

**Abstract Title:** A 10 Year Single Center Experience with Lung Transplantation: The Impact of Elevated Panel Reactive Antibody

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Division of Thoracic Surgery

## Abstract

**Introduction:** Panel reactive antibody (PRA) is an important measurement used to estimate immunosensitization in patients being evaluated for solid organ transplantation. The purpose of this study was to analyze the impact of an elevated PRA on longitudinal survival in lung transplantation at our center.

**Methods:** We reviewed the electronic medical records of all patients who received a lung transplant at our center from the past 10 years (2013-2023). Demographics and relevant peri-operative characteristics were recorded. Continuous variables are presented as median[IQR](range) while categorical variables are presented as N(%). Kaplan-Meier method was used to estimate longitudinal survival in both the low and elevated PRA cohorts.

**Results:** 531/572 transplant recipients had a PRA recorded at the time of transplant (92.8%). 121 of those 531 patients presented to transplantation with an elevated PRA. Median age at transplantation was 61.5[50.6,67.6](1.1,77.1) years and most of our patients were male (299, 56.3%).

Of note:

- Patients with elevated PRA were significantly less likely to be male (42.2% vs. 60.5%,  $p=0.0004$ )
- Patients with elevated PRA were significantly more likely to present with pulmonary hypertension (71.1% vs. 57.1%,  $p=0.06$ ) as well as RV dysfunction (35.5% vs. 24.8%,  $p=0.027$ )
- Patients with elevated PRA were more likely to require ECMO before transplant (16.5% vs. 9.5%,  $p=0.047$ )
- Patients with elevated PRA were less likely to have a negative crossmatch (74.5% vs. 88.7%,  $p<0.0001$ )
- Patients with elevated PRA were more likely to require ECMO post-transplant, (38.8% vs. 24.9%,  $p=0.0039$ ) develop an infection, (61.2% vs. 48.1%,  $p=0.013$ ) or require a tracheostomy (19.8% vs. 11.5%,  $p=0.023$ ). These patients also had significantly longer hospital stays (43[23,97](9,481 vs. 28[17,55.3](0,488),  $p<0.0001$ )

Survival comparison using the Kaplan-Meier method revealed statistically significant differences in survival between low PRA and high PRA patients, with a log rank  $p$ -value of 0.046.

**Conclusions:** Elevated PRA is a significant predictor of mortality for patients undergoing lung transplantation. Future studies should aim to further elucidate the mechanism in which elevated PRA contributes to long term survival in this set of patients, and clinicians should be aware of the increased risk present for immunosensitized patients presenting for lung transplantation.

## The Effect of PCSK9 Inhibitors on Metabolomics and Lipidomics of Abdominal Aortic Aneurysm Formation

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**Introduction** The underlying mechanisms of formation of abdominal aortic aneurysms (AAAs) are not completely understood. There is growing evidence that PCSK9 inhibitors such as evolocumab may have a role in attenuation of AAA growth. It is hypothesized that treatment with PCSK9 inhibitors in mice will significantly alter the metabolome and lipidome seen in AAAs. Our hypothesis is PCSK9 inhibition can result in attenuation of aortic inflammation and vascular remodeling to decrease AAA formation.

**Methods** AAAs were induced in male C57BL/6 mice using the established porcine pancreatic elastase (PPE) model. There were two groups; one was given weekly injections of evolocumab (10mg/kg/mouse/week) and the other was given vehicle (PBS). The aortas were harvested on day 14 and percent increase in diameter of each aorta was measured. Cytokine analysis was performed in aortic tissue using a multiplex ELISA kit. A two tailed unpaired t-test was performed to determine significance. To obtain lipidomic and metabolomic data, aortic tissue was harvested from elastase and deactivated elastase (control) mice on day 14 and analyzed by Matrix-assisted laser desorption/ionization – Mass spectrometry imaging (MALDI-MSI). Metaboanalyst 6.0 software was used for the statistical analysis. Heatmaps were generated using the top 25 significant changes in metabolome of aortic tissue after AAA and statistical significance was determined using students t-test with  $p < 0.05$  considered as statistically significant.

**Results** In the murine AAA model, we observed a significant attenuation of aortic diameter in Evolocumab-treated mice compared to untreated controls (106±24 vs. 146±27;  $n=9-10$ /group,  $p < 0.05$ ). A significant decrease in pro-inflammatory cytokine expression (IL-1b, IL-17, TNF-a, IL-6 and MCP-1) were observed in aortic tissue of evolocumab-treated mice compared to untreated controls. Additionally, lipidomic analysis displayed....(specifics needed)

data shows changes between PCSK9 inhibitor treated and untreated aortic tissue. Metabolomic data shows a lower concentration in several small molecules in aortas without evolocumab treatment.

**Conclusion** Treatment with PCSK9 inhibitors in mice mitigates aortic diameter and AAA formation. This is accompanied with alterations in immunometabolomics in the aortic tissue that likely contribute to attenuation of aortic inflammation and remodeling during AAA formation. Ongoing studies are delineating cell-specific metabolomic changes in the pathogenesis of AAA formation.

**Funding Sources.** [NIH RO1-138931](#)

**Abstract Title:** Incorporating Patient Values in Large Language Model Recommendations for Surrogate and Proxy Decisions.

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## **Abstract**

**Introduction:** Surrogates, proxies, and clinicians making treatment decisions for incapacitated patients often fail to honor their wishes, due to stress, time-pressures, misunderstanding patient values, and projecting personal biases. Advance directives (AD) intend to align care with patient values but are limited by low competition rates and application to only a subset of medical decisions. Here we investigate the potential of artificial intelligence (AI) models such as pre-trained large language models (LLMs) to incorporate patient values in supporting critical care clinical decision-making for incapacitated patients in a proof-of-concept study.

**Methods:** We simulated text-based scenarios for 50 incapacitated patients for whom a medical condition or injury required imminent clinical decisions regarding a specific treatment. For each patient we also simulated five unique value profiles captured using alternative formats: numeric ranking questionnaires, text-based questionnaires, and free-text narratives. We used pre-trained generative LLMs for two tasks: 1) text extraction of the treatment under consideration, and 2) prompt-based question-answering to generate a decision in response to the scenario information, extracted treatment, and patient value profiles. Model outputs were compared with adjudications by three human domain experts who independently evaluated each scenario and decision.

**Results:** The correct treatment was automatically extracted from 88% (N=44/50) of scenarios. AI model treatment recommendations received an average Likert score by the adjudicators of 3.92/5 across all patients for being coherent and sensible treatment recommendations, and 3.58/5 for reflecting the values of the patient recorded in each separate value profile. Recommendation strength was greatest when patient values were captured as short, unstructured, free-text narratives based on simulated patient profiles.

**Conclusions:** This proof-of-concept study demonstrates the potential for LLMs to function as support tools for surrogates, proxies, and clinicians aiming to honor the wishes and values of incapacitated patients facing imminent treatment decisions.

**Funding Sources.** T.J.L. was supported by the National Institute of General Medical Sciences of the National Institutes of Health under Award Numbers K23 GM140268 and R01 GM149657. T.J.L. was also supported by the Thomas Maren Junior Investigator Fund.

**Abstract Title:** Patients with dementia undergoing major limb amputation have poor outcomes

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**Background.** Major limb amputation fundamentally affects patients' function and independence. These impacts may be even more pronounced in patients with dementia. Despite the high impact of amputation on patients living with dementia, there is little information on its frequency and postoperative outcomes, which is important for decision-making. As such, we sought to characterize national patterns of major limb amputation for chronic limb-threatening ischemia (CLTI) and to compare outcomes in patients with and without dementia.

**Methods.** We analyzed Medicare fee-for-service claims from 01/01/2016 to 12/31/2020 in beneficiaries 66 years or older undergoing amputations at or proximal to the ankle for CLTI. We used generalized estimating equations and logistic or linear regression as appropriate. Dementia codes were based on chart validation and expert consensus.

**Results.** We compared 11,879 patients with dementia against 37,231 patients without dementia. Patients with dementia were older (79.7 vs. 73.8,  $y$ ,  $p < .0001$ ), more likely to be female (43.6% vs. 33.4%,  $p < .0001$ ), and more likely to be non-white Hispanic or Black (41.9% vs. 27.8%,  $p < .0001$ ). Patients with dementia underwent more above-knee amputations (AKAs) (59%) compared to those without dementia (59% vs 39.1%). Patients with dementia were more likely to have urgent/emergent cases compared to those without (68.2% vs 62.6%,  $p < .0001$ ) (**Table**). Multivariable analysis showed that mortality at 30 days (15.7%) and 1 year (54.3%) and time-at-home were worse in patients with dementia. The likelihoods of major complications (22.8%) and amputation revision (17.5%) were better in those with dementia and 30-day readmission (28.6%) was similar between the groups.

**Conclusion.** Major limb amputation for CLTI is common among patients living with dementia. Patients with dementia are more likely to undergo urgent procedures and AKAs. Outcomes are sobering (for example, >50% mortality at one year). Outcomes compared to those without dementia are nuanced and include a higher 30-day and 1-year mortality but better rates of complication and amputation revision and a similar 30-day readmission. These are important data that can support goal-concordant decision-making. Additional work is needed to measure impact of amputation on mobility, pain, and other patient-centered outcomes.

**Table.** Patient and Procedural Characteristics by Dementia Status

<b>Feature, No. (%)</b>	<b>Overall (N=49,110)</b>	<b>No Dementia (N=37,231, 76%)</b>	<b>Dementia (N=11,879, 24%)</b>	<b>P- value</b>
<b>Age, years (median)</b>	75.0	73.8	79.7	<.0001
<b>Female sex</b>	35.9%	33.4%	43.6%	<.0001
<b>Race</b>				<.0001
Non-Hispanic White	64.6%	67.8%	54.6%	
Non-Hispanic Black	21.9%	19.1%	30.6%	
Hispanic	9.3%	8.7%	11.3%	
<b>Amputation Characteristics</b>				
Above-knee	44%	39.1%	59%	<.0001
Urgent/Emergent Admission	63.9%	62.6%	68.2%	<.0001

## Postinjury Pneumonia Induces Persistent Sex-specific Alterations in the Gut Microbiome

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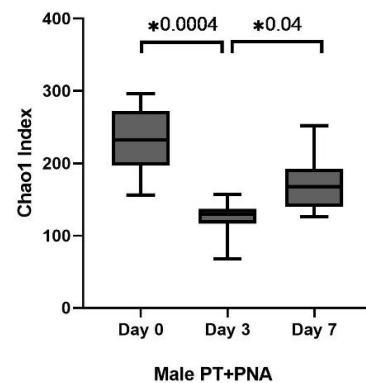
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**Introduction** Previous preclinical studies have demonstrated an altered gut microbiome after traumatic injury; however, the long-term impact of postinjury sepsis on dysbiosis remains unknown. We hypothesized that a rodent model of polytrauma with postinjury pneumonia would result in the development of a pathobiome which would differ between sexes.

**Methods** Male and proestrus female Sprague-Dawley rats (n=16/group) aged 9-11 weeks were subjected to either polytrauma (PT+PNA) (lung contusion, hemorrhagic shock, cecectomy, bifemoral pseudofractures) or PT plus 2-hours daily chronic restraint stress (PT/CS+PNA) with postinjury day 1 inoculation with *Pseudomonas pneumoniae*. Infected cohorts were treated with twice daily imipenem. Fecal microbiome was measured on days 0, 3 and 7 using high-throughput 16S rRNA sequencing and QIIME2 bioinformatics analyses. Microbial alpha diversity was assessed using Chao1 (number of different unique species) and Shannon (species richness and evenness) indices. Beta-diversity was assessed using principle coordinate analysis. Pairwise comparisons were performed in 'R' software package, with significance defined as  $p < 0.05$  between males versus females.

**Results** PT+PNA reduced alpha diversity (Chao1) within 3-days post intervention in males and females ( $p < 0.003$ ), but by day seven only males began to recover ( $p < 0.05$ ) (Fig.). PT/CS+PNA males and females did not recover alpha diversity (Chao1) one-week postinjury compared to baseline ( $p < 0.03$ ) (Fig.). Beta diversity was significantly different among males and females at day 3 and 7 compared to day 0 in both PT+PNA and PT/CS+PNA ( $p < 0.002$ ). By day 7, microbial composition in PT/CS+PNA males was dominated by *Prevotella*, which can be pathogenic, and PT/CS+PNA females by *Parabacteroides*.



**Conclusions** Multicompartmental trauma with postinjury pneumonia induces significant alterations in microbiome diversity and taxa; however, recovery from these acute alterations differs by sex. While both males and females lack resilience, they demonstrate unique pathology in gut microbiome after severe trauma with postinjury sepsis. This sexual dimorphism in the gut microbiome highlights the need for precision medicine in the treatment of trauma patients and further investigation into underlying pathophysiology of these alterations.

**Funding Sources:** NIH R01 GM105893, NIH T32 GM008721.

## Sex-Specific Differences in Human Myeloid-Derived Suppressor Cell Mitochondrial Metabolism after Sepsis

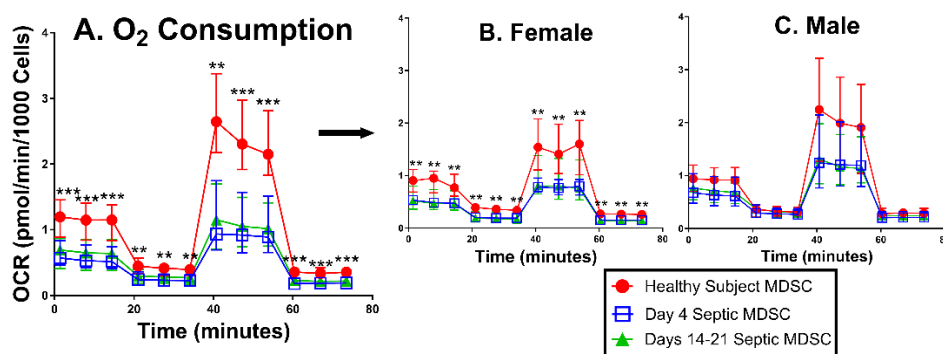
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**Introduction** Sepsis is associated with a dramatic expansion of blood myeloid-derived suppressor cells (MDSCs). In sepsis, the phenotypes and metabolic demands of MDSC as well as the potential impact of sex are unknown. Our objective was to examine MDSC metabolism after sepsis. **Methods** Blood samples were collected from 16 healthy subjects (8 female, 8 male), 40 acutely septic patients (16 female, 24 male) four days after sepsis onset, and 19 patients 14-21 days after sepsis (7 female, 12 male). Peripheral blood mononuclear cells (PBMCs) were isolated, followed by MDSC isolation with CD66b<sup>+</sup> selection. Mitochondrial O<sub>2</sub> consumption (OCR) and glycolysis (ECAR) were analyzed with Agilent XFe™ and compared by Mann-Whitney U and Kruskal Wallis tests. **Results** In all patients, CD66b<sup>+</sup> cell OCR decreased on day 4 compared to healthy subjects ( $p < 0.002$ ) with a sustained decrease at days 14-21 ( $p < 0.008$ ) (Fig A). This was observed in septic female patients compared to healthy females (Fig B), while the reduction in OCR in septic male patients was modest compared to healthy males (Fig C). In contrast, MDSC glycolytic rates were comparable between all septic patients and healthy individuals. However, CD66b<sup>+</sup> MDSCs from septic female patients showed depressed rates of ECAR at day 4 after inhibition of oxidative phosphorylation with oligomycin ( $p < 0.025$ ), indicating a decrease in total glycolytic activity. No differences were observed among males for ECAR. By 14-21 days after sepsis, ECAR returned to baseline for both sexes. **Conclusions.** Patients diagnosed with sepsis exhibit decreased OCR without a compensatory increase in glycolysis. In female patient MDSCs, energy metabolism is impacted both through decreased oxidative and glycolytic metabolism. This study highlights the importance of sex stratification in sepsis research and could result in immunomodulatory development which is sex-specific.

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## Abstract Title: 15-year Single Institutional Analysis of Surgical Approaches and Outcomes for Aortic Coarctation in 132 Neonates and Infants

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### Abstract.

**Introduction:** Our strategy to treat aortic coarctation is designed to match the surgical approach to the individual anatomy of the patient. The objective of this study was to evaluate operative characteristics and outcomes of neonates and infants undergoing repair of coarctation or hypoplastic aortic arch.

**Methods:** We retrospectively reviewed all 132 patients aged 0-1 year at our institution (2006-2021) who underwent surgical repair of coarctation or hypoplastic aortic arch either in isolation or with concomitant repair of ASD and/or VSD.

- Group 1 = Median Sternotomy with cardiopulmonary bypass and continuous antegrade cerebral perfusion (n=110)
- Group 2 = Left Lateral Thoracotomy (n=22).

Left thoracotomy was utilized in patients with focal coarctation without significant hypoplasia of the aortic arch and without hemodynamically significant intracardiac pathology.

Continuous variables are presented as median (range); categorical variables are presented as N (%).

**Results:** The most common operative technique in Group 1 was end-to-side reconstruction with ligation of the aortic isthmus. The most common operative technique in Group 2 was extended end-to-end repair. All patients undergoing concomitant ASD or VSD repair underwent sternotomy. Operative Mortality was one patient (1/132 = 0.76%) in 2007 with coarctation, hypoplastic aortic arch, VSD, and ASD who died after a respiratory arrest on the night of surgery. Vocal cord paralysis occurred in twelve patients (12/132 = 9.09%) and vocal cord paresis occurred in fourteen patients (14/132 = 10.60%). Patients diagnosed with an isolated coarctation of the aorta with arch hypoplasia were most likely to end up with either vocal cord paresis or paralysis (11/132 = 8.33%). Patients with diagnoses of coarctation of the aorta or coarctation of the aorta with VSD and arch hypoplasia had who developed vocal cord paresis were noticeably older in average age compared to other diagnoses.

Table 1 documents patient characteristics and outcomes.

**Conclusions:** A strategy of matching the surgical approach to the anatomy can result in surgical repair with less than one percent Operative Mortality and less than three percent recurrent coarctation requiring reoperation.

	Group 1 = Sternotomy	Group 2 = Thoracotomy
All patients, n	110	22
Age in days: Median (minimum – maximum)	19 (5-306)	57 (4-365)
End-to-side reconstruction with ligation of aortic isthmus	100 (91%)	4 (18%)
Extended end to end repair	6 (5.4%)	18 (82%)
End to side with patch augmentation	4 (3.6%)	0
Mortality	1 (0.9%)	0
Required percutaneous reintervention 1x	3 (2.7%)	2 (9%)
Required percutaneous re-intervention 2x	2 (1.8%)	0
Required surgical re-intervention	3 (2.7%)	0

## **Analysis of 572 Lung Transplants at University of Florida from 2013 to 2023**

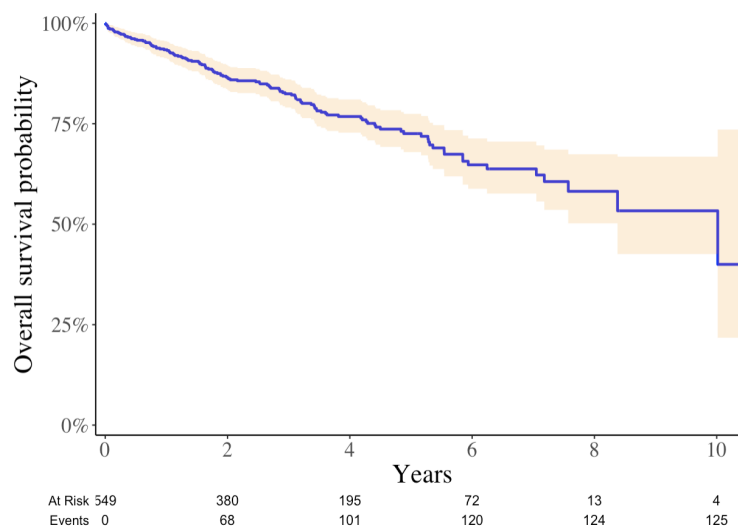
Yuriy Stukov, MD\*, Mindaugas Rackauskas, MD, PhD, Jin Choi, BS, Ahmet Bilgili, BS, Anson Wang, BS, Liam Kugler, BS, Kayla Lucas, BS, Matthew Purlee, BS, Hazel Hutchinson BS, Omar M. Sharaf, BS, Jeffrey P. Jacobs, MD

**Objective:** We reviewed 572 lung transplants performed at the University of Florida from 01/02/2013-4/20/2023 to describe diagnostic characteristics and assess longitudinal survival.

**Methods:** Retrospective review of 572 lung transplants in 553 patients (19 patients underwent retransplantation at our institution). Continuous variables are presented as mean  $\pm$  standard deviation and categorical variables are presented as N (%).

**Results:** At transplant, patients had the following primary diagnoses: Interstitial lung disease: n=284 (49.7%), COPD: n=111 (19.4%), COVID-19 fibrosis: n=38 (6.6%), Cystic fibrosis (CF): n=38 (6.6%), Sarcoidosis: n=24 (4.2%), Pulmonary hypertension: n=18 (3.1%), Non-CF bronchiectasis: n=10 (1.7%), Others: n=49 (8.6%). Mean age for the overall cohort was  $57.1 \pm 14.6$  years, mean weight was  $73.9 \pm 16.9$  kg, and mean body surface area was  $1.8 \pm 0.3$  m<sup>2</sup>. At last follow-up, 136 (23.8%) lung transplant recipients had chronic lung allograft dysfunction. Estimated 1-year, 5-year, and 10-year survival estimates (95% confidence interval) for the entire cohort were 93% (91%-96%), 73% (68%-77%), and 53% (43%-67%) (Figure 1).

**Conclusions:** Although chronic lung allograft dysfunction remains an important complication following lung transplantation, lung transplantation can provide many patients with end-stage lung disease with definitive treatment. Excellent short-term and acceptable mid- and long-term survival can be expected in this cohort of patients with varied diagnoses. Advances in the treatment of chronic lung allograft dysfunction will lead to improvements in long-term survival.



**Figure. Kaplan Meier survival curve with 95% confidence interval for all 572 patients.**

## Exploring Myocardial Recovery in Pediatric Heart Failure Patients Supported with Berlin Heart Ventricular Assist Devices: Who Keeps Their Heart?

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**Introduction:** The Berlin Heart ventricular assist device (VAD) is an effective therapy to support pediatric patients diagnosed with severe heart failure, both acquired and congenital. Although usually utilized as a bridge to cardiac transplantation, in some instances VADs can facilitate myocardial recovery of the native heart. The purpose of this analysis is to compare a series of 6 patients supported with Berlin Heart VADs that were eventually weaned from cardiac support and decannulated to 38 patients with biventricular hearts and acquired heart disease supported as bridge to transplantation.

**Methods:** All patients that underwent Berlin Heart VAD insertion at our center (n=93) had their electronic medical records reviewed. Demographic and VAD characteristics were collected, as well as follow up data and longitudinal outcomes. To create a better control group to compare against the explanted patients (n=6), patients with functionally univentricular physiology or a diagnosis of congenital heart disease were excluded from the comparison group (n=51), leaving only patients with acquired heart disease and biventricular hearts (n=38). Categorical variables are reported as N (%), while continuous variables are reported as median (IQR) [range]. *P*-values were calculated using Fisher's exact t-test.

**Results:** In the overall cohort, median age in days at VAD implantation was 754.5 (89.8-3287.3) [27-6465], and median weight in kilograms at VAD implantation was 11 (5.2-22.3) [2.6-112]. Table 1 lists additional variables for the entire cohort as well as stratified by explant status.

- Patients who had their Berlin heart VAD explanted were significantly younger at the time of implantation (149 (101-224.75) [31-449] vs. 1697.5 (89.3-3346.5) [27-6465], *p*=0.031)

Overall survival at time of last follow up for all patients supported with Berlin Heart was 84.1% with a median follow up time of 5.32 (2.01-9.00) [0.07-17.04] years, although 100% of explanted patients were alive at last follow up.

**Conclusions:** Patients that undergo Berlin Heart VAD implantation can experience myocardial recovery in certain cases. These patients appear to be younger than their counterparts that do not experience recovery and proceed to transplantation. As this population grows and centers build experience with these cases, future studies will likely uncover more characteristics in these patients that allow for myocardial recovery and retention of their native hearts.

	Sample n=44 (All Acquired+Biventricular Berlin Heart Recipients)		Study group n=6 (With ventricular recovery)		Control Group n=38 (Without ventricular recovery)		p- val ue
	Median (IQR)[range]	N (%)	Median (IQR)[range]	N (%)	Median (IQR)[range]	N (%)	
Age at VAD implantation (days)	754.5 (89.8-3287.3) [27-6465]		149 (101-224.8) [31-449]		1697.5 (89.3-3346.5) [27-6465]		<b>0.0 31</b>
Weight at VAD implantation (kg)	11 (5.2-22.3) [2.6-112]		6.1 (5.5-6.3) [2.6-7.1]		14.4 (5.0-24.5) [3.1-112]		0.1 1
Length of VAD support (days)	99 (46-140) [4-315]		135 (103.5-163.5) [76-215]		77.5 (43.8-134.5) [4-315]		0.1 6
Prior ECMO		18 (40.9%)		3 (50%)		15 (39.5% )	0.6 8
Duration of ECMO (days)	9 (8-12.5) [3-23]		21 (15-22) [9-23]		9 (7.5-10.5) [3-20]		<b>0.0 13</b>
LVAD		6 (13.6%)		2 (33.3 %)		4 (10.5% )	
BiVAD		38 (86.4%)		4 (66.7 %)		34 (89.5% )	
Age at VAD removal (days)			277 (211.5-411.5) [183-557]				
Alive at last follow-up		37 (84.1%)		6 (100% )		31 (81.6% )	0.5 7
Length of Follow-up from VAD implantation (years)	5.32 (2.01-9.00) [0.07-17.04]		3.49 (2.23-5.13) [0.61-6.13]		5.69 (2.33-9.71) [0.07-17.04]		0.1 5

## Gastric Perforation Presenting Clinically as Esophageal Perforation

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### Introduction:

We present a case of a patient with a history of Nissen fundoplication (NF) who presented with a gastric perforation (GP) that was originally thought to be of esophageal origin until surgery.

### Methods:

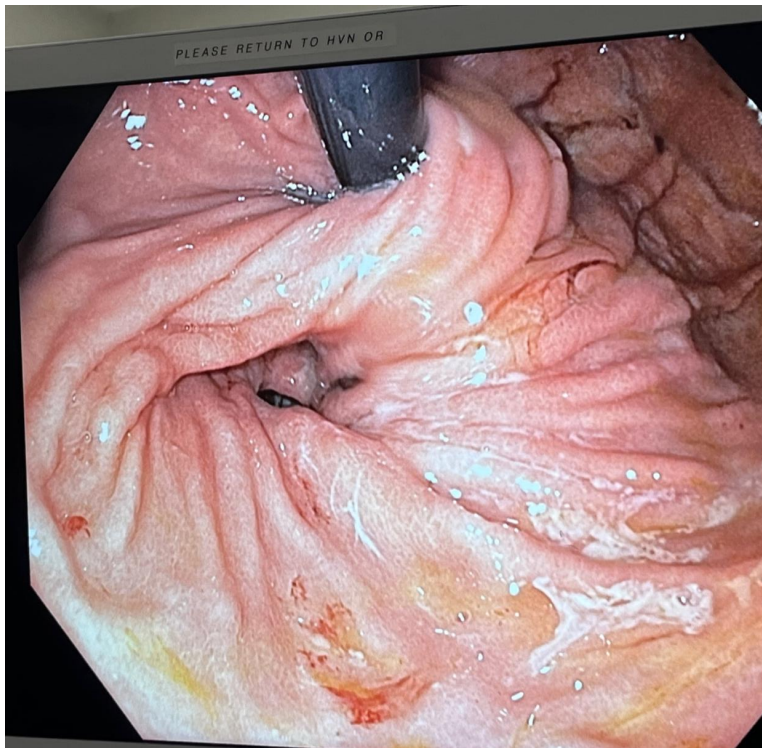
A 50-year-old woman with a past medical history of diabetes mellitus, hypertension, smoking, and chronic GERD s/p NF. She presented to an outside facility with new onset chest pain, fevers, and dyspnea after an episode of retching. CT scan revealed gas in the right pleural space, and findings concerning for perforation of the distal esophagus. She was transferred to our center for definitive surgical management.

### Results:

On arrival to our institution a barium swallow showed extravasation into the right chest. The decision was then made to take the patient to the operating room for suspected esophageal perforation. EGD performed in the OR showed no esophageal perforation, but did reveal a 5 cm GP at the apex of the NF that tracked into the right chest (Figure 1). Via a midline laparotomy extensive lysis of adhesions was performed before the defect could be visualized. A stapler was used to exclude the perforation, then an omental patch was placed over the defect. A J-tube was also placed for feeding access. A full decortication of the right chest was performed with extensive removal of purulent material. The patient had an unremarkable post operative course and was discharged home on POD 17 on full liquid diet and tube feeds.

### Conclusions:

Rarely a gastric perforation can present as clinically identical to an esophageal perforation. The thoracic surgeon must be prepared to perform a major abdominal surgery.



*Figure 1: Intra-operative EGD showing gastric perforation*

## Abstract Title Obesity and Associated Outcomes for Blunt vs. Penetrating Mechanism in Trauma Laparotomy Patients

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Division of Trauma and Acute Care Surgery

### Introduction

Obesity in trauma patients is an established risk factor contributing to post-operative complications, but the relationship between BMI (body mass index) and trauma patient outcomes is not well-defined, especially when stratified by mechanism of injury.

### Methods

We surveyed the trauma laparotomy registry at an academic Level 1 Trauma Center over a three-year period to identify mortality, injury severity score, and hospital length of stay (hLOS) outcome measures across BMI classes, with further stratification by mechanism of injury: blunt vs. penetrating trauma.

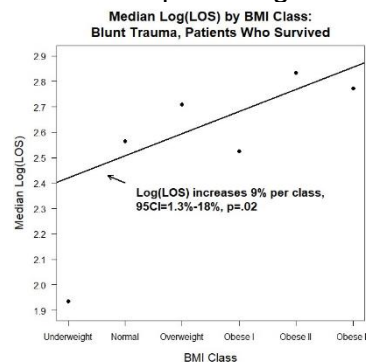
### Results

A total of 442 patients were included with mean age 44.6 (SD=18.7) and mean BMI 28.55 (SD=7.37). These were subdivided into blunt trauma (n=313) and penetrating trauma (n=129). Within the blunt trauma subgroup, the hLOS among patients who survived hospitalization significantly increased 9% for each successive BMI class (p=.022, 95CI= 1.29-17.5).

### Conclusions.

We conclude that successive increase in BMI class is associated with longer hospital stay for blunt trauma patient survivors requiring laparotomy, though additional analysis is needed to establish this relationship to other outcome measures and among penetrating trauma patients.

Fig: Illustration of Relationship of BMI on Hospital Length of Stay in Blunt Trauma Survivors



**BMI, body-mass index; LOS, length of stay**

**Funding Sources.** Division of Trauma and Acute Care Surgery; Division of Minimally Invasive Surgery

**Title: Post Traumatic Vasospasm Surveillance Guided by Timeline, Clinical Predictors and Association with Subarachnoid Hemorrhage in the Fissures and Cisterns**

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**Abstract:**

*Introduction:* Unlike aneurysmal subarachnoid hemorrhage, vasospasm following traumatic brain injury (TBI) is poorly understood and no guidelines-based recommendations for surveillance exist.

*Objectives:* To retrospectively evaluate timing and severity of doppler-diagnosed vasospasm in TBI at a single-center to guide a protocol for surveilling post traumatic vasospasm

*Methods:* TBI patients admitted to the Boston Medical Center surgical ICU from 11/2014 to 12/2020 with two or more instances of transcranial doppler (TCD)-diagnosed vasospasm were included. Clinical timelines, TBI severity by Glasgow Coma Score (GCS) (mild = 13-15, moderate = 9-12, severe = 3-8), presence and location of subarachnoid hemorrhage (tSAH), and vasospasm severity (mild, moderate, or severe) were extracted from records. One-way ANOVA analysis compared the highest severity of vasospasm noted with date of onset and total days of vasospasm. Significant differences in means were further analyzed with Games-Howell post-hoc test. Stata® determined the dependence of vasospasm severity upon imaging findings or the GCS via Chi2 analysis.

*Results:* Forty-four patients were identified (31 male, 13 female, median age 40 (15-92) years). Amongst mild TBIs (13), vasospasm was mild (9), moderate (1), and severe (3). For moderate TBIs (2), vasospasm was mild (1), moderate (0), and severe (1). For severe TBIs (29), vasospasm was mild (16), moderate (6), and severe (7). Thirty-two patients had tSAH; 19 with mild, 6 with moderate, and 7 with severe vasospasm. Of the 12 patients without tSAH, 7 had mild, 1 had moderate, and 4 had severe vasospasm. Of the 32 patients with tSAH, 30 had tSAH in either the sylvian fissure and/or the cisterns; the remaining 2 having only cortical tSAH. Median time to onset did not differ between mild (Hospital Day (HD) 3), moderate (HD 4), and severe (HD 3) vasospasm ( $p=0.47$ ). Mean duration of mild vasospasm (2.35 days) differed from severe vasospasm (6.73 days), ( $p<0.05$ ). Neither presence of tSAH nor severity of TBI was related to severity of vasospasm ( $p= 0.11$  and  $p=0.61$ ).

*Conclusions:* Our study found that where post-traumatic vasospasm can impact TBI patients regardless of TBI severity or the presence of tSAH, there is a strong association between PTV and tSAH in the fissures and cisterns. We thus recommend early and routine surveillance for PTV in all critically ill TBI patients, especially those with hemorrhage in the fissures and cisterns.

## Role of Complement C3a/C5a as a Novel Regulator of Vitamin D Metabolism in Abdominal Aortic Aneurysm Formation

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**Introduction:** Abdominal aortic aneurysms (AAA) are characterized by vascular inflammation and remodeling that can lead to aortic rupture resulting in significant risk of mortality. We sought to investigate the relationship between complement factor C3a and Vitamin D3 in the pathogenesis of AAA formation. **Methods:** A topical elastase (0.4 U/mL type 1 porcine pancreatic elastase) model to induce AAA was performed in C57BL/6 (wild-type, WT) male mice. Blood samples along with the aortic tissue were harvested on days 3, 7, and 14. WT mice were also treated with C3a receptor antagonist (C3aRA) (1mg/kg/day) or saline controls from days 1-13 after surgery and harvested on day 14. WT mice were also treated with C3aRA on days 7-13 to observe the effect of delayed treatment on “preformed” small AAAs. Additionally, separate groups of WT mice were placed on Vitamin D3 (VD3) deficient or VD3 sufficient diets. Mice started this diet 4 weeks before surgery and remained on the diet until harvesting. mRNA expression in aortic tissue were evaluated by RT-PCR on days 3, 7 and 14 in all groups. In a second aortic rupture model, mice were injected with C3aRA from day 14 onwards and analyzed on day 28. Cytokine expression in aortic tissue was quantified by multiplex assay. Groups were compared using t-test or ANOVA and data is displayed as mean $\pm$  SEM with  $p < 0.05$  as statistically significant. **Results:** Aortic diameter was significantly increased in elastase-treated WT mice compared to controls on day 14 ( $181.2 \pm 17.5\%$  vs  $19.5 \pm 6.1\%$ ;  $n=6-10$ /group,  $p < 0.001$ ). mRNA analysis revealed increased C3a and C3aR levels at day 7 in elastase-treated WT mice compared to controls (1.48-fold;  $p < 0.01$ ). Treatment with C3aRA antibody significantly decreased AAA formation compared to mice treated with saline ( $105.2 \pm 9.1\%$  vs.  $166.0 \pm 15.2\%$ ;  $n=7-9$ /group,  $p < 0.01$ ). Moreover, a significant decrease in proinflammatory cytokine expression (IL-6, CXCL1, MCP-1, MIP-2, RANTES) was also observed in elastase-treated mice administered with C3aRA antagonist compared to untreated mice. In a separate group of mice undergoing treatment of C3aRA antagonist from days 7 through 13 in a preformed AAA, we also observed a decrease in aortic diameter compared to vehicle-treated controls ( $99.2 \pm 10.2\%$  vs.  $152.3.0 \pm 15.2\%$ ;  $n=9$ /group,  $p=0.03$ ). VD3 deficient mice had a significantly larger AAA compared to match control diet mice ( $169.8\% \pm 37.3\%$  vs.  $138\% \pm 27.7\%$  ( $n= 11-19$ ;  $p=0.02$ ). Histology showed interruption of both the smooth muscle (SMA) and elastin (VVG) in the VD3 deficient mice when compared to the VD3 sufficient mice. Mice with VD3 deficient diet displayed a significant increase in the mRNA expression of C3a compared to mice with VD3 sufficient diet ( $P = 0.0355$ ). Mice in our BAPN model saw trends towards a decreased AAA size when treated with C3aRA from days 14-28 when compared to control mice ( $359.0\% \pm 25.8$  vs.  $462.7\% \pm 69.5\%$ ;  $n=8-9$ /group;  $p=0.4$ ). **Conclusion:** These results suggest that complement C3a signaling pathway is associated with exacerbation of AAA formation in Vitamin D3 deficiency.

NIH RO1HL153341 and R01HL138931 (GRU and AKS)

## **The Utility of Primary Excision and Direct Closure Approach to Burn Wounds: A Literature Review and Case Report**

**Nhan Trieu, BS\*, Jonathan Butts, MD, Peter Vonu, MD, Pavel Mazirka, MD, Shawn Larson, MD, Kalyan Dadireddy, MD**

Division of Plastic and Reconstructive Surgery

**Introduction** In the last 50 years, the mainstay of burn treatment is early tangential excision and skin grafting. Primary excision with direct closure is another reconstructive approach to deep burn. However, among the burn surgeons, this method is met with great reluctance, primarily due to the concerns of scar hypertrophy and wound dehiscence even though there has been limited evidence to support these apprehensions. This study aims to review the existing literature on the utility of primary excision and direct closure and to present our case report of a 12-year-old patient with bilateral breast burns treated with reduction mammoplasty.

**Methods** The types of literatures being examined include survey and prospective series, case series, correspondence, randomized controlled trial, and other literature reviews. The study also includes a case report of a 12-year-old female who sustains self-inflicted burns totaling to 35% TBSA and undergoes bilateral mammoplasty, consistent with the primary excision and direct closure technique.

**Results** Among all literatures reviewed, one common requirement for direct closure of burn wounds is the availability of sufficient tissue laxity to allow tension-free closure. Compared to skin-grafting, direct closure uses healthy skin as barrier for the wound and effectively eliminates exposure of burn tissue to the element, thereby reducing the risks of hypermetabolism and decreasing the rate of infection as it removes the portal entry to bacteria. This strategy also demonstrates quicker healing time, shorter hospital stays, and lower health care costs. Direct skin closure removes the need for donor site which further contributes to the shortened healing time, reduction of overall burn and graft donor wound size, ultimately resulting in better aesthetic outcomes.

In the case of our 12-year-old patient, she is initially treated with tangential excision with allograft and autograft. However, the healing of her breast wounds is complicated by large volume breasts that contributes to difficulty dressing management, poor allograft adhesion and pseudomonal growth around the chest. The plastic surgery team is consulted and performs excision of burnt breast tissue and reduction mammoplasty using the superomedial-central pedicles. The direct closure of breast burns not relieved wound and dressing burden but also reduced patient's pre-injury body dysmorphia and depression related to large breast size. No additional breast surgery is needed during the patient's remaining hospital stay.

**Conclusions** While having similar rates of postoperative complications as the mainstay for burn treatment, direct closure provides additional aesthetics and body contouring effects for selected patient populations. It also shortens healing time, reduces risks of hypermetabolism, infection, and overall health care costs. This technique should be further investigated as treatment for selective burn population.

**Abstract Title** Direct Thrombin Inhibition as an Anticoagulation Strategy for Impella 5.5: Safety and Hemocompatibility

**Authors** Fabian Jimenez Contreras, MD, MMCi; Griffin Stinson\*, BS; Carlos Valdes, BS; Omar Sharaf, BS; Alex Parker, MD; Mohammad Al-Ani, MD; Juan Vilaro, MD; Mustafa Ahmed, MD; Eric Jeng, MD

Division of Thoracic and Cardiovascular Surgery

**Abstract**

*Introduction* The Impella 5.5® (Abiomed, Danvers) has become one of the most clinically utilized temporary left ventricular assist devices since its FDA approval in late 2019. As with any mechanical circulatory support device, it is critical to assess the hemocompatibility in pursuit of limiting thrombotic and hemorrhagic events. The safety of anticoagulation (AC) with direct thrombin inhibitors (DTI) during Impella support has not been well described.

*Methods* We retrospectively reviewed adult patients (≥18 years old) supported with Impella 5.5® at our institution (May 2020-April 2023) used as bridge to durable support, and/or transplantation. Baseline demographics were collected on all patients. Number of blood products given during Impella support was recorded. Haptoglobin, plasma free hemoglobin, lactate dehydrogenase, and unconjugated bilirubin were collected at several time points. Rates of in-hospital mortality, 30-day mortality, Impella-associated access site complications, and arterial thromboembolic events were recorded.

*Results* A total of 31 patients were supported with Impella 5.5® during the study period. There was no difference in baseline demographics. The duration of support was 28.06±32.56 days. The AC agent was heparin in 27 and DTI in 4 patients. Vascular access was axillary artery in 77% and direct aortic placement in 23%. There was no difference in baseline characteristics between groups. In 19% of patients, there was concomitant veno-arterial ECMO support. In-hospital mortality was 33% for heparin and 25% for DTI patients (p=0.739). The mean number of blood products given during support was 7.71±11.76 units; however, 42% of the entire cohort and 75% of the DTI cohort required no transfusions. The heparin group required a greater mean number of transfusions 8.7 vs 1 units (p=0.133). Aggregate total blood products per day of Impella support was low at 0.28 units/day. DTI patients had lower rates of total product transfusions per day 0.03 vs 0.32, p-value=0.0329, lower pRBC 0.03 vs 0.22, p-value=0.0332, lower platelets 0.00 vs 0.07, p-value=0.0466. Hemolysis markers were not significantly different pre and post-implant or by AC strategy. Overall thromboembolic event rate was low at 3% and not different among AC strategy.

*Conclusions* Support with Impella 5.5® showed high rates of hemocompatibility with many patients requiring no transfusions during their support. In this limited cohort, we found anticoagulation with DTI to be associated with fewer transfusions than heparin and no statistically significant increase in hemolysis markers.

**Funding Sources** None

## **Abstract Title Imaging Surveillance Adherence for Acute Uncomplicated Type B Aortic Dissection at a Regional Referral Center**

**Authors** Griffin P Stinson\*, BS; Jonathan R Krebs, MD; Liam Kugler, BS; Brian Fazzone, MD; Zain Shahid, MD; Martin Back, MD; Salvatore Scali, MD; Samir Shah, MD; Gilbert R Upchurch, Jr., MD; Michol A Cooper, MD, PhD

Division of Vascular Surgery and Endovascular Therapy

### **Abstract**

*Introduction* Though anti-impulse therapy and imaging surveillance (IS) is the standard of care for uncomplicated type B aortic dissections (auTBAD), nonadherence to IS may increase the likelihood of aortic sequela and affect long-term mortality. We sought to analyze adherence to imaging surveillance and identify risk factors for nonadherence in our practice.

*Methods* In this single-center, retrospective cohort study, demographics, follow-up, and outcomes of auTBAD patients 8/2011-11/2021 were analyzed. IS was aorta-directed imaging with associated in-person/telephone encounter  $\geq 3$  months from index hospitalization. Univariate analysis compared patients with and without IS. Multivariate logistic regression identified factors related to increased odds of adherence to IS.

*Results* A total of 152 medically managed auTBAD patients were identified. Seventy (43%) patients underwent IS for a median of 16 (IQR 25) months. There were no differences in age, sex, race, insurance status, or smoking status between groups. Median patient home address was 96.1 miles from our center, with no difference between the surveillance (85.7 IQR 86.4) versus no surveillance (104.9 IQR 91.5) groups ( $p=.29$ ). Prior aortic surgery (20% vs 6%,  $p=.01$ ) and diabetes (15% vs 6%,  $p=.05$ ) were more common in those without IS. Most patients (95%) presented as hospital transfers, with no difference between groups ( $p=.06$ ). Patients with IS were more likely to be discharged home (93% vs 71%,  $p<.01$ ). Post-discharge thoracic endovascular aortic repair (TEVAR) occurred in 23% of patients and was more common in the IS group (26% vs 4%,  $p<.01$ ). In TEVAR patients, there was no difference between the rate of urgent/emergent intervention ( $p=0.30$ ), and no difference in the median time to TEVAR ( $p=0.61$ ). Discharge home (5.78, 95% CI [1.86-17.95],  $p=.002$ ) was associated with greater odds of IS adherence. Previous cardiovascular surgery (.21, 95% CI [.06-.73],  $p=.015$ ), history of drug use (.31 95%CI [.10-.97],  $p=.045$ ), and increased age (.96 [per unit increase], 95% CI [.93-.99],  $p=.022$ ) were associated with worse odds of IS. There was no difference in 5-year survival (log-rank  $p=0.26$ )

*Conclusions* Adherence to auTBAD IS was low and did not vary by patient demographics or distance from hospital. Patients with imaging surveillance were more likely to undergo TEVAR, although there were no differences in 5-year all cause survival between groups. Home discharge was associated with the greatest odds of imaging surveillance adherence. This study highlights the difficulty in regional referral center care coordination for treatment of medically-managed auTBAD and identifies several factors that may help identify at-risk patients.

**Funding Sources** None

## Abstract Title: Pharmacologic Inhibition of Ferroptosis Attenuates Experimental Abdominal Aortic Aneurysm Formation

**Authors:** Jonathan R. Krebs\*<sup>1</sup>, Paolo Bellotti<sup>1</sup>, Michael Spinosa<sup>1</sup>, Jeff A. Valisno<sup>1</sup>, Gang Su<sup>1</sup>, Joseph B. Hartman<sup>1</sup>, Chelsea Viscardi<sup>1</sup>, Yogesh Scindia<sup>2</sup>, Guoshuai Cai<sup>1</sup>, Ashish K. Sharma<sup>1,2,3</sup>, Gilbert R. Upchurch Jr.<sup>1</sup>

<sup>1</sup>Division of Vascular and Endovascular Surgery, <sup>2</sup>Department of Medicine, <sup>3</sup>Department of Pharmacology & Therapeutics

### Abstract

**Introduction** The pathogenesis of abdominal aortic aneurysm (AAA) formation involves vascular inflammation, thrombosis formation and programmed cell death leading to vascular remodeling of the affected tissue. The role of ferroptosis, an iron-mediated cell death causing lipid peroxidation, and its role in immune cells like macrophages and ferroptosis-related genes in AAA formation remains to be deciphered. **Methods** Single-cell RNA sequencing of human AAA tissue from a published dataset was performed evaluating for differentially expressed genes (DEGs) identified via edgeR. Ferroptosis-related genes (FRGs) were recognized from GeneCards. AAAs were induced in male C57BL/6 mice using elastase or deactivated elastase in an acute 14-day model and a chronic 28-day elastase+BAPN model. Mice were treated with vehicle or liproxstatin-1 (ferroptosis inhibitor, 5mg/kg i.p.) on days 1-7 (acute) or 14-28 (chronic). Aortic diameter, histology, inflammatory cytokines, and ferroptosis markers (malondialdehyde (MDA) and glutathione (GSH)) were analyzed. F4/80+ macrophages were exposed to elastase with/without liproxstatin-1 treatment and MDA/GSH levels measured using colorimetric assay kits. Conditioned media transfer (CMT) from elastase exposed macrophages with/without liproxstatin-1 to SMCs was performed, measuring cytokines and MMP2 in SMC culture supernatants. Data is presented as mean +/- SD and statistical analysis was performed by ANOVA and p<0.05 considered significant. **Results** Differential analysis revealed 1,917 DEGs between human AAA (n=4) and control (n=2), with 287 differentially expressed FRGs. A reduction in diameter was observed in liproxstatin-1 treated mice compared to elastase treated mice in the acute (63±14 vs. 156±9%; n=10-15/group; p<0.01) and chronic (276±22 vs. 507±41; n=20-30/group; p<0.01) models. Histological analysis showed a decrease in immune cell (neutrophil/macrophage) infiltration, preservation of aortic morphology (increased smooth muscle  $\alpha$ -actin, decreased elastin breaks) after liproxstatin-1-treatment compared to untreated mice (n=4-8/group, p<0.05). In both models, a reduction in pro-inflammatory cytokines and lipid peroxidation (MDA), and increased GSH was observed in liproxstatin-1 treated mice (n=5/group, p<0.001). Macrophages exposed to elastase demonstrated increased MDA levels and reduced GSH which was attenuated by Liproxstatin-1 (n=8/group, p<0.01). CMT from elastase-exposed macrophages to SMCs induced a significant decrease in MMP2 expression which was attenuated by liproxstatin-1 treatment (n=8/group, p<0.01). **Conclusions** This study demonstrates that pharmacologic inhibition by liproxstatin-1 mitigates macrophage-dependent ferroptosis and decreases SMC activation that contributes to inhibition of aortic inflammation and remodeling during AAA formation.

**Funding Sources.** R01 HL138931-01A1 (GRU and AKS) R01 HL153341-01 (GRU and AKS) T32 HL160491 (GRU and JRK)

**Abstract Title:** Proprotein Convertase Subtilisin/Kexin Type 9 Inhibition is Associated with Survival Advantage in Aortic Aneurysm Patients

**Authors:** \*Gwendolyn S. Gillies, MD, Griffin P. Stinson, BS, Chelsea Viscardi, MD, Jonathan R. Krebs, MD, Ashish K. Sharma, MD PhD, Gilbert R. Upchurch, Jr., MD

Division of Vascular Surgery and Endovascular Therapy

**Abstract: Introduction:** Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) is an important enzyme that regulates cholesterol metabolism, and is known to reduce low density lipoprotein receptor (LDL-R) activity, thereby increasing plasma LDL levels. Animal studies have suggested that PCSK9 also promotes ferroptosis in aortic aneurysm development, while PCSK9 inhibition or absence decreases aneurysm growth. Although PCSK9 inhibitor (PCSK9i) medications are approved to treat hypercholesterolemia, their effect on human abdominal aortic aneurysmal (AAA) growth and mortality from AAA rupture has yet to be explored. The aim of this study was to investigate the effect of PCSK9 inhibition on AAA progression and overall patient outcomes in comparison to statin therapy or neither medication. **Methods:** A retrospective chart review was performed of patients aged 18 or older who were diagnosed with AAA between 2015 and 2023 and treated with PCSK9i medications evolocumab or alirocumab (n=54), HMG-CoA reductase inhibitors (statins) alone (n=3665), or neither medication (n=645). Demographic and comorbidity data at time of diagnosis were collected. Total cholesterol, LDL, HDL, and hemoglobin A1C were collected at time of diagnosis and at last follow up. Survival or death was assessed based on patient reports and social security data. Comparisons between PCSK9i, statins, and neither medication groups were performed using GraphPad Prism with two-tailed t-tests, ANOVA, or their non-parametric counterparts, as applicable. Kaplan-Meier analysis was used to estimate survival. Significance was defined as  $p < 0.05$ . **Results:** The percentage of patients with hypertension, atherosclerosis, and/or diabetes was highest in the PCSK9i group. Mean total cholesterol at time of diagnosis was significantly higher in the PCSK9i group compared to the statin and neither medication groups ( $193.3 \pm 59.3$  vs.  $146.3 \pm 44.9$  ( $p < 0.0001$ ) and  $159.5 \pm 51.6$  mg/dL ( $p = 0.0015$ ), respectively). Mean LDL was significantly higher in the PCSK9i group compared to the statin group ( $100.8 \pm 46.5$  vs.  $77.4 \pm 35.2$  mg/dL,  $p = 0.0048$ ). Hemoglobin A1C and body mass index (BMI) were significantly higher in the PCSK9i group compared to the neither medication group, but not significantly different compared to the statin group ( $6.1 \pm 0.8$  vs.  $5.5 \pm 0.5\%$ ,  $p < 0.0001$ ;  $28.0 \pm 5.3$  vs.  $25.0 \pm 5.6$  kg/m<sup>2</sup>,  $p = 0.0054$ , respectively). Freedom from all-cause mortality at time of last follow up was best in the PCSK9i group (85.2%) compared to the statins (72.4%) and neither medication (68.7%) groups (log-rank  $p < 0.001$ ). Within the PCSK9i group, there was no difference in survival based on sex, diabetic status, or smoking status. **Conclusions:** PCSK9 inhibitors are class of medications currently used to treat hypercholesterolemia, which show promise in the mortality in patients with aortic aneurysm disease. Our preliminary data suggest that even in a cohort of patients with worse risk factors for mortality, treatment with a PCSK9i was associated with significantly longer overall survival compared to treatment with statins or neither medication in patients with AAAs. Further investigation is ongoing with the aim of repeating statistical analysis after propensity matching, analyzing major adverse cardiovascular endpoints and determining the effect of PCSK9 inhibition on aortic aneurysm growth. **Funding Sources:** NIH NHLBI T32 HL-160491 (GRU).