. Univariate and regression analyses were performed to identify factors predictive of AFG.

Results: Five-hundred twenty-nine patients were included in our analysis, with 43% having AFG. The grafting cohort was younger (P<.0001) and less likely to have undergone radiation therapy (p=.0457). Mean implant size was larger in the AFG cohort (*p*=.0375). Univariate regression displayed single-stage reconstruction (OR=0.53, 95% 0.37-0.75) and previous radiation (OR 0.59, 95% 0.35-0.99) negatively predicted the need for AFG, while bilateral breast reconstruction (BBR) was a predictor (OR 2.32, 95% 1.58-3.4). On multivariate analysis, decreasing age and BBR remained predictive of AFG. The odds of AFG decreased by 3% for every one-unit increase in age (95% CI [0.96, 0.99]). Interestingly, neither pre-pectoral breast reconstruction nor specimen weight : implant ratio was associated with increased need for AFG on univariate/multivariate analysis.

Conclusions: Patients requiring AFG were likely younger and had undergone BBR with tissue expanders. Plane of implant did not appear to affect need for AFG. Knowledge of these predictive factors may help plastic surgeons in preoperative counseling before implant-based breast reconstruction.

	AFG [*N* (% or IQR)	No AFG [*N* (% or IQR)	Combined	p-value
Oncologic Details				
Unilateral	54 (10.2)	126 (23.8)	180 (34.0)	**<0.0001***
Bilateral	174 (32.9)	175 (33.1)	349 (66.0)	
NSM	121 (26.1)	138 (22.9)	259 (49.0)	0.19*
SSM	99 (18.7)	146 (27.6)	245 (46.3)	
SRM	8 (1.51)	17 (3.2)	25 (4.73)	
Median mastectomy specimen weight (g)	441.8 (276-638.5)	438 (280.5-688.0)	440.5 (227.5-657.5)	0.84+
Reconstructive Details				
Direct-to-Implant	116 (21.9)	199 (37.6)	315 (59.6)	**0.0004***
Tissue Expander	112 (21.2)	102 (19.3)	214 (40.5)	
Pre-pectoral	134 (25.3)	191 (36.1)	325 (61.4)	0.27*
Sub-pectoral	94 (17.8)	110 (20.8)	204 (38.6)	
Average Implant Size (cc) $\pm$ SD	444.6 $\pm$ 136.8	419.7 $\pm$ 135.0	430.4 $\pm$ 136.2	0.038*
Specimen weight (g) to implant ratio	0.99 (0.75-1.37)	1.06 (0.76-1.43)	1.03 (0.76-1.40)	0.19+

Table 1. Oncologic and reconstruction characteristics
*Pearson chi-square test
+Wilcoxon test

10:20AM

#C36 - Diagnosis and Disparity: Characteristics of Patients Presenting with Breast Cancer at the Instituto Oncológico del Oriente Boliviano

Constance Harrell Shreckengost, Mauricio Andres Villarroel Garrón, Estefany Copa, Lauren Postlewait, Steven Roser, Esteban Foianini, Carolina Henestrosa

INTRODUCTION: Breast cancer is the second most common cancer among women in Bolivia, but data regarding its presentation are scarce. We describe a sample of patients with breast cancer at the Instituto Oncológico del Oriente Boliviano (IOOB), Bolivia's largest and oldest public cancer hospital.

METHODS: Retrospective review of medical records at the IOOB from 2021 identified patients age 18+ diagnosed with invasive breast cancer. Researchers then contacted patients via telephone to obtain clinical data not available from the medical record.

RESULTS: Of the 119 patients included, one was male. Median age at presentation was 51 (range 24-86). Nearly all (95%, n=97/102) patients presented after palpating a mass, while only 2% (n=2/102) presented after a lesion was identified on screening mammography. Histologically, 88% (n=103/117) had invasive ductal carcinoma. Specimens were 66% (n=57/86) hormone-receptor-positive, 15% (n=13/86) HER2-positive, and 26% (n=22/86) triple-negative. Thirty percent (n=37/53) of patients presented with Stage IV disease. Only 34% (n=41/119) underwent surgical treatment; of these, 93% (n=38/41) underwent modified radical mastectomy. Only one patient had a sentinel lymph node biopsy. Forty-two percent (n=44/106) underwent systemic chemotherapy.

CONCLUSION: While breast cancer patients at the IOOB present at a median age of only 51, 30% are diagnosed with Stage IV disease. In comparison, US patients are diagnosed at a median age of 63, and only 6% present with metastatic disease. Further research will be needed to determine whether these data are representative of Bolivian breast cancer at the national level and what factors influence its presentation.

10:25AM

#C39 - The impact of social determinates of health on ICU admissions in pediatric trauma

Katya Van Anderlecht, Valerie Dutreuil, Goeto Dantes, Allison Linden

Introduction: Trauma is the leading cause of death in children and social determinants of health (SDOH) have been shown to influence pediatric trauma outcomes. Trauma patients requiring pediatric intensive care are among the most critical and require an extensive amount of resources. The purpose of this study is to identify the effect of social determinants of health on pediatric trauma requiring a PICU admission.

Methods: A retrospective review of children (age 0-21) admitted to a level 1 pediatric trauma center between February 2018 and December 2021 was conducted. Demographic and clinical data were collected. SDOH factors included race, insurance, and childhood opportunity index (COI) score. Univariate and multivariate logistic regression models were performed with the latter adjusted for age, race, COI, insurance, and ISS in relation to PICU admission.

Results: A total of 12,244 patients were treated for trauma of which 1,141 (9.32%) were admitted to the PICU. Compared to patients not requiring PICU admission, those that did require a PICU admission were more likely to have government insurance (72.3% vs. 59.2% p<0.001), were more likely to be black (47.5% vs. 37.65%, p<0.001), and were more likely to live in areas defined as “very low opportunity” in composite COI (36% vs. 28%, p < 0.001). PICU patients had increased hospital length of stay (117 hours vs 23 hours; p<0.01) and mortality (7% vs. 0.25%; p<0.01). On univariable analysis, age (p=0.001), race (p=0.001), insurance status (p=0.001), and COI (p<0.01) were all associated with the need for PICU admission. On multivariable analysis, insurance status (p=0.003) and COI (p=0.021) remained significantly associated with PICU admission.

Conclusion: Social determinates of health represented by COI and insurance status were found to have a significant impact in pediatric trauma patients requiring a PICU admission. These patients subsequently had worse outcomes, including mortality. As we seek to provide quality and equitable pediatric care, further investigation into these socioeconomic disparities is warranted to mitigate this risk and improve outcomes.

ORAL PRESENTATIONS: SESSION 2

Moderators/Judges: Olamide Alabi, Kendra Grubb & Michael Lowe
Location: EUH Auditorium

10:45AM

#C21 - Neoadjuvant Chemoradiation Does Not Improve Outcomes for Patients Undergoing Resection for Upper Rectal Cancer: A US Rectal Cancer Consortium Analysis

Caroline Medin Goel

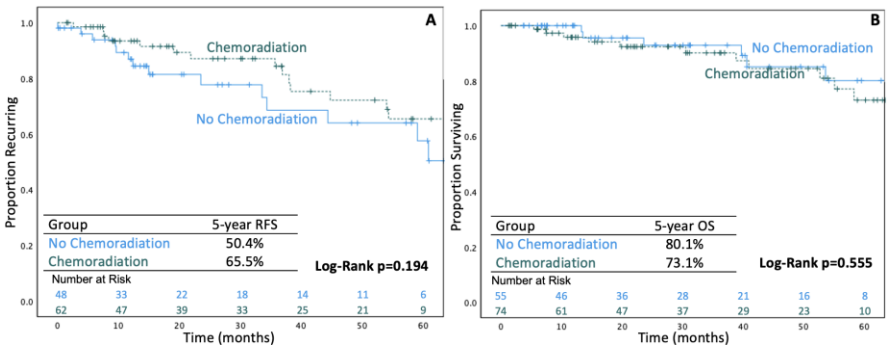
Introduction: The use of neoadjuvant chemoradiation (NCRT) for upper rectal cancer remains controversial. We sought to determine whether NCRT was associated with improved outcomes.

Methods: The US Rectal Cancer Consortium was queried for patients who underwent resection of non-metastatic upper rectal cancer (≥12cm from anal verge) from 2007-2017. Primary outcomes were recurrence-free (RFS) and overall survival (OS). Secondary outcomes were postoperative complications.

Results: 193 patients met inclusion criteria; 100 (52%) did not receive NCRT and 93 (48%) did. Median age was similar between groups (non-NCRT: 62 years; NCRT: 57 years; p=0.71), as was gender and stage (non-NCRT: 22% stage I, 32% stage II, 36% stage III; NCRT: 21% stage I, 23% stage II, 33% stage III; p=0.143). Median follow-up was 31 months (non-NCRT) and 34 months (NCRT). On Kaplan-Meier analysis of Stage II/III patients, NCRT was not associated with improved 5-year RFS compared to non-NCRT (65.5% vs. 50.4%; p=0.194) or 5-year OS (73.1% vs. 80.1%; p=0.555; Figure 1). This finding persisted on multivariable cox regression. R0-resection rate was similar between groups at 99% (non-NCRT) and 96.7% (NCRT; p=0.27). Anastomotic leak occurred in 11% of both cohorts. Creation of a diverting loop ileostomy (DLI) was nearly 3-times higher following NCRT (82%) versus non-NCRT (29%; p<0.001).

Conclusions: Among patients with non-metastatic upper rectal cancer, NCRT did not improve survival or recurrence, but was associated with nearly threefold higher DLI rate. Although NCRT is a mainstay of treatment for lower rectal cancer, our results do not support its use in upper rectal cancer.

Figure 1. Kaplan-Meier Survival Analysis for Recurrence-Free (A) and Overall (B) Survival.



11:00AM

#B9 - Inhibition of CD154/CD11b Interaction Using a Novel Nanotherapeutic Improves Allograft Survival

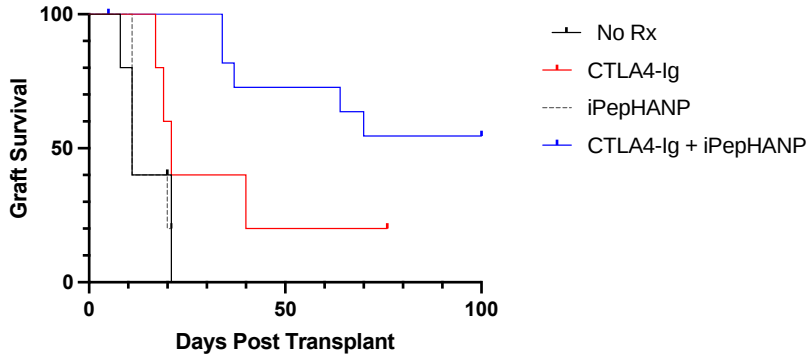
Bahn-Humphrey, A. Liu, D. Zhu, L. Yang, L. Ford, ML

CD154 blockade is among the most effective methods to prolong allograft survival. However, thrombotic complications prevented clinical use of anti-CD154 antibodies. Recently, we showed that CD11b functions as an alternate CD154 receptor during alloimmunity. Here, we developed a novel nanobiologic that prevents CD154:CD11b binding and determined the impact of this therapeutic approach on allograft survival.

Methods: Hyaluronic acid nanoparticles (HANP) labeled with a near infrared dye, NIR 830, were conjugated to the CD154:CD11b peptide inhibitor (iPep), generating the CD154:CD11b-blocking nanoparticle (iPep-HANP). Murine allogeneic skin graft recipients were treated with CTLA4-Ig+empty HANP, CTLA4-Ig+iPep, CTLA4-Ig+iPep-HANP, or vehicle alone on postoperative day 0/2/4/6, then q7days. Nanoparticle trafficking post-injection was assessed with serial IVIS imaging.

Results: In recipients treated with CTLA4-Ig+iPep-HANP, radiance efficiency within the graft increased by 188.3% at 48h post-injection, demonstrating nanoparticle localization within the allograft. Recipients treated with CTLA4-Ig+iPep-HANP exhibited superior graft survival compared to CTLA-4Ig+emptyHANP (MST 77d vs. 47d, n=4-5/group, *p=0.0009*). Mechanistically, animals treated with CTLA-4Ig+iPepHANP exhibited increased FoxP3$^+$ CD4$^+$ Treg within allografts compared to animals treated with CTLA-4Ig alone *(p=0.0406).* In addition, mice treated with CTLA-4Ig+iPepHANP exhibited increased expression of CD80 on CD8$^+$ T cells, as compared to either CTLA-4Ig-treated or untreated animals (*p=0.0055,p=0.0324, respectively*). In DLN, treatment with CTLA-4Ig+iPepHANP resulted in increased expression of CD25 on CD8$^+$ T cells relative to treatment with CTLA4-Ig alone *(p=0.0061)*

Conclusions: These results illuminate the role of CD11b/CD154 interactions in promoting alloimmunity and demonstrate that utilization of nanotechnology to block this pathway in combination with CD28 blockade improves allograft outcomes.



11:15AM

#C32 - Utilizing time-specific machine learning models to predict mortality in trauma-related ultra-massive transfusion

Courtney H. Meyer, Andrew ElHabr, John Lyons, Jason D. Sciarretta, Jonathan H. Nguyen, Randi N. Smith

Introduction: Despite the widespread use of ultra-massive transfusion (≥ 20 red blood cell products within 24h) in trauma resuscitation, mortality rates remain as high and the parameters in which this resource-demanding intervention is most beneficial are unknown. Therefore, this study sought to investigate the utility of using machine learning models to address this critical gap in the current literature.

Methods: A retrospective review was conducted at a Level I Trauma Center from 2018-2021. Patients with a traumatic mechanism of injury and meeting criteria for UMT were included. The primary outcome of interest was in-hospital mortality. Data was obtained from the institutional trauma registry and served as input to develop time-specific decision tree machine learning models for 4, 8, 12, 16, 24 and 48 hours after the initiation of transfusion. A 75% train/25% test split was used and predictive accuracy was evaluated.

Results: The six time-specific decision tree models generated were able to predict mortality for trauma-related UMT with an accuracy of 61-75%, the greatest being the 0-4 hour and 16-24 hour models. The strongest predictive factors for mortality immediately following the initiation of transfusion were GCS and heart rate. In the later time intervals (> 16 hours) serum lactic acid, pRBC:FFP ratios and total blood products transfused became more heavily predictive for mortality.

Conclusions: Time-specific decision tree models were able to predict mortality with an accuracy as high as 76% and have the potential to serve as real-time, evidence-based decision making tools for providers faced with the clinical and ethical challenges of UMT resuscitation.

Table 1: Accuracy of time-specific decision tree models predicting mortality in trauma-related ultra-massive transfusion

Time Window	Number of Patients		Observations		ROC AUC (95% CI)
	N	% Survive	N	% Survive	
0-4 Hours	160	49%	690	53%	0.75 (0.66-0.85)
4-8 Hours	74	60%	252	63%	0.69 (0.55-0.82)
8-12 Hours	117	65%	399	66%	0.69 (0.59-0.80)
12-16 Hours	102	73%	348	68%	0.70 (0.59-0.81)
16-24 Hours	116	72%	569	75%	0.76 (0.67-0.84)
24-48 Hours	115	75%	1,613	78%	0.61 (0.55-0.67)

11:30AM

#B18 - A Transcatheter Beating Heart Neoleaflet Device to Treat Mitral Valve Prolapse

Stephanie K. Tom, Julia Toma, Muralidhar Padala

Objective: Leakage of valves in the human heart is one of the most common cardiac lesions among adults >70 years of age. In this population, nearly 3% have mitral valve prolapse (MVP), in which leakage of blood through the mitral valve occurs and can cause heart failure or sudden death. Surgical repair of these valves is effective, yet not all patients are eligible for open heart surgery due to comorbidities. In our lab, we have developed a new transcatheter device that achieves beating heart correction of MVP, by implanting a neoleaflet that replaces the diseased section of the native valve. In this study, the efficacy of this new technology is reported in an ex vivo mitral valve disease simulator.

Methods: Mitral valve prolapse (MVP) was created on healthy pig valves by rupturing the marginal chordae, and the efficacy of repairing MVP in this model was studied in a pulsatile left heart model (**Figure 1a**) Our device consists of bovine pericardium reinforced with nitinol wire (**Figure 1b**), and was implanted onto the prolapsing section to replace it. Mitral regurgitation was measured before and after MVP induction, and upon repair with the device.

Results: In 10 replicative experiments, the regurgitation fraction (RF) increased from baseline vs. prolapse (0.1104 ± 0.21 vs. 4.8040 ± 3.58, p < 0.001) and decreased from prolapse vs. device (4.804 ± 3.58 vs. 1.400 ± 1.55, p=0.006) (**Figure 1c**)**.** Regurgitant volume (RV) increased from baseline vs. prolapse (0.0636 ± 0.11 vs 2.480 ± 1.54, p< 0.001) and decreased from prolapse vs. device (2.480 ± 1.55 vs. 0.7536 ± 0.83, p= 0.011).

Conclusion: In this work, we demonstrated complete encircling of the flail segment and decrease of RF following device implantation in 8 of 10 experiments.

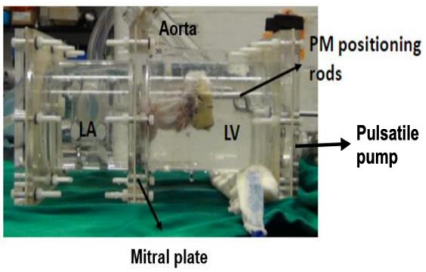


Figure 1a - ex-vivo pulsatile pump

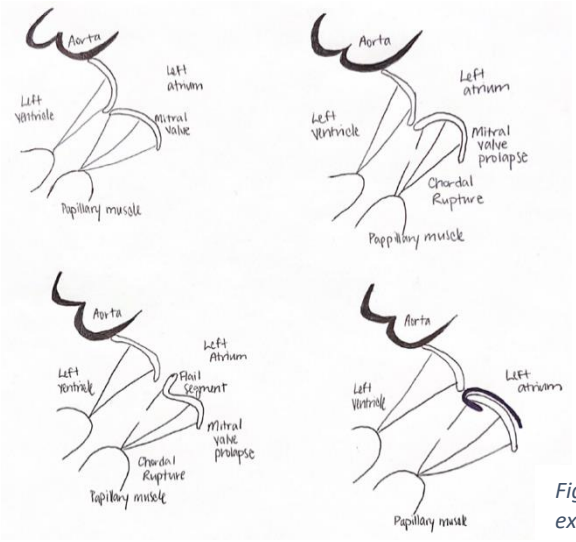


Figure 1b Schematic of normal valve, MVP due to chordal rupture, MVP with flail segment, and novel neoleaflet device encircling prolapsing segment.

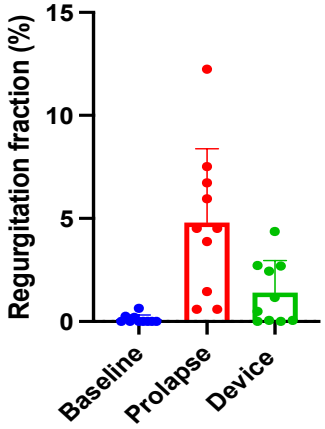


Figure 1c - Regurgitation Fraction experiments 1-10 at three different conditions for each experiment.

11:45AM

#C35 - Head and Neck Melanoma: An International Outcomes Analysis in the Post-MSLT-II Era

Baecher KM, Broman KK, Hughes T, Dossett LA, Carr M, Bartlett E, Sharma A, Thompson JF, Nijhuis A, Hieken TJ, Kottschade L, Gyorki DE, Downs J, vanAkkooi A, Stahlie E, Zuur C, Boere T, Ollila D, O'Shea K, Moncrieff M, Nobes J, Han D, Vetto J, Farma J, Karakousis G, Song Y, Deneve J, Fleming M, Delman KA, Perez M, Olofsson Bagge R, Mattsson J, Lee AY, Berman R, Chai H, Kroon H, Beasley G, Farrow N, Teras J, Teras RM, Hui J, Kruijff S, Been LB, Zager JS and Lowe MC

Objectives: Recent trials (MSLT-II and DeCOG-SLT) have transformed the management of sentinel lymph node (SLN)-positive melanoma patients. However, questions persist about the applicability of these trials to patients with head and neck (H&N) primaries (excluded from DeCOG-SLT). This study aims to assess outcomes of SLN-positive H&N melanoma patients undergoing nodal surveillance in the post-MSLT-II era.

Methods: SLN-positive H&N melanoma patients from 21 International High-Risk Melanoma Collaborative institutions undergoing nodal surveillance were included. Data were analyzed via univariate and multivariate Cox regression; multivariate analysis of a 1:1 propensity matched cohort compared outcomes between H&N and non-H&N patients.

Results: Of 1147 patients, 154 (13.4%) had H&N melanomas. H&N patients were more likely to be male (76.62% versus 58.01%, p=<0.001) and have multiple positive lymph nodes (38.7% versus 29.1%, p=0.038) than non-H&N patients. On univariate analysis, increased age, depth, T, N, and overall stage and number of positive SLNs, were associated with worse melanoma-specific survival (MSS). On multivariate analysis, increased age and primary tumor depth but not location predicted worse MSS. Propensity matched sample analysis with 208 patients demonstrated no difference in MSS (HR 1.82, CI 0.71-4.68), recurrence-free survival (HR 1.02, CI 0.66-1.59) or overall survival (HR 1.93, CI 0.87-4.30) between patients with H&N versus non-H&N melanomas.

Conclusions: This analysis showed similar outcomes for nodal surveillance of SLN-positive patients with H&N and non-H&N primary melanomas. These data suggest nodal surveillance without immediate completion lymphadenectomy is an a

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