2018 Department of Medicine
Research Symposium

Changing What’s Possible
Department of Medicine Research Symposium
March 30, 2018

We would like to thank all the participants for sharing their innovative research, as well as those who coordinated and attended this event. Your support for our research mission is greatly appreciated.

Many thanks to the judges who contributed their time and effort to make the 12th annual Department of Medicine Research Symposium a successful event.

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Sincerely,

Jim Oates, M.D.  
Professor, Division of Rheumatology and Immunology  
Vice Chairman for Research, Department of Medicine
Department of Medicine Research Symposium
Award Recipients

2015

Craig Kutz, Graduate Student, Cardiology
Jennifer Scott, Graduate Student, Rheumatology & Immunology
Akash Naik, Medical Student (1st & 2nd Year), Surgery
Coti Phillips, Medical Student (1st & 2nd Year), Urology
Christian Hicks, Medical Student (3rd & 4th Year), Memorial Sloan-Kettering Cancer Center
Kathryn Appleton, Postdoctoral Fellow, Endocrinology
Neeti Kanodra, MD, Resident/Fellow, Pulmonary & Critical Care
Takamitsu Saigusa, MD, Junior Faculty, Nephrology
Mara Lennard Richard, PhD, Other, Rheumatology & Immunology

Oral Presenters:
- Joy Buie, Rheumatology Immunology
- Melissa Cunningham, MD, Rheumatology & Immunology
- Lillianne Harris, PhD, Cardiology
- Mukoso Ozieh, MD, General Internal Medicine & Geriatrics

2016

Mohammed Dany, Graduate Student, Hematology/Oncology
Michael Lugo, Medical Student (1st & 2nd Year), Other
Muyi Li, Medical Student (3rd & 4th Year), Rheumatology & Immunology
Mona Haj, Postdoctoral Fellow, Gastroenterology & Hepatology
Sara Matar, MD, Resident/Fellow, Hematology/Oncology
Daena Peterson, MD, Resident/Fellow, Infectious Diseases
Sang-Ho Kwon, MD, Basic Junior Faculty, Nephrology
Rebekah Walker, PhD, Clinical Junior Faculty, General Internal Medicine

Oral Presenters:
- Erik Strungs, Endocrinology
- Keri Holmes-Maybank, MD, General Internal Medicine
- David Daly, MD, Cardiology
2017

Daniel Herr, Graduate Student, Cardiology
Tanjina Akter, Graduate Student, Rheumatology & Immunology
Diana Fulmer, Graduate Student, Department of Regenerative Medicine and Cell Biology
Andrew Hill, Medical Student (1st & 2nd Year), Endocrinology
Christopher Duckworth, Medical Student (1st & 2nd Year), Department of Pathology and Laboratory Medicine
Joseph Tracey, Medical Student (1st & 2nd Year), Department of Orthopedics
Mohammed Dany, Medical Student (3rd & 4th Year), Department of Biochemistry and Molecular Biology
Samuel Dickey, Medical Student (3rd & 4th Year), Gastroenterology & Hepatology
Samuel Feldman, Medical Student (3rd & 4th Year), Department of Ophthalmology
Lillianne Wright, PhD, Postdoctoral Fellow, Cardiology
Kamala Sundararaj, PhD, Postdoctoral Fellow, Cardiology
Cindy Wang, PhD, Postdoctoral Fellow, Gastroenterology & Hepatology
Deanna Baker Frost, MD, PhD, Resident/Fellow, Rheumatology & Immunology
Stephanie El Hajj, MD, Resident/Fellow, Cardiology
Alexandra Monroe, MD, Resident/Fellow, Department of Emergency Medicine
Rahul Argula, MD, Clinical Junior Faculty, Pulmonary & Critical Care
Ming Lim, MD, Clinical Junior Faculty, General Internal Medicine
Diann Krywko, MD, Clinical Junior Faculty, Department of Emergency Medicine
Ehtesham Arif, PhD, Basic Junior Faculty, Nephrology
Suchit Kumbhare, Other, Pulmonary & Critical Care

Oral Presenters:

- Ludivine Renaud, Ph.D., Division of Nephrology
- Myroslawa Happe, Department of Surgery
- Hesham El-Shewy, Ph.D., Division of Nephrology
- Samuel Schumann, M.D., General Internal Medicine
Formoterol induced mitochondrial biogenesis accelerates podocyte recovery from acute injury

Ehtesham Arif¹, Ashish K. Solanki¹, Pankaj Srivastava¹, Judit Megyesi³, Michael Janech, Sang-Ho Kwon¹, Justin Collier², Rick G. Schnellmann²,⁴, Deepak Nihalani¹

¹Department of Medicine, Nephrology Division, Medical University of South Carolina, Charleston, SC
²Department of Pharmacology and Toxicology, University of Arizona, Tucson, AZ
³John C McClelland VA Hospital, Little Rock, AR
⁴Southern Arizona VA Health Care System, Tucson, AZ

Introduction: Mitochondrial biogenesis (MB) is an adaptive response required to meet the metabolic and energy demand during acute injury to various organs, including kidney. This suggests that MB plays a central role in cellular recovery from injury. There are a limited number of chemicals known to induce MB. Therefore, targeted stimulation of MB may be a valuable approach in the development of new therapies for treatment of diseases characterized by mitochondrial impairment. In this report, we demonstrate that an increase in MB using β2-adrenergic receptor (ADRB2) agonist Formoterol accelerates the recovery of podocytes and hence glomerular function from acute injury.

Methods: RNA-Sequencing was performed to identify the differential gene expression pattern of mitochondrial electron transport chain (ETC). Formoterol induced oxygen consumption rate (OCR) was measured using sea-horse approach. Protamine sulphate/Nephrotoxic serum induced injured podocytes were treated with Formoterol and actin cytoskeleton arrangement and localization of slit-diaphragm protein Neph1 was analyzed using confocal microscopy. Efficacy of Formoterol was further tested in mouse model of NTS-induced glomerulonephritis. Formoterol (1mg/kg body weight/day) was used to treat post-NTS injured mice for day 7. Urine of these mice was analyzed by determining Albumin/Creatinine ratio, and the histological and ultrastructural analysis of kidney sections was performed. Immunostaining with various MB markers and slit diaphragm proteins was performed to further clarify the mechanisms involved.

Results: Initial studies using mRNA profiling of cultured podocytes treated with PAN (puromycin aminonucleoside), showed that podocyte injury induced differential expression of key components of ETC and PGC1α, a co-activator of MB. Injured podocytes treated with Formoterol, restored injury-induced damage to actin cytoskeleton organization and loss of slit-diaphragm protein Neph1 at the podocyte cell membrane. Importantly, in a mouse model of NTS-induced glomerulonephritis, 6 hr post injury, when glomerular dysfunction was established, treatment with Formoterol accelerated the recovery of glomerular function by reducing proteinuria and restored kidney pathology. Immunoblotting and qPCR showed that multiple proteins of ETC were elevated and the glomerular expression of MB marker PGC1α was significantly elevated. Finally, TUNEL staining of kidney sections showed reduced cellular apoptosis in the glomeruli of Formoterol-treated mice.

Conclusion: Present investigation revealed ADRB2 as a novel therapeutic target and Formoterol as a lead therapeutic compound that has potential to be commercially employed in treatment of podocytopathies.

Category: Basic Junior Faculty, Basic Science
Mentor: Deepak Nihalani, Ph.D., Division of Nephrology
The Protective Effects of Atrial Natriuretic Peptide Infusion in Salt-Sensitive Hypertension
Daria Ilatovskaya¹, Vladislav Levchenko², Adrian Zietara², Alexander Staruschenko²
¹Medical University of South Carolina, Department of Medicine, Division of Nephrology, Charleston, SC
²Medical College of Wisconsin, Department of Physiology, Milwaukee, WI

Introduction. Atrial Natriuretic Peptide (ANP) is a hormone secreted by cardiomyocytes; it stimulates water and sodium excretion by the kidneys to relieve pressure on the circulatory system. In our previous studies we compared wild type Dahl Salt Sensitive (SS) rats to SS rats lacking the Nppa gene which encodes ANP (SS\textsuperscript{Nppa-/-}). Salt-induced blood pressure development was exacerbated in the SS\textsuperscript{Nppa-/-} rats. Furthermore, SS\textsuperscript{Nppa-/-} rats exhibited reduced urinary sodium excretion and diuresis, as well as aggravated kidney damage compared to wild type controls. These data led to a hypothesis that ANP infusion may have beneficial effects during the development of salt-induced hypertension.

Methods. Wild type Dahl SS rats were fed a high salt diet (HS, 4% NaCl) for 21 days, with a continuous i.v. infusion of ANP (100 ng/kg/day) administered from day 0 or day 14 onward. Blood pressure was monitored throughout the study, and urine samples were collected in metabolic cages on days 0 and 21. At the end of the protocol, animals were sacrificed; fibrosis, glomerular injury, and protein casts formation were assessed in renal tissues stained with Masson trichrome. Urine and plasma samples were analyzed to estimate electrolyte homeostasis.

Results. We observed a decrease in blood pressure in both groups infused with ANP during 0-21 days (21D) and 14-21 days (7D) of a HS challenge. We observed reduced renal hypertrophy in the 21D animals. Metabolic cage studies revealed no changes in diuresis; urinary electrolyte analysis showed a more effective sodium excretion in the 21D rats. Assessment of kidney damage demonstrated a decrease in protein casts in both 7D and 21D rats: 3.8% ± 0.47%, 2.7% ± 0.24%, and 2.0% ± 0.41% of the tissue surface in the control, 7D and 21D groups, respectively. Glomerular injury had a similar pattern: scores were 2.86 ± 0.09, 2.62 ± 0.07, and 2.41 ± 0.06. Renal fibrosis was alleviated in the 21D group (1.4% ± 0.18%, compared to 1.9% ± 0.49% and 3.1% ± 0.31% in the 7D and control groups).

Conclusion. ANP infusion had beneficial (preventive and therapeutic) effects on BP and renal function compared to control animals. ANP administration during the HS diet challenge resulted in decreased BP, increased electrolyte excretion, and reduced tissue damage.

Category: Basic Junior Faculty, Basic Science
β-Arrestin plays a critical role in eNOS signaling

1Songling Liu, 1Louis M. Luttrell, 2Richard T. Premont, and 1Don C. Rockey

From the 1Medical University of South Carolina, Department of Medicine, Charleston, SC 29425 and 2Duke University Medical Center, Department of Medicine, Durham, NC

Introduction: Endothelial cell nitric oxide (NO) synthase (eNOS), the enzyme responsible for synthesis of NO in endothelial cells, undergoes extensive post-translational modifications that modulate its activity. In liver fibrosis, sinusoidal endothelial cell (SEC) injury is associated with dysregulation of eNOS, with resultant reduced enzyme activity and NO production reduction - and sinusoidal portal hypertension. We previously identified a novel eNOS interactor, G-protein-coupled receptor kinase interactor-1 (GIT1), which we found to play an unexpected stimulatory role in G-protein-coupled receptor (GPCR)-stimulated NO signaling. Since the β-arrestins are key participants in GPCR desensitization/resensitization, we hypothesized that they may be important in eNOS signaling. Therefore, we examined β-arrestin 2 (β-Arr2) and asked whether it is involved in GIT1/eNOS/NO signaling in either normal or injured SECs.

Methods: Portal hypertension was induced in rats and mice by bile duct ligation (BDL). SECs were isolated using pronase/collagenase digestion and primary cells were used for all studies. NO production and portal pressure were measured by standard techniques. SECs were infected with adenovirus expressing β-Arr2 or GIT1 constructs. β-Arr2/eNOS interaction was evaluated using novel super-resolution imaging.

Results: By immunofluorescence microscopy and immunoblotting pull down assays in SECs, β-Arr2/eNOS were found to be co-localized. Additionally, β-Arr2 expression was reduced in injured SECs (Figure, panel A) and β-Arr2/eNOS co-localization was reduced in injured SECs. Over-expression of β-Arr2 in injured or β-Arr2 KO SECs rescued eNOS function in these cells, increasing NO production and eNOS activity(Figure, panel B/C). In β-Arr2 KO mice compared to wild type mice, BDL led to an increase in portal pressure from 5.23±1.20 mmHg to 6.46±0.58 mmHg, and reduced eNOS activity (in SECs). A ternary complex of β-Arr2, GIT1 and eNOS was formed after stimulation of SECs with the GPCR activating agent, ET-1, and was attenuated in injured SECs. Over-expression of β-Arr2 in injured SECs resulted in increased GIT1/eNOS co-localization (and greater NO production).

Conclusions: The data suggest that β-Arr2 promotes GIT1/eNOS complex formation (in particular after stimulation with GPCR agonists such as ET-1). The reduction of eNOS activity in injury SECs may also be related to reduced β-Arr2 expression. Finally, the data emphasize the role of GPCR signaling partners in eNOS function and have fundamental implications for the pathogenesis of sinusoidal portal hypertension.

Category: Basic Junior Faculty, Basic Science
Mentor: Don C. Rockey, M.D., Division of Gastroenterology and Hepatology
Delirium screening as a tool to reduce falls and mechanical restraint use in hospitalized patients.

Benjamin Kalivas, MD.  Department of Medicine.
Kristine Harper, MSN, RN, NE-BC.  Patient Safety

Introduction: Delirium is a common neuropsychiatric condition associated with medical illness that occurs frequently in elderly patients. Delirium is associated with significant morbidity and mortality. Delayed or missed diagnosis of delirium can contribute to these poor outcomes. Screening for delirium is part of the critical care guidelines for ICU care, but is not currently part of non-ICU care. This project set out to pilot the use of delirium screening as well as a nursing driven care plan to help reduce falls and the use of mechanical restraints in screened patients.

Methods: Nursing began conducting a validated delirium screening tool on all patients twice daily. When patients screened positive for delirium, the “Acute Confusion Nursing Care Plan” was initiated. The care plan consisted of non-pharmacologic interventions for delirium. Rates of patient falls and the use of mechanical restraints are measured on all nursing units. The intervention began in December 2016 on one, 32 bed med-surg, non-ICU medical unit. After initiation of the screening tool and nursing care plan, data was compared from January to September 2017 to the same months in 2016

Results: Total patient falls was reduced from 26 before the intervention to 18 after the intervention. Mechanical restraint use was reduced from 43 before the intervention to 27 after.

Conclusion: The use of delirium screening and a nursing driven delirium care plan reduces falls and mechanical restraints in screened patients. The use of standardized screening and nursing management tools should be considered standard of care of non-ICU care as it is in the ICU.

Category: Clinical Junior Faculty, Clinical Science
Mentor: William Moran, M.D., MS, Division of General Internal Medicine and Geriatrics
Managing the influx of remotely obtained patient data: The provider’s perspective
Elizabeth B Kirkland, William P Moran
Division of General Internal Medicine and Geriatrics

Introduction
Patients are increasingly tracking their own health metrics, yet it is unclear how medical professionals should handle the onslaught of remotely obtained data. At MUSC, the Technology Assisted Case Management-2 program was initiated in 2016 as a method of engaging rural, underserved patient populations in chronic disease management through telemedicine. We examine the impact of remote data on chronic disease management as well as provider perspectives on the utility of remotely obtained data.

Methods
Patients are selected to participate based on an A1c of 8% or higher and agreement to monitor blood glucose and blood pressure with a 2-in-1 automated wireless device. Faculty and resident providers are responsible for overseeing remotely obtained data from patients of their continuity clinic. PGY3+ residents monitor the remote data on a biweekly basis and make changes to diabetes and/or hypertension treatment plans based on those values, with faculty supervision. We measure the impact of the remote data by analyzing the number of medication titrations recommended each week based on the remotely obtained data. We assess provider behavior with respect to this data by determining the severity and frequency of abnormal values which trigger a change in treatment.

Results
In November 2017, this program was introduced to the University Internal Medicine clinic. Within the first six weeks, 38 patients were enrolled. Of the enrolled and actively transmitting patients, an average of 75% were recommended to have medication titrations at the biweekly data review. Results from the survey of providers are currently being aggregated for statistical analysis. Preliminary data suggests that severely abnormal results trigger immediate change to treatment, while less aberrant results require several abnormal data points before triggering a change.

Conclusion
The influx of remotely obtained data will continue to grow in the coming years. Patterns of provider response to this data have not been studied. We attempt to characterize the severity and frequency of abnormal data points that lead providers to alter the treatment plan based on out-of-office health metrics. This information will help guide development of triage tools and flagging algorithms which will be imperative in the future, as the breadth of incoming data will overwhelm the individual provider’s ability to review in real-time.

Category: Clinical Junior Faculty, Clinical Science
Mentor: William Moran, M.D., MS, Division of General Internal Medicine and Geriatrics
Integration of an HIV Patient Reported Outcome Tool in the Electronic Medical Record
Eric G. Meissner, Bryan N. Rogers, Lucas Moreira, John Gnann, Cassandra D. Salgado, Melissa L. Habrat
Division of Infectious Diseases

Background: Assessing medication adherence, depression, and alcohol use are important components of delivering effective care for persons living with HIV infection. Patient reported outcome (PRO) tools can facilitate communication between patients and providers and identify areas for intervention that may not arise in the context of a routine clinical visit.

Methods: We developed a focused PRO tool within the electronic health record (EHR) that includes questions about HIV medication adherence, a depression screen (PHQ-8), and an alcohol abuse screen (AUDIT-C). At the time of rooming, patients use a secure touch screen on an EHR connected tablet or on a desktop computer using a mouse. Patients enrolled in MyChart can complete PRO assessments within a week of their appointment. Scores are immediately available for clinicians to review in the EHR communication inbox and discuss with the patient during the visit.

Results: Scores can be graphed longitudinally in the results review flowsheet and can be viewed by social workers and case managers providing services for patients. Use of a smart-phrase allows immediate inclusion of PRO answers into the physician’s clinical documentation. Thus far PROs have been completed by 95 patients. Multiple patients reported missing at least 1 day of medication within the last 2 weeks (n=22) and/or missing more than 3 days of medication since their last visit (n=24, with 4 patients missing more than 10 doses). PHQ-8 scores suggested 17/95 patients met criteria for major or severe major depression while 27/95 patients had higher risk scores for alcohol abuse on the AUDIT-C.

Conclusions: Implementation of a PRO tool that interfaces with the EHR represents an important tool to facilitate patient-provider communication and assess issues germane to delivering care for patients living with HIV infection.

Category: Clinical Junior Faculty, Clinical Science
Potential for the Current National Healthcare Safety Network (NHSN) >3 Days after Admission Definition of LabID Healthcare Facility Onset-Clostridium difficile Infection (HO-CDI) to Overestimate Rates

Participants: Heather Y. Hughes, MD, MPH¹,², Monica D. McCrackin, MSN, RN, CIC¹, Robert Williford, MS², Cassandra Salgado, MD, MS², and Scott Curry, MD²

Affiliations: Ralph H. Johnson VAMC, Medicine Service, Infectious Diseases Section¹ and the Medical University of South Carolina, Department of Medicine, Infectious Diseases Division²

Introduction: While the incubation period for CDIs is not precisely known, since 2013, all hospitals receiving payment from the Centers for Medicare and Medicaid Services are required to report CDI LabID events to NHSN. A HO-CDI LabID event is defined by NHSN as a positive CDI lab specimen collected >3 days after admission to the facility (on or after calendar day 4). We hypothesize that the current NHSN definition classifies a significant number of specimens collected between 48 and 72 hours from admission as HO-CDI. Such classification may over-estimate HO-CDI rates by including cases which may have been incubating on admission.

Methods: A retrospective cohort study was conducted at the Ralph H. Johnson VAMC (VA) and the Medical University of South Carolina (MUSC). All LabID cases classified as HO-CDI by the current NHSN definition with available data (time of admission and CDI specimen collection) from 2011-2016 (VA) and 1/2014-6/2017 (MUSC) were included. HO-CDI incidence was calculated using the current NHSN >3 days after admission definition and compared to HO-CDI incidence defined as any positive CDI lab specimen collected ≥ 72 hours from admission using R version 3.4.0.

Results: A total of 552 HO-CDI cases were included in the study. 43 (9.3%) cases at MUSC and 7 (8%) cases at the VA identified as HO-CDI by the current NHSN definition were collected 48-72 hours from admission [Figure]. The effect of removing these cases to include only those meeting the ≥ 72 hours after admission definition is shown in the Table.

Conclusion: Our study suggests that the current definition utilized by NHSN (on or after calendar day 4) may overestimate HO-CDI incidence by 8-9% compared to a definition based on a more granular use of time data of ≥72 hours after admission. This overestimation may influence the accuracy of HO-CDI rates and possibly impact interpretation of CDI data comparison.

Category: Clinical Junior Faculty, Clinical Science

Mentor: Julie Westerink, M.D., and Cassandra Salgado, M.D., MS, Division of Infectious Diseases
Nebulized Vasopressin to Control Hematemesis and Hemoptysis in a Child at the End-of-Life
Jennifer Dulin, MD, Palliative Care, Division of General Internal Medicine, Department of Medicine, Medical University of South Carolina
Patrick Coyne, APRN, Palliative Care, Division of General Internal Medicine, Department of Medicine, Medical University of South Carolina

Introduction: Bleeding occurs with some regularity at the end-of-life. Patients often endure resulting fatigue, weakness, pain, dyspnea and anxiety. These symptoms are magnified in visually apparent bleeds. Management can be particularly challenging as we attempt to balance therapies with goals of care. This challenge is greater in the pediatric population: children are often more sensitive to symptoms and less tolerant of therapies.

Case Description: A 7-year-old male with recurrent, refractory Burkitt’s lymphoma was frequently hospitalized for palliative chemotherapy and disease complications. On his final admission, he experienced gross hemoptysis and hematemesis: he was short of breath, fatigued and anxious due to his blood loss. His and his family’s angst were heightened by “seeing” him bleed. Potential, especially invasive, treatments were limited by our goals to promote comfort, limit interventions, maintain alertness, poor intravenous access and a small bowel obstruction. Nebulized vasopressin, 20 units in 4ml of normal saline given over 10 minutes, provided our patient with needed relief. His bleeding remitted and he tolerated the medication’s administration.

Conclusion: Many treatments for hemorrhage exist. In the palliative care population, however, goals of care, administration, side-effects and tolerability all present unique complications to treatment. Given our success and the unobtrusive nature of its administration, further investigation into nebulized vasopressin as a potential therapy for hemoptysis and hematemesis at the end-of-life is warranted.

Category: Clinical Junior Faculty, Clinical Science
Mentor: Patrick Coyne, MSN, Division of General Internal Medicine and Geriatrics
Formative Research to Assess Family Experiences with Inter-ICU Transfers of Ventilator Dependent Respiratory Failure Patients -Perspectives of Multiple Stakeholders
N.R. Nadig1, K. Sterba2, E. Johnson3, A.J. Goodwin1, D.W. Ford1
1Medical University of South Carolina - Charleston, SC/US Division of Pulmonary and Critical Care, 2Medical university of South Carolina – Department of Public Health Sciences, 3Medical university of South Carolina-College of Nursing

**Rationale**- Patients with ventilator dependent respiratory failure (VDRF) are among the most seriously ill ICU patients and thus theoretically should benefit from treatment in centers with greater expertise necessitating inter-ICU transfer. While intended to benefit patients, transfer may impact patient’s family who are removed from their local support systems and may experience substantial burdens to be near their family member. It is widely recognized that family of ICU survivors experience depression, post-traumatic stress and anxiety at rates higher than that of the US population but the influence that an inter-ICU transfer has on psychological outcomes in families is entirely unknown. Thus, our objective was to utilize a qualitative approach to gather insights into the psychological impact of inter-ICU transfer on families from multiple stakeholders in the transfer triad.

**Methods**-We prospectively identified VDRF patients transferred to adult ICU’s at the Medical University of South Carolina (MUSC) and then recruited stakeholders associated with the patient:1) family members 2) transferring ICU clinicians from referring hospitals and 3) receiving ICU clinicians at MUSC. We then used qualitative, semi-structured interviews that explored factors regarding the transfer including patient, family, health system, transfer timing, communication, coping and support factors. Interviews were transcribed and template analysis was used to identify key themes within and across stakeholder groups.

**Results**-Our results suggest that clinicians viewed inter-ICU transfers as burdensome to family and perceived few family-centered resources available. Further, the role of tertiary care hospitals was seen as peripheral to routine critical care and sought primarily for highly specific reasons. Family members were rarely engaged in the decision to transfer and highlighted that psychological strains were time-dependent and most prominent during the care transition. Our interviewees offered examples of general awareness and strategies they felt would be most beneficial to improving the experiences of family members that undergo inter-ICU transfer.

**Conclusions**-Findings from the interviews indicated the reasons for patient transfers were driven by perspectives of clinicians, patients and families more so than clear clinical, organizational or health system factors. The study highlights the common lack of engagement of family members in the decision to transfer as well as financial challenges and inadequate support networks through the process of inter-ICU transfer for family members. In light of these findings, it is critical to develop and evaluate family-focused tools and resources to optimize family experiences with ICU transfer.

**Category:** Clinical Junior Faculty, Clinical Science
**Mentor:** Dee Ford, M.D., MSCR, Division of Pulmonary and Critical Care
Essential Complex in the Etiology of Mitral Valve Prolapse

Lilong Guo, Departments of Medicine & Regenerative Medicine and Cell Biology

**Introduction:** Mitral Valve Prolapse (MVP) affects 1 in 40 individuals and is associated with secondary complications (e.g. arrhythmia's, heart failure, and sudden death). Although the genetic etiology of MVP has been known for decades, only recently have disease genes been identified. We identified mutations in the cilia gene DZIP1 in multiple families with MVP. To initially determine the function of DZIP1 in promoting cilia function, we used proteomics-based approaches with the goal of identifying unique binding partners for DZIP1. These studies revealed a direct interaction with Chibby1 (CBY1), a protein known to be involved in shuttling polycystin-2 (encoded by the polycystic kidney disease gene PKD2) to the cilia. As patients with PKD2 mutations are known to have a 10-fold increased incidence of MVP, we hypothesized that DZIP1 interacts with PKD2 through a CBY1 linker in a trafficking complex to the primary cilia.

**Methods:** 3D reconstruction of mice mitral valves was used to evaluate valvular phenotypes in knock out mice. Co-immunoprecipitation was performed to demonstrate an interaction between proteins in this complex. Immunofluorescence was performed to evaluate proliferation, MAPK pathway activity, protein localization and ECM synthesis in Cby1-/- mouse tissue.

**Results:** Genetically knocking out genes in this complex lead to enlarged mitral valves. The interaction domain between Dzip1 and Cby1 is at the C-terminus. No proliferation and cell number alterations were observed in Cby1-/- mouse mitral valve tissue. Phosphorylated (active) Erk (pERK) was increased in Cby1-/- tissue. ECM synthesis was decreased in Cby1-/- valve tissue.

**Conclusions:** The function of polycystin-2 in primary cilia on other tissues (e.g. kidney), is associated with mechanosensing. Thus, conservation of PKD2 function in the mitral valves supports primary cilia as a mechanosensor that relies on an intact DZIP1-PKD2 trafficking complex through CBY1.

**Category:** Graduate Student, Basic Science

**Mentor:** Joshua Lipschutz, M.D., Division of Nephrology, Russell Norris, Ph.D., Department of Regenerative Medicine and Cell Biology
Single Cell Genomic Profiling of Human B cells that Play a Role in Producing Immune Response against Pneumococcal Polysaccharides in Aging HIV-negative and HIV-positive Individuals

Myroslawa Happe, Devadoss Samuvel, Julie Westerink

**Background:** The introduction of combined anti-retroviral therapy has resulted in a significant improvement of life expectancy of HIV-positive individuals leading to a rapid growth of an aging HIV-positive population. Together, aging and HIV infection, increase susceptibility to life-threatening infections caused by *Streptococcus pneumoniae*. Despite preventative strategies, such as pneumococcal vaccination, it remains a challenge to induce potent and durable immune responses against pneumococcal polysaccharides (PPS) possibly due to poorly characterized perturbations in the B cell compartment of immune system of HIV-positive persons. The goal of this study is to characterize individual cellular changes in IgM memory B cell population that is largely responsible for producing immune responses to PPS, identify variations in inter-cellular gene expression that shape polysaccharide-specific B cell responses, and determine how aging affects these gene expressions.

**Methods:** Blood samples were collected pre- and post-pneumococcal vaccination from healthy and HIV+ individuals ages 21-40 and 50-65 according to guidelines of institutional review board of Medical University of South Carolina. Isolated B cells were used for FACS analysis and sorting. Single-cell qPCR was performed using Fluidigm BiomarkHD instrument.

**Results:** We have shown that the phenotype of polysaccharide specific B cells changes with age from predominantly IgM-memory to switched memory in HIV-negative individuals. However, in aging HIV-positive individuals, it resembles the phenotype of HIV-negative young adults in significantly reduced percentages. Single-cell genomic studies of IgM memory B cells revealed differential expression of genes that play an important role in T-cell independent immune responses (TACI, BAFF-R, CD21, TLR9, AICDA and other), B cell proliferation, and signaling between HIV-positive and HIV-negative persons in all age groups. Furthermore, unbiased clustering analysis identified distinct subgroups within IgM memory B cell population.

**Conclusions:** Together, these data significantly increase our knowledge of the genetic identities of B cells in aging HIV+ individuals uncovering their complexity and diversity and revealing insights into mechanisms underlying B cell dysfunctional phenotype that leads to poor responses to pneumococcal vaccination.

This project was supported by South Carolina Clinical & Translational Research (SCTR) Institute, with an academic home at the Medical University of South Carolina, NIH-NCATS UL1 TR001450 and NIH NCATS TL1 TR0011415. RO1 A081558

**Category:** Graduate Student, Basic Science

**Mentor:** Julie Westerink, M.D., Division of Infectious Diseases
Does PKC mediate the high risk of preeclampsia in pregnant women with diabetes?

Authors: Rebecca P. Chow¹,², Jiawu Zhao¹, Tim M. Curtis¹, Timothy J. Lyons¹,², Jeremy Y. Yu¹,²

¹Centre for Experimental Medicine, Queen's University of Belfast, UK
²Division of Endocrinology and Diabetes, Medical University of South Carolina, USA

Introduction: Preeclampsia (PE) is a leading cause of pregnancy-related mortality and morbidity, and its prevalence is 4-fold higher in women with diabetes vs. those without, but the underlying mechanism is unclear. The anti-angiogenic factor soluble fms-like tyrosine kinase-1 (sFlt1) plays an important role in the pathogenesis of PE. Evidence suggests that PKC activation, which is associated with the development of diabetic vascular complications, may mediate the enhanced sFlt1 release in non-trophoblast cell types; but it is unclear whether this mechanism occurs in the placenta and thus mediate the high risk of PE in diabetes. We aimed to determine: (1) the role of PKC in the regulation of sFlt1 expression in a human placental trophoblast cell line (2) whether diabetes-relevant conditions promote sFlt1 expression via the PKC pathway.

Methods: Quiescent human trophoblast HTR-8/SVneo cells were treated with the PKC activator phorbol-12-myristate-13-acetate (PMA), or the diabetes stimuli 'heavily oxidized, glycated' low-density lipoproteins (HOG-LDL) vs. native LDL ± glucose, over 24hrs, with or without PKC inhibitor GF109203X. Both sFlt1 mRNA expression (RT-PCR) and protein release (ELISA) were measured.

Results: We found that 5nM PMA increased sFlt1 mRNA expression (p ≤ 0.001 for sFlt1a) and protein release (p ≤ 0.001) in HTR-8/SVneo cells; this effect was abrogated by the pre-treatment of 5µM GF109203X (p ≤ 0.001 for sFlt1a expression, p ≤ 0.001 for protein). Similarly, 50 µg/ml HOG-LDL increased sFlt1a expression (p ≤ 0.001) and protein release (p ≤0.001), which were attenuated by GF109203X. However, glucose did not appear enhance the effect of HOG-LDL.

Conclusions: The results are consistent with the possibility that modified lipoproteins may promote PE development in women with diabetes, likely via a PKC-mediated up-regulation and release of sFlt1. These findings provide new insights into the disease mechanism, and potential targets for developing preventative and interventional measures for PE.

Category: Graduate Student, Basic Science
Mentor: Jeremy Yu, Ph.D., Timothy Lyons, M.D., Division of Endocrinology
**Effects of modified lipoproteins on first trimester trophoblast cells: a role in pre-eclampsia in pregnancies complicated by diabetes**

Rebecca H. McLeese¹,², Jiawu Zhao², Jeremy Y. Yu¹, Derek P. Brazil², Timothy J. Lyons¹

¹Division of Endocrinology and Diabetes, Medical University of South Carolina, Charleston SC 29425, USA; ²Centre for Experimental Medicine, Queen’s University Belfast, Belfast, Northern Ireland, UK

Introduction: Pre-eclampsia (PE) complicates 2-8% of pregnancies worldwide. In women with diabetes, the risk for PE is increased 4-fold. Trophoblast cells are involved in angiogenesis, producing growth factors to promote vascularization of the developing placenta. In women destined to develop PE, trophoblast invasion is impaired, leading to incomplete spiral artery remodelling. Soluble fms-like tyrosine kinase (sFlt-1) and soluble endoglin (sEng) are anti-angiogenic factors, secreted from many cell types and tissues including placental trophoblast. Evidence suggests that increased release of these factors from the trophoblast into the maternal circulation may promote endothelial dysfunction associated with the development of PE. In this study, we investigated sFlt-1 and sEng release from the placental trophoblast cell line, HTR8/svneo, in response to modified lipoproteins (which accumulate in vascular tissues of patients with diabetes) and/or elevated glucose. Methods: HTR8/svneo cells were exposed to highly-oxidized glycated low density lipoprotein (HOG-LDL) vs native LDL (N-LDL) (0-200µg protein/ml) for 24h. To investigate the effect of hyperglycaemia, HTR8/svneo cells were pre-treated (72h) with 30mM glucose followed by exposure to HOG-LDL vs N-LDL for 24h. Transcriptional expression of the two main sFlt-1 isoforms, i13 and e15a, endoglin and its major shedding protease, MMP-14, were measured by RT-PCR. sFlt-1 and sEng secretion in cell supernatants were measured by ELISA. Results: HOG-LDL increased sFlt-1 mRNA expression (i13, p<0.05; e15a, p<0.01) and protein secretion (p<0.05). HOG-LDL increased mRNA expression of endoglin and MMP-14 (p<0.05) and secretion of sEng (p<0.01). N-LDL had no effect on HTR8/svneo cells. High glucose potentiated the effects of HOG-LDL, but alone had no effect. Conclusion: Exposure of trophoblasts to modified lipoproteins may contribute to the development of PE in diabetes, and the presence of high glucose may amplify the effect. These findings may explain the increased risk of PE in women with diabetes.

Keywords: pre-eclampsia, diabetes, trophoblast, lipoprotein, hyperglycaemia, anti-angiogenesis

**Category:** Graduate Student, Basic Science

**Mentors:** Timothy Lyons, M.D., Division of Endocrinology
M10, a 10 Amino Acid Peptide, Regulates the Extracellular Matrix Expression via a Dual Mechanism in Scleroderma Associated Lung Fibrosis

Akter T, Atanelishvili I, Silver RM, and Bogatkevich GS

Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina, USA.

Rationale. Interstitial lung disease (ILD) is the major cause of mortality among scleroderma (systemic sclerosis, SSc) patients. Extracellular matrix (ECM) deposition is a hallmark of fibrotic diseases. TGFβ plays a crucial role in ECM protein expression via regulation of intra-cellular Ca²⁺ level, and matrix metalloproteinases (MMPs). We recently demonstrated that M10 peptide, naturally derived from the cytosolic fragment of the hepatocyte growth factor receptor, blocks the TGFβ-mediated canonical pathway via interaction with SMAD2 and reduces fibrosis in vivo. In this study, we investigate the efficacy of M10 in the regulation of intracellular Ca²⁺ levels, ECM gene transcriptions, and MMPs/TIMPs expression in normal and SSc lung fibroblasts.

Methods. Primary human lung fibroblasts were derived from autopsy specimens from SSc-ILD patients and matched healthy individuals. Ca²⁺ was measured by FLIPR Tetra cellular screening system equipped with Molecular Devices ScreenWorks® software. Expression of collagen I, connective tissue growth factor (CTGF), fibronectin and tenascin were measured by real-time PCR. Expression of MMP-1, MMP -2, MMP -3, MMP -8, MMP -9, MMP -10, MMP -13, TIMP-1, TIMP -2, and TIMP -4 was determined by human MMP antibody array. Statistical analysis was performed using GraphPad Prism 7 software.

Results. In both normal and SSc-ILD lung fibroblasts, an acute increase of intracellular Ca²⁺ was observed 15sec following TGFβ administration, with a second peak of delayed Ca²⁺ efflux at 60sec. A high level of Ca²⁺ was maintained throughout the 10 min of the cellular screening process. In the presence of M10 peptide, TGFβ-mediated Ca²⁺ was significantly (p < 0.001) reduced in both acute and delayed states maintaining overall lower amplitude. M10 consistently suppressed TGFβ-mediated mRNA expression of collagen I, CTGF, fibronectin, and tenascin. M10 downregulated the expression of MMP 3 in SSc-ILD fibroblasts, suggesting that it can prevent the latent TGFβ from activation. M10 upregulated the expression of MMP10 in normal lung fibroblasts, suggesting that it can promote Collagen-I degradation.

Conclusions. M10 peptide reduces mRNA of ECM proteins, inhibits TGFβ-mediated Ca²⁺ efflux, regulates MMPs, induces degradation of collagen and other ECM proteins. These data suggest that M10 peptide possesses great potential to reduce TGFβ-mediated outcomes in SSc-ILD.

Category: Graduate Student, Basic Science
Mentor: Richard M. Silver, M.D. and Galina Bogatkevich, M.D., Ph.D., Division of Infectious Diseases
Lupus Serum Induces Glomerular Endothelial Cell Neutrophil Adhesion and Migration in Association with Soluble Mediators of Adhesion and Chemotaxis

Dayvia Russell¹, Margaret Markiewicz², Jim C. Oates²,³

¹Research Service, Ralph H. Johnson VA Medical Center, Charleston, SC, ²Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, ³Medical Service, Ralph H. Johnson VA Medical Center, Charleston, SC

Introduction
Systemic lupus erythematosus (SLE) is a chronic inflammatory disease associated with endothelial cell dysfunction (ECD), a key modulator of inflammatory renal disease, found in up to 50% of SLE patients. ECD leads to upregulation of adhesion molecules, release of inflammatory chemokines, and ingress of neutrophils into glomerular tissue. Understanding how ECD processes lead to neutrophil influx across the endothelium is essential to finding therapeutic targets for SLE. The aim of this study is to uncover the functional ability of SLE serum from patients with active disease to induce adhesion and chemotaxis of neutrophils towards glomerular endothelial cells.

Methods
Serum was collected during paired visits (during active and inactive disease) from SLE patients and healthy controls with and without hypertension. To assess the functional ability of serum to induce adhesion molecule expression in endothelial cells, primary human renal glomerular endothelial cells (HRGECs) were treated with SLE serum. Neutrophils were then cultured with HRGECs, and neutrophil adherence was determined. To assess the functional ability of SLE serum to induce neutrophil chemotaxis, HRGECs were treated with SLE serum, then conditioned media (CM) was collected. Migration of neutrophils towards CM was calculated.

Results
Neutrophil adherence to HRGECs was significantly increased during the visits with higher SLE disease activity. HRGECs treated with SLE serum induced significantly greater neutrophil chemotaxis than control serum. Lupus nephritis serum induced chemotaxis more than serum from SLE patients without nephritis. Finally, serum from both SLE and control patients with hypertension induced more chemotaxis than disease-matched non-hypertensives.

Conclusion
This study suggests SLE serum induces expression of mediators by glomerular endothelial cells that promote neutrophil adhesion and migration, furthering our understanding of how ECD processes lead to renal impairment in SLE. Hypertension may be an independent mediator of consequence of ECD induced by circulating factors in SLE.

Category: Medical Students (1st – 2nd Year), Basic Science
Mentor: James C. Oates, M.D., Division of Rheumatology and Immunology
Glycosphingolipids as Biomarkers of Lupus Nephritis

Jessalyn Rodgers, 1Kamala Sundararaj, 2Richard Drake, 1Michael Janech, 1James Oates, and 1Tamara Nowling

1Department of Medicine and 2Department of Pharmacology, Medical University of South Carolina, Charleston, SC

Introduction: Glycosphingolipid (GSL) levels and activity/expression of neuraminidase (NEU), which mediates GSL catabolism, are elevated in kidneys and/or urine of lupus mice and nephritic human patients compared to controls. Exosomes, 20-100nm extracellular vesicles, contain lipids, proteins and RNA representative of the cells from which they were derived and are abundant in human urine. Thus, exosomes are a potential source of biomarkers of renal disease in lupus nephritis (LN) patients. We hypothesize: 1) levels of GSL molecules may be potential biomarkers of flare and therapeutic response and 2) decreasing NEU activity will reduce proteinuria and/or progression of nephritis in lupus.

Methods: We have collected exosomes from LN patient urine samples taken during quiescent disease and during a disease flare. The exosomes were used: 1) to measure GSL levels by MALD-FTICR, 2) to measure NEU1/3 and exosome marker levels by western immunoblot, and 3) for proteomic discovery analysis. In addition, we have generated a NEU1 heterozygote on the B6.SLE1/2/3 lupus prone mouse strain for analyses of decreasing NEU1 levels (and GSL catabolism) on the progression of LN.

Results: Preliminary results measuring GSL levels in exosomes from LN patient urine showed significant differences between patients who responded or failed to respond to treatment. A pilot study of urine exosomes from five LN patients taken during quiescent disease and a disease flare and from five lupus non-nephritic patients show: 1) increased GSL levels in flare samples compared to non-flare, and/or control samples; and 2) differences in the levels of proteins between flare, non-flare, and/or control samples. We have generated a NEU1 heterozygote (Neu1+/−) on the B6.SLE1/2/3 lupus prone mouse strain, and are assessing for effects on disease development. Preliminary data indicate that the Neu1+/− lupus mice have decreased/delayed development of proteinuria.

Conclusions: Data suggests that molecules in this pathway may serve as biomarkers of flare and/or response to therapy in LN patients and GSL catabolism as a potential target for therapeutic intervention.

Category: Medical Students (1st – 2nd Year), Basic Science
Mentor: Tamara Nowling, Ph.D., Division of Rheumatology and Immunology
A Cadaveric Load Analysis of the Supramalleolar Osteotomy In The Setting of an Osteochondral Pseudolesion: Quantifying Chondral Off-loading

Introduction
The supramalleolar osteotomy (SMO) serves as a means to alter joint load transmission and shield damaged areas of cartilage within the tibiotalar joint. The aim of this study was to directly measure the changes in pressure attributed to varying degrees of SMOs (varus and valgus); with and without an osteochondral (OCD) pseudolesion, and in multiple ankle alignments (Dorsiflexion, neutral, and plantarflexion). We hypothesize measurement metrics to be reduced with increasing degrees of SMO.

Methods
6 cadaver specimens were included in the biomechanical study (sectioned at the mid-tibia). A pressure sensor was used to measure load, load area, and peak pressure within the tibiotalar joint. SMOs of 3, 6, 9, and 12 degrees in varus or valgus were performed. A servohydraulic machine was used to transmit 400 and 800N through the specimens; in 10 degrees of dorsiflexion, neutral, or in 10 degrees of plantarflexion during load transmission. Measurements were performed in undisturbed joints, followed by re-measurement in the presence of a created 9mm diameter pseudolesion.

Results
Load was not changed (only significant changes reported) in the presence of a lesion. For the load, it was more influenceable at 800 N, changes were observed in higher degree SMOs, and changes were only observed in neutral and dorsiflexion. Changes in area were only observed when 12 degrees of varus or valgus SMOs were used. Peak Pressure was the only modifiable metric in the presence of a pseudo-lesion, reductions were more common at 800 N, and in the absence of a pseudolesion there was an incremental reduction in medial peak pressure when increasing varus SMOs were performed (dorsiflexion).

Conclusion
Medial peak pressure tended to decrease with varus SMOs in neutral and dorsiflexion. Medial load tended to decrease with varus osteotomies in 10 degrees of dorsiflexion. A 12 degree varus SMO was the only SMO to influence a pseudolesion.

Category: Medical Students (1st – 2nd Year), Basic Science
Mentor: Christopher Gross, M.D., Department of Orthopedics and Physical Medicine
Characterization of Pericytes from Normal and Idiopathic Pulmonary Fibrosis (IPF) Human Lungs

Seth E. Bollenbecker*, Sarah E. Falta*, Sarah E. Stephenson, Carole L. Wilson, and Lynn M. Schnapp
Division of Pulmonary, Critical Care, Allergy, and Sleep Medicine, Department of Medicine
*Co-first authors

Introduction: Pericytes are key regulators of blood vessel development and function. However, pericytes may play additional roles in tissue homeostasis and repair through their ability to upregulate immune response genes and transdifferentiate into myofibroblasts. Accumulation of myofibroblasts is a hallmark of fibrotic diseases such as Idiopathic Pulmonary Fibrosis (IPF).

Methods: To understand the role of pericytes in lung fibrosis, we isolated these cells from normal and IPF lungs to compare their properties and responses to fibrotic and inflammatory stimuli in vitro. Pericytes were selected from explanted human lung digests based on PDGFRβ expression as we previously described for mouse cells.

Results: We found that IPF cells migrated significantly more rapidly and invaded a matrix more readily than normal pericytes. TGFβ, a major fibrotic cytokine, caused both normal and IPF pericytes to shift to a myofibroblastic phenotype, with increased expression of collagen, αSMA, and fibronectin. Given that pericytes are uniquely positioned in vivo to respond to danger signals of both systemic and local origin, we stimulated pericytes with agonists having damage-associated molecular patterns (DAMPs) or pathogen-associated molecular patterns (PAMPs). Both normal and IPF lung pericytes showed increased expression of proinflammatory chemokines in response to PAMPs and DAMPs.

Conclusion: Our results demonstrate that human lung pericytes can transition to myofibroblasts, and IPF pericytes are more invasive than normal. IPF and normal pericytes both respond to danger signals through elaboration of proinflammatory chemokines. Further understanding the biology of normal and IPF pericytes will assist in developing targeted therapeutics for treatment of fibrosis.

Category: Medical Students (1st – 2nd Year), Basic Science
Mentor: Lynn Schnapp, M.D., Carole Wilson, Ph.D., Division of Pulmonary and Critical Care
Effect of Alcohol Septal Ablation on Renal function of patients with Hypertrophic Obstructive Cardiomyopathy. Does relief of obstruction ameliorate Acute Contrast-Induced Nephropathy?
Alex Canova, Mira Patel, Billy Mullinax, Ashley Waring MD, Chris Capps MD, Christopher Nielsen MD, Valerian Fernandes MD

BACKGROUND: Alcohol septal ablation (ASA), a catheter based treatment for hypertrophic obstructive cardiomyopathy (HOCM) uses contrast to visualize coronaries while targeting the septal artery for ablation. Alcohol infarcts the hypertrophied obstructive basal septum and relieves LV outflow obstruction. There is a risk of renal dysfunction and contrast induced nephropathy (CIN) with the use of angiographic contrast. This study evaluates the incidence of renal dysfunction after ASA in our center.

METHODS: Renal function data of consecutive patients who underwent ASA at MUSC between January 2007 and May 2017 were retrospectively analyzed. CIN was defined as a ≥0.5mg/dL or ≥25% increase in serum creatinine after the procedure.

RESULTS: A total of 218 patients (age 60.39 ± 14.08y, 124F, 111M) who underwent 235 ASA procedures were included in this study. Alcohol (2.10 ± 0.68 cc) was injected into 1.22 ± 0.52 septal arteries, thereby relieving LVOT gradient from 71.65 ± 41.27mmHg at baseline to 5.68 ± 11.16mmHg after ablation. A mean volume of 114.4 ± 56.2mL of contrast (Omnipaque/Visipaque) was used for ASA. In the entire cohort there was a significant decrease in serum creatinine and BUN after ASA. Creatinine decreased from 1.05 ± 0.68mg/dL to 1.00 ± 0.72mg/dL while BUN decreased from 16.32 ± 9.09mg/dL to 14.91 ± 8.25mg/dL after procedure (P<0.05 for both). Predefined CIN was seen in 10/233 (4.3%) cases. The creatinine in these patients increased from 0.86 ± 0.23mg/dL to 1.29 ± 0.51mg/dL after ASA. None of these patients needed renal support.

CONCLUSION: The use of contrast with ASA did not have a detrimental effect on renal function. Renal indices improved after ASA suggesting that the relief of LVOT obstruction and thus improvement in renal perfusion may have ameliorated the detrimental effect of contrast on the kidneys. The incidence of CIN was low at 4.3% with no one needing renal support.

Category: Medical Students (1st – 2nd Year), Clinical Science
Mentor: Valerian Fernandes, M.D., Division of Cardiology
Opioid addiction is an increasingly prevalent problem. Patients prescribed higher doses of opioids are at added risk of overdose. Opioid prescriptions for musculoskeletal pain, acute and chronic, increased from 2001-2010. It has never been examined which medical specialties are prescribing the patients of South Carolina opioid prescriptions for low back pain. We examined opioid prescribing habits of different specialties for non-surgical low back pain at MUSC. The sample size was 2790 patients (age > 18) diagnosed with ICD-9 codes 724.2, 724.3, 724.5, or 54.5 and has prescribed an opioid during outpatient visits between 1/01/2013-12/31/2016. De-identified data was stratified examining the most commonly prescribed opioids and the prescribing specialty. This overview explored the gross numbers associated with low back pain and opioid prescription habits without additional statistical analysis. For 2790 patients there were 5303 opioid prescriptions. Only 3861 prescriptions had a prescribing specialty listed. Thus, prescriptions with no specialty assigned were the largest group in the study (1442 prescriptions written (27%)). Family medicine wrote 986 (18.5%) of the prescriptions, followed by Internal Medicine with 795 (15%), Anesthesiology with 419 (8%), Neurosurgery with 283 (5.5%), and Pain Medicine with 230 (4.5%). These five specialties comprised 51.5% of the total prescriptions. Combining the top five prescribing specialties and prescriptions with no specialty listed yields ~78% of the total prescriptions written for low back pain. Interestingly, only 65 prescriptions (1.2%) were written by orthopedic surgeons for non-surgical low back pain. The three most commonly prescribed opioids were Oxycodone (29%), Hydrocodone (26.5%), and Tramadol (15.5%). More analysis is still being performed; however, this could potentially lead to more effective education and interventions to prevent opioid abuse and overdose. By elucidating which specialties are prescribing, focused education pertaining to each specialty will aid in decreasing rates of unnecessary opioid prescriptions.

**Category:** Medical Students (1st – 2nd Year), Clinical Science  
**Mentor:** Christopher Gross, M.D., Department of Orthopedic Surgery
Effect of Alcohol Septal Ablation on cardiac enzymes in patients with Hypertrophic Obstructive Cardiomyopathy. Does volume of alcohol used for ablation matter?

Mira Patel, Brian Blaker MD, Alex Canova, Billy Mullinax, Ashley Waring MD, Chris Capps MD, Christopher Nielsen MD, Valerian Fernandes MD

Background:
In acute MI, cardiac enzymes used to assess the extent of myocardial necrosis have evolved over time from LDH to SGOT/SGPT to CK, then CK-MB and now to Troponin. In Alcohol septal ablation (ASA), alcohol is used to infarct the hypertrophied obstructive basal septum and relieve LV outflow obstruction. The effect of this iatrogenic infarction on cardiac enzymes has been inadequately studied. We undertook this study to assess the effect of ASA on present day cardiac enzymes.

Methods:
Serial CK and Troponin enzymes of consecutive patients who underwent ASA at MUSC between January 2007 and May 2017 were retrospectively analyzed. The peak level of enzymes was correlated to the volume of alcohol injected. The enzymes curves were compared to the historical curves of enzyme release after MI.

Results:
A total of 160 patients (age 60.39 y ± 14.08 y, 68 F, 92 M) who underwent 173 ASA procedures were included in this study. Alcohol (1.82 cc ± 0.43 cc) was injected into 1.22 ± 0.52 septal arteries, thereby relieving LVOT gradient from 71.65 mmHg ± 41.27 mmHg at baseline to 5.68 mmHg ± 11.16 mmHg after ablation. CK enzyme reached peak at 24 hours while Troponin peaked at 13 hours after the alcohol injection. Both peak CK and peak Troponin correlated with the amount of alcohol injected (R = 0.05) but the correlation was stronger for CK than for Troponin. On average 2 cc of alcohol produced an infarct releasing 702.9 U/l of CK or 17.04 ng/ml of troponin.

Conclusion:
In Alcohol septal ablation the amount of alcohol used directly affected infarct size in terms of troponin and CK enzyme release. Similar to acute MI the CK enzyme peaked around 24 hours but unlike AMI the troponins peaked earlier at 13 hours.

Category: Medical Students (1st – 2nd Year), Clinical Science
Mentor: Valerian Fernandes, M.D., Division of Cardiology
Alcohol Septal Ablation Produces Similar Changes to CBC as Atherosclerotic Myocardial Infarction but Platelet Counts Are Not Elevated. Is There Less Inflammation With ASA?

Billy J Mullinax1, Mira Patel1, Alex Canova1, Ashley Waring MD2, Christopher Nielsen MD2, and Valerian Fernandes MD2.

1College of Medicine, Medical University of South Carolina, Charleston, SC. 2Department of Cardiology, Medical University of South Carolina, Charleston, SC.

Objectives
To study blood cell count changes after alcohol induced septal infarct in Hypertrophic Obstructive Cardiomyopathy (HOCM) patients.

Background
Atherosclerotic myocardial infarction (MI) is a pro-inflammatory and prothrombotic state associated with neutrophilic leukocytosis, anemia, and increased platelet count and platelet size. The degree of leukocytosis correlates with infarction size and, together with increased platelets, amplifies myocardial inflammation. Alcohol Septal Ablation (ASA) produces a targeted infarction in the hypertrophied septum to reduce left ventricular outflow obstruction. The inflammatory and thrombotic effects of this iatrogenic alcohol induced infarction have not been studied.

Methods
We evaluated 314 consecutive patients who underwent ASA with pre- and post-ASA hemoglobin, WBC count, platelet counts, and troponin.

Results
A total of 314 patients (age 61.14 ± 13.00, 139M, 175F) who underwent ASA were included in the study. Alcohol (2.08 ± 0.65cc) was injected into a targeted septal artery producing a peak troponin of 53.60 ± 42.77 ng/ml. After ASA, WBC increased from 6.95 ± 1.95 to 8.16 ± 2.48 (p<0.001), hemoglobin decreased from 13.42 ± 1.77 to 12.31 ± 1.91 (p<0.001), and platelet counts decreased from 200 ± 56 to 177 ± 49 (p <0.001). Different tertiles of hemoglobin, WBC, and platelet counts showed no correlation to peak troponin values following ASA. The volume of alcohol injected did not affect the pre and post-ASA hemoglobin, WBC, and platelet counts.

Conclusions
Compared to atherosclerotic MI, alcohol induced infarction also leads to increase in WBC count and anemia but unlike atherosclerotic MI there is a reduction in platelet count. This suggests that ASA produces a similar inflammatory response with a reduced thrombotic state. The size of the ASA infarct did not correlate with blood count indices, possibly suggesting that unlike atherosclerotic MI infarct with ASA is independent of physiologic inflammatory or thrombotic states.

Category: Medical Students (3rd – 4th Year), Clinical Science
Mentor: Valerian Fernandes, M.D., and Christopher Nielsen, M.D., Division of Cardiology
MRI Utilization by Orthopaedic and Non-orthopaedic providers for acute or chronic ankle pain

Durante, E., MS4¹, Chapin, R. MD¹, Palanca, A. MD², Hocking, D., MS3¹, Hermann, J.², Gross, C. MD¹
Department of Orthopaedics, Medical University of South Carolina¹, Stanford University²

Healthcare costs are an increasingly significant burden on society. Advanced imaging comprises a large component of these costs. Many professional groups (American Academy of Family Physicians (AAFP), American College of Radiology (ACR)) recommend use of plain film radiographs prior to magnetic resonance imaging (MRI). We examined the compliance rate of this recommendation at our institution between orthopaedic providers (Orthopaedic surgeons, non-operative physicians employed in the Department of Orthopedics, and Orthopaedic Physician Assistants) compared to other physicians. We hypothesized that there is an over utilization of resources by non-orthopaedic providers. This was a retrospective chart review of patients who had had MRIs of their ankles from April 2015-June 2016 (total of 721 charts). We assessed whether the ordering physician had obtained an ankle radiograph prior to the MRI. The diagnosis listed as the reason for the study was also recorded. We determined that 222 of the 259 (85.7%) of the orthopaedic providers obtained radiographs prior to MRI while only 271 of 462 (58.7%) non-orthopaedic providers followed these criteria (p<0.0001). Overall, 493 out of 721 (68.4%) providers obtained radiographs prior to MRI. The orthopaedic providers who did not comply with ACR criteria were evaluating diagnoses of tendinopathy or did not obtain new radiographs when the plain films were more than 6 months old. Non-orthopaedic providers failed to follow ACR criteria when evaluating edema and tendinopathy. Orthopaedic providers complied with ACR criteria more closely, but there is an appreciable over-utilization of advanced imaging by all providers. There was an overall inappropriate use percentage of 32.1%. Increasing compliance to the ACR criteria would allow for decreased cost of healthcare in the treatment of ankle pain.

Category: Medical Students (3rd – 4th Year), Clinical Science
Mentor: Christopher Gross, M.D., Department of Orthopedics and Russel Chapin, Department of Radiology
Case Report of Sustained Response to Oral Propranolol as an Adjunct to Cytotoxic Chemotherapy and Radiation Therapy in Treatment of Large Cutaneous Angiosarcoma

Emily Nyers, MUSC Department of Dermatology

Introduction: Angiosarcoma is an aggressive, heterogeneous malignancy of the vascular or lymphatic endothelium that most commonly presents cutaneously with a high rate of recurrence following treatment. Sporadic disease occurs most commonly in elderly men presenting as an asymptomatic ecchymotic patch or plaque. Historically, cutaneous angiosarcoma is associated with poor outcomes, with an overall 10-50% survival and 0% survival at two years for tumors >10cm. Factors portending a worse prognosis include age >70, size, scalp location, and positive margins on histology. Treatment modalities have traditionally included surgical excision, with targeted radiation and cytotoxic chemotherapy for nonsurgical candidates in spite of unclear survival benefit. Tyrosine kinase inhibitors and VEGF inhibitors such as bevacizumab have more recently been added to the treatment arsenal. While these agents have been shown to slow or stabilize tumor growth, response is often incomplete. Laboratory models have demonstrated the increased expression of beta-adrenergic receptors in these tumors, and several previous case reports suggest that a daily regimen of oral propranolol may afford additional treatment benefit.

Methods: Here we report a case of a 78-year-old male who presented to care with a several-month history of a purplish bruise beginning on the forehead and extending to the preauricular and parietal scalp.

Results: Staged as a T2bN0M0, the lesion was treated with a regimen of radiation, paclitaxel, and 40mg oral propranolol BID, to which the lesion responded with regression at 1 month and ultimate complete response.

Conclusion: The patient remains in remission approximately 3 years following treatment with no evidence of recurrence or metastasis. While larger, randomized controlled trials are warranted to fully elucidate therapeutic benefit of propranolol, the dramatic and sustained response exhibited here is promising.

Category: Medical Students (3rd – 4th Year), Clinical Science
Mentor: Graciela de Jesus, M.D. and David Perry M.D., Ph.D., Department of Dermatology and Dermatologic Surgery
An Updated Meta-Analysis of Ankle Fusions and Third Generation Ankle Replacements
Jesse Morris

**Background:** The effectiveness of total ankle replacement (TAR) compared with that of ankle arthrodesis remains a hotly debated topic. The purpose of this study was to clinically compare the two procedures. A systematic review of the literature addressing the intermediate- long-term outcomes of interest in total ankle arthroplasty and ankle arthrodesis was performed.

**Methods:** A comprehensive search of MEDLINE for all articles published from 3/25/2006 to 2/1/2017 was conducted with a minimum two-year follow-up. Two reviewers evaluated each study to determine whether it was eligible for inclusion and abstracted the data of interest. Meta-analytic pooling of group results across studies was performed for the two procedures. The analysis focused on third-generation ankle implants.

**Results:** The systematic review identified 58 primary studies, 40 of which evaluated TAR in a total of 4853 patients and 24 of which evaluated ankle arthrodesis in a total of 761 patients. The mean post-operative AOFAS-Ankle-Hindfoot score was 79 points for TAR patients; 75 points in fusion patients (p=0.013). Meta-analytic mean results showed 84.2% of the patients treated with TAR had an excellent/good result; in the fusion group, 76.2% of the patients excellent/good results arthrodesis group (p=0.001). The five-year implant survival rate was 86% and the ten-year survival rate was 76%. The revision rate following TAR was 9.6% compared with a 5.0% revision rate for arthrodesis (p=0.001). In TAR the primary reason for revisions was loosening of either tibial or talar component (3.5%); in the arthrodesis group the main revision reason was nonunion (3.9%) (p=0.58).

**Conclusions:** Based on these findings, the intermediate outcome of TAR appears to be better than fusion. Comparative studies are needed to strengthen this conclusion.

**Category:** Medical Students (3rd – 4th Year), Clinical Science
**Mentor:** Christopher Gross, M.D., Department of Orthopedics
Case series of dabigatran-associated intracranial hemorrhages treated with and without idarucizumab

Authors: John Mark Sawyer, College of Medicine
Nicholas J. Connors, Assistant Professor, Department of Emergency Medicine

Introduction: Intracranial hemorrhage (ICH) is a rare, but serious event affecting those taking dabigatran. Idarucizumab is an antidote that lowers dabigatran concentrations. Clinical outcomes and comparative data are lacking.

Methods: This case series used Epic SlicerDicer and chart review to identify all patients between 7/1/2014 and 7/1/2016 who were taking dabigatran at the time of their admission for ICH. Information on demographics, clinical presentation, discharge disposition, laboratory values, home medications, ICU days, and total cost of hospitalization was collected and entered into a REDCap database for review.

Results: All patients took dabigatran for nonvalvular atrial fibrillation.
Case 1: A 74-year-old man has a large right ICH. He receives idarucizumab and platelets, and aPTT decreases from 35.2 to 23.7 seconds. On hospital day (HD) #2, he has an enlarging right ICH prompting surgery. On HD#38, he is discharged to a skilled nursing facility ventilated, and able to respond “yes” or “no.” Hospitalization cost: $478,326.07.
Case 2- An 87-year-old man has a right parietal-occipital ICH and is administered idarucizumab. On HD#4, a new cerebellar infarction is found. He is stabilized, but has multiple splenic and renal infarcts. On HD#12, he is discharged to hospice. Hospitalization cost: $119,088.10.
Case 3- A 58-year-old man presents with a traumatic frontal subdural hematoma. He is administered FEIBA and platelets. Repeat imaging reveals a stable SDH. He is discharged on HD#6. Hospitalization cost: $60,909.00.
Case 4- A 71-year-old woman has a massive left frontal ICH. After consultation with family, comfort care is initiated. Hospitalization cost: $14,622.00.

Conclusion: This series demonstrates varied outcomes in patients on dabigatran with ICH. Two cases result in poor outcomes despite receiving idarucizumab. While idarucizumab is the only reversal agent for dabigatran, clinical benefit is undocumented in regards to patient-centered outcomes, cost, and length of stay.

Category: Medical Students (3rd – 4th Year), Clinical Science
Mentor: Nicholas Connors, M.D., Department of Emergency Medicine
Proud to be GIM Event Increases Medical Student Interest and Knowledge about General Internal Medicine Careers

Leah Snipe, Zemin Su, William Moran, Patrick Mauldin, Keri Holmes-Maybank
General Internal Medicine and Geriatrics

Introduction: The number of medical students choosing Internal Medicine (IM) residencies has declined with only 20-25% of those who chose IM making a career in General Internal Medicine (GIM). We hosted a Proud to be GIM (PTBG) event with the objectives to: 1) Increase student knowledge and interest in GIM; 2) Assess student attitudes regarding career and lifestyle factors; 3) Evaluate the effect of a resident panel and faculty speed-dating on student knowledge and interest in GIM.

Methods: In January 2017, 51 medical students participated in a PTBG event that included faculty speed-dating, a resident panel, and multimedia presentation. A pre-event survey included demographics and assessed interest in GIM, knowledge of GIM, and the importance of lifestyle and career factors in considering GIM. The post-event survey had additional questions to evaluate the event’s impact on student interest in and knowledge of GIM.

Results:
Participant characteristics were: 50% male; 54% pre-clinical (years 1 and 2); 60% white, 30% black, 4.7% Hispanic, 4.7% Asian; 40% had completed a 3rd year IM clerkship; and 25% had rotated in an IM subspecialty. The majority of students were preclinical and had not completed an IM clerkship or subspecialty rotation. Pre-post survey comparison suggests the PTBG event led to a statistically significant increase in knowledge of GIM careers ($p<0.0001$) and a non-significant increase in interest in GIM ($p=0.064$). 100% of students felt that faculty speed-dating and resident panel increased interest and knowledge in GIM. After the event the importance of mentorship increased significantly ($p=0.012$). 80% of student respondents ranked lifestyle as important as well as patient population (53%), intellectual challenge (73.3%), commitment to patients (70%), and career opportunities (63.5%). Several areas were not considered for “important” including income (26.7%), work hours (20%), and mentorship (13.3%). After participating in the event the importance of mentorship increased significantly ($p=0.012$).

Conclusion
The PTBG event held at our institution significantly increased knowledge and increased interest in GIM. This interaction with faculty likely also led to the increased recognition of the importance of mentorship. The survey suggests that an event incorporating multimedia presentations, resident opinions, and interactions with faculty can successfully educate students about careers in GIM as well as increase their interest in the field.

Category: Medical Students (3rd – 4th Year), Clinical Science
Mentor: Keri Holmes-Maybank, M.D., Division of General Internal Medicine and Geriatrics
Improving lupus patients’ disease-specific knowledge through educational modules

Maham Awan, B.S., Diane L. Kamen, M.D., M.S.C.R, Department of Medicine, Division of Rheumatology & Immunology

Introduction:
Living with systemic lupus erythematosus (SLE), a chronic autoimmune disease, often requires patients to implement drastic lifestyle changes. However, providing sufficient education to ensure patients enact appropriate and well-informed changes remains a challenge. This study aims to create and evaluate the effectiveness of educational modules detailing SLE activity triggers, symptom management, and disease-specific lifestyle modifications.

Methods:
SLE education modules were crafted using peer-reviewed literature sources and further evaluated and critiqued by three volunteer key informants who were patients with long-standing SLE. A guided interview took place with the informants to determine what information in the modules were unclear and what topics needed to be added. After the modules were finalized, a test was constructed to assess if patients understood the content and “take home messages” of the modules. The test would be given prior to and after the patient went through the modules.

Results:
The key informant interviews revealed that patients needed clarification on the etiology of SLE and the concept that SLE is an incurable disease. Informants appreciated detailed tables of different medication options that included side effects. All 3 key informants requested current information about research trials and study results. The informants appreciated information regarding smoking cessation and sun protection included in the modules. A larger scale educational intervention utilizing the finalized modules is now planned.

Conclusion:
Patients with SLE desire detailed information regarding the pathophysiology and pharmacologic management of SLE. Further studies with pre- and post-testing will determine the effectiveness of these patient education modules in improving disease-related knowledge.

Category: Medical Students (3rd – 4th Year), Clinical Science
Mentor: Diane Kamen, M.D., MSCR, Division of Rheumatology and Immunology
Utility of Bronchoscopy in Diagnosis of Lung Cancer
Mary Brooks, Ben Bevill MD, Nicholas J. Pastis MD, Gerard Silvestri MD, MS
Division of Pulmonary, Critical Care, Allergy, and Sleep Medicine
Medical University of South Carolina, Charleston, SC

Introduction: Bronchoscopy is a commonly used tool for the evaluation of suspicious lung lesions. Earlier studies have shown that the sensitivity for standard bronchoscopy as well as endobronchial ultrasound (EBUS), electromagnetic navigation (EMN) and radial probe EBUS (r-EBUS) range from 67% to 89% for the diagnosis of cancer.1-3 However recent data suggest that the diagnostic yield is somewhat lower ranging from 39% with EMN to 64% with flexible bronchoscopy.4 The Airway Epithelial Gene Expression in the Diagnosis of Lung Cancer (AEGIS) trial sought to validate a bronchial genomic classifier for lung cancer diagnosis.5 The study found that 43% of bronchoscopies were non-diagnostic for lung cancer, and that 35% of patients with benign lesions underwent invasive diagnostic procedures after bronchoscopy. This finding calls into question the utility of bronchoscopy as a stand-alone diagnostic tool for lung cancer. Our study seeks to further evaluate the performance of bronchoscopy through analysis of the AEGIS trial.

Methods: Descriptive statistics were performed on the raw data acquired from the AEGIS trial. The percentage of positive and negative lung cancer diagnoses were determined for the following categories: physician derived patient pretest probability of cancer (pCA), procedure type, size of lesion, location of lesion, and presence of lymphadenopathy.

Results: 817 patients were evaluated for the performance of bronchoscopy, of which 45% were non-diagnostic. EBUS was the most prevalent procedure performed in the positive bronchoscopy group (55%). More combination bronchoscopies were performed in the negative bronchoscopy group. Lesion size was >3cm in 69% of patients in the positive bronchoscopy group, and were more likely to be centrally located (40%) or both centrally and peripherally located (35%). Of the lesions in the negative bronchoscopy group, 24% were 1-2cm and only 32% were >3cm, with 27% in the central location and 23% in both central and peripheral locations. Lymphadenopathy was present in 65% of the positive bronchoscopy group, yet present in only 36% of the negative bronchoscopy group.

Conclusion: In this large prospective, multicenter trial the diagnostic yield from bronchoscopy was only 55%, lower than previously reported in the literature. Predictors of a positive bronchoscopy include those where physicians have a high clinical suspicion of cancer (pCA>60%), have larger, centrally located lesions and have adenopathy present and utilize EBUS. Patients were more likely to have a non-diagnostic procedure when the clinical suspicion of lung cancer is low, the lesion is small and peripheral, and there is no adenopathy. Our findings highlight a need for reassessing guideline recommendations for the utilization of bronchoscopy in those suspected of having lung cancer. Future research should develop a clinical prediction rule which can aid physicians in if, when, and what type of bronchoscopy would aid clinical decision-making surrounding the workup of suspicious lung lesions.

Category: Medical Students (3rd – 4th Year), Clinical Science
Mentor: Gerard Silvestri, M.D., Ben Bevill, M.D., Nicholas Pastis, M.D., Division of Pulmonary and Critical Care

Ankyloglossia, Frenectomy, and Frenotomy effects on Length of Stay and Total Cost for Newborns

Authors:
Suqrat Munawar, BS. Elizabeth Durante, BA/BS. Clarice Clemmens, M.D.

Department of Otolaryngology – Head and Neck Surgery, Medical University of South Carolina, Charleston, SC, USA

Objectives:
Explain the differences in length of stay (LOS) & cost for neonates with ankyloglossia compared to those without ankyloglossia. Recognize the differences in length of stay & cost for neonates who undergo frenectomy or frenotomy compared to those who do not undergo a procedure for ankyloglossia. Compare demographics between neonates with ankyloglossia (stratified by procedure) versus those without ankyloglossia

Design: Retrospective Database Review

Setting: Database

Methods:
Newborn admissions from 2009 were identified in the HCUP KID database and stratified by those with ankyloglossia and/or those who underwent frenotomy or frenectomy and were examined for descriptive statistics and frequencies using SPSS v. 24. Variables examined include sex, race, median income of patient residence, hospital characteristics: size, location, and region; disposition, and total cost. Independent sample t-tests were then performed for LOS and cost. Chi-squared was used for demographics.

Results:
With a sample of 15762 patients with ankyloglossia and 3443798 patients without ankyloglossia, ankyloglossia patients had an average LOS of 3.08 days and average total cost of $5880.20. Ankyloglossia patients who had either frenectomy or frenotomy had an average LOS of 3.42 days while those who did not have a procedure had an average LOS of 2.8 days; average total cost was $6814.51 and $9114.99, respectively. Patients without ankyloglossia had an average LOS of 3.38 days and average total cost of $9124.97 (all had p-value of <0.001).

Conclusion:
While overall patients with ankyloglossia had a shorter average LOS compared to neonates without ankyloglossia, those who underwent a procedure had a longer average LOS compared to patients without ankyloglossia. Total cost was greater for those without ankyloglossia and ankyloglossia patients who did not undergo a procedure.

Category: Medical Students (3rd – 4th Year), Clinical Science
Mentor: Clarice Clemmens, M.D., Department of Otolaryngology
Comparison of Psychosocial Factors Over Time among HPV-positive Oropharyngeal Cancer and Tobacco-Related Oral Cavity Cancer Patients

Authors: Janz, T., Momin, S., Sterba, K., Garris, T.K., Armeson, K., Scallion, M., and Day, T.

Introduction: Patients with head and neck cancer (HNC) experience physical and emotional challenges during their care that may impact long-term quality of life (QoL). The role of the human papilloma virus (HPV) in the pathogenesis of oropharyngeal squamous cell carcinoma (OPSCC) is well documented, as is the excellent prognosis of these patients. In contrast, oral cavity squamous cell carcinoma (OCSCC) is associated with tobacco and alcohol use and has a worse prognosis. While causative factors have been identified for both cancer subsets, few studies have compared whether psychosocial factors differ in these groups.

Methods: Head and neck cancer patients from a multidisciplinary, tertiary care HNC center were enrolled in a prospective study and completed self-administered questionnaires before starting treatment and at 12 months assessing demographics, behaviors, self-efficacy, symptoms, cancer worry and depression.

Results: A total of 34 (18 HPV+ OPSCC/16 OCSCC) patients (mean age: 57 [32-76], 73.6% male, 79.4% Caucasian, 68% stage IV) met inclusion criteria. OPSCC patients tended to be of male sex, Caucasian race, and single. Furthermore, OPSCC patients were more likely than OCSCC patients to have private insurance, be employed, and use alcohol and tobacco less frequently. Regarding psychosocial factors, while no statistically significant differences were found, the HPV+ OPSCC patients reported lower symptom severity (2.5 versus 3.1), depression (11.9 versus 13.9) and cancer worry (2.8 versus 3.2), and higher self-efficacy for coping with treatment (7.07 versus 6.88) at baseline. No differences were noted between groups when assessing for changes over time.

Discussion/conclusion: This ongoing study highlighted that while OCSCC patients had higher symptom, depression, and self-efficacy scores at baseline as compared to the OPSCC cohort, no differences existed in these scores over time. Although different in cancer etiology, HPV-associated OPSCC and tobacco-related OCSCC patients both require multidisciplinary cancer care plans that address their psychosocial concerns.

Category: Medical Students (3rd – 4th Year), Basic Science
Mentor: Terry Day, M.D., Department of Otolaryngology and Katherine Sterba, Ph.D., Department of Public Health Sciences
Title: A novel cell-based assay for diagnosing recurrent FSGS

Ashish Solanki¹, Pankaj Srivastava¹, Ehtesham Arif¹, Peifeng Deng¹, Bethany J Wolf², Kenneth Kwon¹, Milos Budisavljevic¹, Michael Janech¹, Deepak Nihalani¹#

¹Div. of Nephrology, Dept. of Medicine, MUSC, ²Dept. of Public Health Sciences, MUSC.
# Corresponding Author

Introduction: FSGS (focal and segmental glomerulosclerosis), is a disease that primarily targets kidney podocytes (an important constituent of kidney’s filtration barrier) and whose dysfunction leads to progressive renal failure. Here, we report the development of a human podocyte cell-based assay that will serve as a non-invasive diagnostic clinical tool to detect recurrent FSGS. The concepts and approaches demonstrated are widely applicable in designing assays for other forms of FSGS, which are the leading causes of ESRD and their diagnostic gold standard remains the invasive kidney biopsy method. This assay is specifically aimed at diagnosing rFSGS to avert the ineffective renal transplant in FSGS patients.

Methods: We identified rFSGS responsive genes by profiling (RNASeq) human podocytes treated with plasma derived from human rFSGS and control patients, which also induced significant alterations to podocyte actin cytoskeleton partially mimicking the disease processes. 3 unique candidate genes (proprietary information) based on profiling data from control and rFSGS patients were selected. Next, their promoter regions were cloned into a promoterless reporter vector, transduced into podocytes and luciferase assay was performed.

Results: Interestingly, when these cell lines were exposed to plasma from rFSGS patients, increased reporter activity was noted; whereas no reporter activity was noted in controls. The cell lines were also tested for their response to other glomerular diseases including non-rFSGS and membranous nephropathy patients. The statistical analysis showed that the estimated AUCs for model fits discriminating between rFSGS and all other nephropathies and between rFGSG and non-recurrent FSGS ranged from 0.93 to 0.96. Additionally, the estimated sensitivities and specificities of detection were greater than 86% and 82% respectively for all genes.

Conclusion: The developed assay is noninvasive, sensitive, specific, accurate and studies are being planned for conducting clinical trials to utilize its full diagnostic potential.

Category: Postdoctoral Fellow, Basic Science
Mentor: Deepak Nihalani, Ph.D., Division of Nephrology
Title: Haptoglobin phenotype modulates lipoprotein-associated risk for preeclampsia in women with Type 1 diabetes

Clare B. Kelly, PhD1, Jeremy Y. Yu, MD, PhD1, Alicia J. Jenkins, MD1,2, Alison Nankervis, MD3, Kristian F. Hanssen, MD1, Tore Henriksen, MD5, Satish K. Garg, MD6, Christopher E. Aston, PhD7, and Timothy J. Lyons, MD1

Author affiliations: 1Division of Endocrinology, Medical University of South Carolina, Charleston, South Carolina, USA. 2University of Sydney, NHMRC Clinical Trials Centre, Camperdown, Sydney, NSW, Australia. 3Royal Women's Hospital, Melbourne, Australia. 4Department of Endocrinology, Oslo University Hospital, Oslo, Norway. 5University of Oslo, Oslo, Norway. 6Barbara Davis Center for Childhood Diabetes, University of Colorado, Denver, USA. 7The Department of Pediatrics, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA.

Preeclampsia (PE) occurs more frequently in pregnant diabetic than non-diabetic women (~20% vs ~5%). Early identification of high-risk women is needed. Dyslipidemia is implicated: increased cholesterol-rich lipoproteins, early in pregnancy, are associated with subsequent PE in type 1 diabetes (T1D). Haptoglobin (Hp) is a plasma protein that binds free hemoglobin, and has two allelic forms, Hp-1, Hp-2, hence three phenotypes. Among people with diabetes, Hp 2-2 phenotype (present in ≈50%) has been associated with oxidative stress, cardiovascular risk and renal decline.

We investigated whether maternal Hp phenotype is associated with PE in T1D, and/or modulates lipoprotein-related risks for PE. A prospective study of pregnancy included 23 T1D women (cases) who developed PE, and 24 T1D (controls) who remained normotensive. Hp phenotype was determined by ELISA (Savyon Diagnostics Ltd.). Lipid profiles were measured at three study visits (V1-V3), all preceding PE onset: (mean ± SD) 12.4 ± 1.8, 21.7 ± 1.4, and 31.3 ± 1.4 weeks gestation.

Results: Hp phenotype did not differ between women with and without PE, and lipid profiles did not differ by Hp phenotype. In PE cases vs. controls, by univariate analysis, HDL-C was lower at V1, while LDL-C was higher at V2, as were triacylglycerols (p<0.05). In Hp 2-2 women, these associations were stronger: in 2-2 cases (n=11) vs 2-2 controls (n=9), HDL-C was lower at all visits (V1: p<0.05; V2, V3: p<0.01) and LDL-C was higher at V1 (p<0.01) and V2 (p<0.05). In contrast, in women with one or two Hp-1 alleles, no associations between lipids and PE were observed.

Conclusion: In T1D women, lipoprotein-related risks for PE may be limited to those with Hp 2-2 phenotype. The data provide further evidence of a role for Hp phenotype as a modulator of vascular risk in diabetes.

Category: Postdoctoral Fellow, Basic Science
Mentor: Timothy Lyons, M.D., Division of Endocrinology
PDGFR-ß+ Cells: a Novel Reservoirs for HIV in the Lungs

Sarah E Stephenson¹, Carole L Wilson¹, Lindsey M Felton¹, Lynn M Schnapp¹

¹Pulmonary, Critical Care, Allergy and Sleep Medicine, Medicine, Medical University of South Carolina, Charleston, SC

Background: The success of anti-retroviral therapy (ART) in HIV patients has lengthened life span. However, HIV infection is not completely eradicated due to reservoirs of virus. The lung has been proposed as an important reservoir of HIV. This may contribute to the increased risk of chronic pulmonary complications, including COPD. The lung pericyte is a mesenchymal-derived cell that is critical for vascular homeostasis, through secretion of pro-survival molecules such as angiopoietin-1 (Angpt-1). It has been shown in vitro that HIV can directly infect brain pericytes, leading to reduced endothelial cell association and increased leakiness of the blood-brain barrier. We hypothesize that lung pericytes can also be infected by HIV and may serve as a reservoir for the virus. Furthermore, we propose that HIV infection switches pericytes to an activated state in which Angpt-1 secretion is decreased and pro-inflammatory cytokine production is increased. To test this hypothesis, we isolated pericytes from digested human lung tissue by selecting for PDGFR-ß, a common marker for pericytes.

Results: We found that lung pericytes express key co-receptors for HIV, including CD4, CXCR4 and CCR5. Furthermore, lung pericytes are directly infected by HIV-1, as determined by p24 production and RT-PCR for HIV-1. Infected pericytes show increased expression of the pro-inflammatory genes CXCL1, CXCL2, CXCL10 and IL-8. In addition, HIV infection decreased Angpt-1 expression and, following exposure to TGFß1, transiently decreased myofibroblast markers.

Conclusion: Taken together, our data demonstrate that HIV directly infects lung pericytes, which may represent a previously unrecognized reservoir of HIV in the lung.

Category: Postdoctoral Fellow, Basic Science
Mentor: Lynn Schnapp, M.D., Division of Pulmonary and Critical Care
Ammonia levels do not guide clinical management in patients admitted with hepatic encephalopathy

Mona Haj

Objective: Ammonia is believed to play a major role in the pathophysiology of hepatic encephalopathy. However, its role in guiding management is unclear. Our aim was to understand the impact of ammonia levels on inpatient HE management. We hypothesized that patients with an elevated ammonia level drawn would receive more aggressive lactulose therapy than patients with a normal ammonia or no ammonia level drawn.

Design: Cirrhotics admitted to the Medical University of South Carolina for management of HE from 2005-2015 were evaluated. Patients with and without an admission ammonia level were included, and were matched using propensity matching. Patients with an ammonia level taken were further separated into those with normal or elevated ammonia levels. The primary endpoint was total lactulose given in the first 48 hours of management.

Results: 1202 admissions were identified. Ammonia levels were drawn in 551 (46%) patients; 328 patients (60%) had an abnormal ammonia level (>72 µmol/L). There were no significant differences in Child-Pugh, MELD, or Charlson Comorbidity Index between groups. The average total lactulose dosage (mL) over 48 hours in the no ammonia group was 167 mL vs 171 mL in the ammonia group (p=0.42). The average lactulose dose in those with an elevated ammonia level was 161mL. There was no correlation between lactulose dose and ammonia level (R²=0.0026).

Conclusions: The amount of lactulose administered to treat inpatients with HE did not differ whether ammonia was measured or whether it was abnormal or not, suggesting that ammonia levels in clinical practice do not guide lactulose therapy.

Category: Postdoctoral Fellow, Clinical Science
Mentor: Don C. Rockey, M.D., Division of Gastroenterology and Hepatology
miRmapper: A tool for interpretation of miRNA-mRNAs interaction networks

da Silveira W.A¹, Renaud L.²,³, Simpson J.¹, Glen W.B Jr¹, Hazard E.S¹,⁴, Chung D.⁵, Hardiman G.¹,²,³,⁵,

¹Center for Genomic Medicine, Bioinformatics, Medical University of South Carolina (MUSC), Charleston, SC 29425, USA.
²Division of Nephrology, Department of Medicine, Medical University of South Carolina (MUSC), Charleston, SC 29425, USA.
³Laboratory for Marine Systems Biology, Hollings Marine Laboratory, Charleston, SC 29412, USA.
⁴Library Science and Informatics, Medical University of South Carolina (MUSC), Charleston, SC 29425, USA.
⁵Department of Public Health Sciences, Medical University of South Carolina (MUSC), Charleston, SC 29425, USA.

Abstract

Current estimates predict that miRNAs potentially regulate up to 30% of the protein-coding genes in the human genome. Differentially expressed (DE) miRNAs that modulate a large number of mRNA transcripts ultimately have a greater influence in determining biological outcomes, a concept we term ‘miRNA network centrality’. Here we describe the development of a tool, ‘miRmapper’ which identifies the most dominant miRNAs and modulated mRNAs in a miRNA-mRNA network, and recognizes similarities between miRNAs based on commonly regulated mRNAs. Using a list of miRNA-Target gene interactions and a list of DE transcripts, miRmapper provides several outputs: 1) an adjacency matrix that is used to calculate miRNA similarity utilizing the Jaccard distance, 2) a dendrogram and 3) an identity heatmap displaying miRNA clusters based on their effect on mRNA expression, 4) an microRNA impact table and 5) a barplot that provides a visual illustration of this impact. We tested this tool using non-metastatic and metastatic bladder cancer cell lines and demonstrated that the most relevant miRNAs in a cellular context are not necessarily those with the greatest fold change. Additionally, by exploiting the Jaccard distance, we unraveled novel cooperative interactions between miRNAs from independent families in regulating common target mRNAs; i.e. 5 of the top 10 most influential miRNAs regulate the same biological pathway.

Category: Postdoctoral Fellow, Basic Science

Mentor: Gary Hardiman, Ph.D., Division of Nephrology
A Positive Feedback Loop between Estrogen and IL-6 leads to Fibrosis in Human Skin

DeAnna Baker Frost, MD, PhD¹,³, Carol Feghali-Bostwick, PhD²,³
¹Rheumatology Fellow, ²Professor, Kitty Trask Holt Endowed Chair for Scleroderma Research, ³Department of Medicine, Division of Rheumatology and Immunology, Medical University of South Carolina 96 Jonathan Lucas Street, Charleston, SC 29425

Background: Systemic Sclerosis (SSc), a disease characterized by increased extracellular matrix (ECM) synthesis in organs, including skin, results in morbidity. SSc is female predominant, increasing during childbearing years. Post-menopausal SSc patients have higher circulating estradiol (E2) levels compared to age-matched controls. E2 exerts pro-fibrotic and pro-inflammatory activity, increasing ECM and IL-6, both of which are increased in SSc patients. Aromatase, a cytochrome p450 enzyme active in extra-gonadal tissues, including skin, is responsible for aromatization of androgens into estrogens. Increased aromatase activity may underlie increased E2 levels in SSc patients. Since SSc dermal fibroblasts secrete increased IL-6 levels, and SSc patients have increased E2 levels, we hypothesize an interplay between E2 and IL-6, contributing to fibrosis.

Methods: Human skin in organ culture was stimulated with E2 or IL-6 and its soluble receptor, sIL6R, for 24 or 48 hours. Aromatase, IL-6, and ECM transcript levels were measured using real-time PCR. Aromatase activity was measured using an ELISA-based testosterone conversion assay. Statistical significance was based on t-test or ANOVA, with p≤0.05 defined as significant.

Results: Human skin stimulated with E2 or IL-6 + sIL-6R ex vivo showed increased transcripts of ECM components. E2 stimulation resulted in increased IL-6 transcript and protein levels. Human skin stimulated with IL-6 and sIL-6R led to increases aromatase mRNA. Skin samples stimulated with IL-6 and sIL-6R had increased aromatase activity, translating into increased testosterone to E2 conversion. Aromatase activity decreased significantly after treatment with anastrozole, an aromatase inhibitor.

Conclusion: Our data show that E2 exerts pro-fibrotic effects in human skin and further establish a positive feedback loop between E2 and IL-6, supporting a pro-fibrotic cycle that leads to increased ECM and fibrosis. Our results implicate E2 and IL-6 in dermal fibrosis in SSc and suggest that effective therapies for SSc may require concomitant inhibition of E2 and IL-6.

Category: Resident/Fellow, Basic Science
Mentor: Carol Feghali-Bostwick, Ph.D., Division of Rheumatology and Immunology

Poster # 37
Perception of Metal Detector usage in the Emergency Department.

Russell Allinder MD, Diann Krywko MD

Department of Emergency Medicine, Medical University of South Carolina, Charleston, South Carolina

Background: Healthcare workers are at high risk for workplace violence. Widely varying policies exist regarding the use of metal detectors (MDs) as screening tools to enhance safety. Our institution policy mandates activation of walk-through MDs (WTMDs) only when EMS arrival of gunshot wound victims is identified. Administrative concerns as to whether the presence of WTMDs worsens the public perception of ED safety, thus deterring visits, has precluded ubiquitous usage. This study was intended to understand current perception of security measures, with future goal to address utilization concerns, change policy, and increase ED occupant safety.

Methods: The study was conducted from June to July, 2017 via a voluntary, confidential REDCap™ survey distributed to eligible ED patients, visitors, and staff at an academic level-1 trauma center. Data collected included: demographics (gender, age, race, ED entry time and method), presence/absence of WTMD awareness, if MDs affected their safety perception, and whether the presence of a MD would affect future ED use.

Results: 307 participants enrolled. A majority of participants (75%) stated they would feel safer if a WTMD was in use. African-Americans (AA) (87%) and Caucasians (64%) alike reported increased safety perception if WTMDs were in use, with AA reporting greater perceived safety benefit than Caucasians, p<0.001. Security officer visibility increased safety perception in 72%. WTMD usage at entrance would not negatively affect ED return usage in 99% of respondents.

Conclusion: Surveyed participants would not perceive the ED as a more dangerous place if WTMDs were routinely utilized. Conversely, the majority would perceive these measures as providing increased safety. ED utilization rates would not be affected adversely by usage of WTMDs at the entrance. This data should be considered by administration to routinely utilize MDs, thus potentially decreasing dangerous weapon entry into the ED and increasing safety and well-being of ED occupants.

Category: Resident/Fellow, Basic Science
Mentor: Diann Krywko, M.D., Department of Emergency Medicine
Title: Lung Protective Ventilation Adherence Rates Among ICUs in a Tertiary Care Medical Center

Authors: Adam Kouns MD, Andrew Goodwin MD MSCR, Kit N Simpson DrPH, Dee Ford MD MSCR Medical University of South Carolina Division of Pulmonary, Critical care, sleep and allergy

Rationale: Ventilator-Dependent Respiratory Failure (VDRF) is a common critical care illness with high morbidity and mortality. Lung Protective Ventilation (LPV) with tidal volumes of ≤6cc/kg of ideal body weight (IBW) has been shown over decades of research to improve outcomes including mortality, ventilator-free days and ICU length of stay. Two recent reports found that adherence to LPV was sub-optimal including in academic medical centers. We investigated adherence to LPV at our tertiary care medical center and sought to explore potential practice variation by ICU type (e.g. medical, surgical) and associations with duration of mechanical ventilation, length of stay, and patient mortality.

Methods: We performed a retrospective, observational review of patients, diagnosed with VDRF, admitted to the Medical University of South Carolina (MUSC). To develop our patient cohort, we extracted all admissions, for patients 18 years of age or older, to any MUSC ICU from 1/1/2016 through 6/30/2016. Patients with VDRF were identified using ICD codes 96.xx, as the operational definition of VDRF. We then used this patient list to extract outcomes and measures of interest from MUSC’s electronic medical record (EPIC). We retrieved patient demographic characteristics, data for the construction of Sequential Organ Failure Assessment (SOFA) scores, and ICU type where patients were treated. Because we were specifically focused on adherence to LPV, we extracted comprehensive and detailed mechanical ventilation variables including: mode, tidal volumes, ideal body weight (IBW, calculated from height), and plateau pressures (PPlat). Statistical analysis included descriptive statistics and multiple logistic regression with patient mortality as the outcome. The primary predictor of interest was the percent of recorded tidal volumes falling within 3-6.4 cc/kg IBW.

Results: We identified 1124 unique VDRF patients with a total of 8833 recorded mechanical ventilation observations documenting tidal volumes. Mean patient age was 56.1 years with 40% females, 44% Minority race and a mortality rate of 29.9%. Overall, LPV adherence rate was 33.7%. When ICU location was considered we found LPV adherence rates to be higher among Medical and Med-Surgical ICU patients than those in Surgical-Trauma ICU with the proportions of LPV tidal volumes of 36.6, 38.1, and 17.2. Clinical outcome of observed duration of mechanical ventilation was shorter among the MICU and MSICU (mean 6.8 and 6.9 days) compared to STICU (mean 8.9). ICU length of stay was decreased in the MICU and MSICU (7.2 and 8.0) compared to STICU (8.8). And Hospital LOS was decreased in MICU and MSICU (10.4 and 11.3) compared to STICU (16.1). Logistic regression analysis identified a positive association between proportion of tidal volume measures adherent to LPV and survival with a 10% increase in adherence associated with a 9% reduction in risk of mortality.

Conclusion: Despite widely accepted guidelines, and robust research showing improved outcomes among patients with VDRF treated with LPV, adherence remains disappointing with our highest performing ICU having 38.1% of all tidal volumes adherent to LPV. We found our STICU to have significantly lower adherence than our two ICU’s with medically critically ill population. Future investigation should focus on identifying underlying barriers to LPV adherence and strategies to overcome them.

Category: Resident/Fellow, Clinical Science
Mentor: Dee Ford, M.D., Division of Pulmonary and Critical Care, Andrew Goodwin, M.D., MSCR, Division of Pulmonary and Critical Care, and Kit Simpson, Dr.PH., Department of Healthcare Leadership and Management
Abstract Title: Diagnostic accuracy of Non-Invasive Blood Markers and Liver Stiffness Measurements in Non-Alcoholic Fatty Liver Disease.

Author Names: Shetty, Akshay; Oliver, Lisa; Syn, Wing-kin
1 Department of GI & Hepatology, RHJ VAMC, MUSC

Abstract Text
Introduction:
In the US, prevalence of non-alcoholic fatty liver disease (NAFLD) is rising in association with obesity and type 2 diabetes mellitus. Among those with NAFLD, the presence of significant liver fibrosis (i.e. F2 or higher) is associated with increased liver-related morbidity and mortality. The 2-D shear wave elastography (SWE) is a new ultrasound-based tool that allows point of care measurement of liver stiffness.

Objectives:
In a pilot study, we compared liver stiffness measurement by 2-D shear wave elastography (SWE) with blood fibrosis test for the diagnosis of significant NAFLD fibrosis

Methods:
Diagnostic accuracy was evaluated in a cross-sectional study of Veterans who had undergone a liver biopsy, SWE, and blood fibrosis tests (FIB-4, APRI, BARD, and NAFLD fibrosis score) as part of NAFLD evaluation.

Results:
27 patients with NAFLD had undergone a liver biopsy and a SWE within a year of each other. A SWE reading of >8 kPa positively correlated with significant liver biopsy (i.e. >F2) (r = 0.68, P<0.05). Blood markers of fibrosis were found to be highly variable in their correlation to SWE ( r<0.5), and showed poor accuracy in identifying those with significant liver fibrosis. 40% (8/20) of those with significant liver fibrosis exhibited normal liver enzyme studies.

Conclusions:
SWE is an accurate non-invasive modality in assessing liver fibrosis. By contrast, commonly used blood fibrosis tests exhibited significant variability and correlated poorly with liver stiffness by SWE and liver biopsy stage. A larger cohort of patients will be needed to validate these findings.

Category: Resident/Fellow, Clinical Science
Mentor: Wing Syn, M.B.Ch.B., Division of Gastroenterology and Hepatology
Effect of Methotrexate on Infliximab Trough Levels in Sarcoidosis Patients

Bevill BT¹, Zollars ES², James WE¹
1. Division of Pulmonary, Critical Care, and Sleep Medicine, Medical University of South Carolina
2. Division of Rheumatology and Immunology, Medical University of South Carolina

**Introduction** Sarcoidosis is a systemic granulomatous disease of unknown etiology[1]. When indicated, first line treatment typically includes systemic corticosteroids. Methotrexate is the most commonly used second-line agent[2]. Infliximab is a monoclonal antibody against tumor necrosis factor (TNF)-α which is used as third line therapy in refractory sarcoidosis[3, 4]. Infliximab dosing and medication monitoring vary widely, as do practice patterns regarding use of concomitant medications such as methotrexate. Monitoring for infliximab antibody formation and titrating infliximab dose to serum trough levels is beneficial in other chronic diseases[5-7], but its role in sarcoidosis is unclear. We sought to evaluate infliximab trough levels in a predominantly African American sarcoidosis cohort, and to evaluate the effect of concomitant methotrexate use.

**Methods** Included patients were followed at an academic medical center sarcoidosis clinic and had a diagnosis of sarcoidosis according to accepted criteria[1]. In all cases patients had been on stable doses of infliximab alone or in combination with methotrexate for at least 3 months. Trough infliximab drug and antibody levels were drawn immediately prior to infliximab infusions. Total infliximab dose, interval, gender, race, presence of infliximab antibodies and concomitant methotrexate usage were included in a multivariate model to evaluate their relative effect on infliximab trough levels.

**Results** A total of 15 patients with 18 infliximab levels (60% female, 80% African American) met inclusion criteria. Seven patients (38.8%), each with one infliximab level drawn, were on concomitant methotrexate. The median infliximab dose and interval were 5mg/kg every 6 weeks. Mean infliximab trough level was 17.5µg/mL (median 17.2µg/mL). Of the included variables, gender (p<0.0001), concomitant methotrexate usage (p=0.0002), and presence of antibodies (p=0.0142) had a significant effect on infliximab trough levels, with higher levels in females and ones on concomitant methotrexate. One patient taking only infliximab developed infliximab antibodies and had undetectable trough levels. Trough levels increased significantly after starting methotrexate and she had resolution of antibodies and improvement in symptoms.

**Discussion** In a multivariate analysis, female gender and the concomitant use of methotrexate were associated with higher infliximab trough levels. One patient did have an improved clinical outcome associated with higher infliximab trough levels and the resolution of antibodies that occurred after the addition of methotrexate. The potential effects this has on clinical outcomes across the population is unclear, but warrants additional evaluation in a larger cohort.

**Category:** Resident/Fellow, Clinical Science

**Mentor:** Walter Ennis James, M.D., Division of Pulmonary and Critical Care

Identifying Point of Care Echo Parameters for Predicting Renal Recovery in Cirrhotics with Ascites

Brad Petkovich M.D
Pulmonary Division, Department of Medicine

Introduction:
Renal dysfunction is common among liver cirrhotic patients likely attributable to the complex hemodynamic changes that arises from the systemic and splanchnic vasodilation combined with renal vasoconstriction. Renal failure in these patients portends a particularly poor prognosis – 50% mortality at 1 month and 20% at 6 months (1). Thus predicting patients who are going to respond to an intervention becomes of the utmost importance. We have recorded data in 30 patients with cirrhosis, ascites and an acute kidney injury who subsequently underwent a large volume paracentesis. We recorded the echocardiography variables of IVC assessment, mitral inflow E velocity and Velocity Time Integral (a surrogate for stroke volume) before and after paracentesis. There appears to be a correlation for the percent increase in Velocity Time Integral and improvement in kidney function parameters.

Methods:
We evaluated 30 patients on the Hepatology service over 3 years with point of care echocardiography who have received large volume paracentesis with >/= 5L of ascites removal with pre and post cardiac echocardiography. We assessed for urine output, serum creatinine and Acute Kidney Injury Network (AKIN) stage reduction. We have also recorded intraperitoneal pressures with a disposable pressure transducer.

Results:
In patients not requiring hemodialysis and with >5L of volume removed, 5 of the 30 patients had incomplete data, 4 patients had evidence of intrinsic renal disease. Of the remaining 21 patients, only 2 patients did not have an AKIN stage reduction. The variable most consistently identifiable as predicting improvement in renal function was the velocity time integral. 9 patients with VTI % increases above 15% after paracentesis had greater than or equal 1 AKIN Stage reduction.

Discussion:
The complex physiological changes that go along with liver cirrhosis makes predicting who will respond to interventions provided by medicine providers. Point of care echocardiography and easily obtainable skill as well as a safe and cost effective intervention that allows providers to assess complex hemodynamic parameters for guiding patients back onto the steep end of the Frank Starling when providing care to the complex patient. Currently, it appears that the percent increase in the velocity time integral provides valuable information for predicting renal recovery for cirrhotic patient with acute kidney injury undergoing large volume paracentesis. As a future endeavor we hope to capture the hemodynamic information of patients admitted with cirrhosis, ascites and acute kidney injury undergoing standard of care therapy, to ultimately better provide a more personalized approach to medicine.

Category: Resident/Fellow, Clinical Science
Mentor: Terri Huggins, M.D., Division of Pulmonary and Critical Care
TITLE: The Utilization and Performance of FDG-PET Imaging Based on Pretest Probability in Lung Nodule Management

AUTHORS: Branden W. Luna1, Nichole Tanner1,3, Amanda Walker1, Bastien Bacro-Duverger2  Gerard Silvestri1

INSTITUTION:
1. Division of Pulmonary, Sleep, Allergy, and Critical Care Medicine. The Medical University of South Carolina, Charleston, South Carolina.
2. The Medical University of South Carolina, College of Medicine.
3. Health Equity and Rural Outreach Innovation Center (HEROIC). Ralph H. Johnson Veterans Affairs Hospital, Charleston, South Carolina.

RATIONALE:
Pulmonary nodules are both a common and diagnostically challenging finding for clinicians and patients. While ensuring adequate evaluation of the malignant nodules is paramount, limiting invasive procedures, surgery, and unnecessary imaging in benign nodules is equally as important. The pretest probability of malignancy (pCA) informs subsequent management decisions. Evaluation with Positron Emission Tomography (PET) imaging is incorporated into both the American College of Chest Physicians (ACCP) and British Thoracic Society (BTS) guidelines in the management of intermediate risk nodules. The purpose of this study was to evaluate the performance of PET imaging in the clinical context of pretest probability of malignancy in pulmonary nodules.

METHODS:
This was a retrospective review of prospectively collected data from a multicenter observational trial. The pCA was determined by the treating physician at the time of enrollment. These were grouped into low (<5%), intermediate (5-65%), and high (>65%) risk for malignancy. PET findings including maximum standardized uptake values (SUVmax), PET positivity, and use of PET for staging purposes were recorded. The clinical course after PET imaging was tracked to evaluate if PET findings informed the clinical decision making. The performance of PET in differentiating benign from malignant disease was evaluated based on each risk category.

RESULTS:
Of the 392 patients enrolled, we separated patients that had a PET scan performed as part of their diagnostic workup (Cohort 1) from patients that did not have a diagnostic PET (Cohort 2). We analyzed 151 patients in Cohort 1 and 108 patients in Cohort 2. In Cohort 1, 97 patients had a positive PET scan and of those 18 (18.6%) had benign disease and 79 (81.4%) had malignancy. Cohort 1 patients with a negative PET were found to have benign disease in 41 patients (75.9%) and 13 (24.1%) had malignancy. Patients in Cohort 2 were found to have benign disease in 86 patients (79.6%) and malignancy in 22 patients (20.4%). The pooled sensitivity and specificity of PET scans was found to be 0.859 and 0.695 respectively. Sensitivity in the intermediate pCA group was 0.625 with a specificity of 0.805. Positive predictive value (PPV) and negative predictive value (NPV) were 0.556 and 0.846 respectively. Sensitivity and PPV were better in the high pCA group of cohort 1 at 0.920 and 0.885 but specificity was 0.357 with a NPV of 0.455.

CONCLUSIONS:
The utilization of PET imaging as recommended in guideline statements underperformed specifically in patients with intermediate pretest probability nodules.

Category: Resident/Fellow, Clinical Science
Mentor: Gerard Silvestri, M.D., and Nichole Tanner, M.D., MSCR, Division of Pulmonary and Critical Care
Should routine blood cultures be drawn in hematology/oncology patients receiving broad-spectrum antibiotics?
Clark Alsfeld, MD¹; Don C. Rockey, MD²
¹Division of Hematology/Oncology, MUSC; ²Department of Medicine, MUSC

Introduction:
Blood cultures are drawn regularly on Hematology/Oncology inpatients due to concern for new or uncontrolled infection even if they are on broad-spectrum antibiotics. However, there are limited data about this practice, and there are no guidelines from national societies regarding how frequently or under what circumstances blood cultures should be drawn. In our experience, blood cultures are positive in very few patients receiving broad-spectrum antibiotics, raising questions about the cost effectiveness of obtaining routine blood cultures in these patients. Thus, we aimed to understand the incidence of positive blood cultures in Hematology/Oncology inpatients.

Methods:
We performed a single-center cohort analysis of Hematology/Oncology inpatients in whom blood cultures were drawn between July 1, 2013 and June 30, 2014, including 1,437 blood cultures from 220 unique patients. We reviewed characteristics of the blood cultures in an effort to predict which patients would have a positive blood culture. We also defined the blood usage and cost for blood cultures for this fiscal year on these patients.

Results:
Of the 1,437 blood cultures drawn during the study period, 111 (8%) of the blood cultures grew clinically significant organisms. Gram-positive organisms were more likely than gram-negative organisms, with Coagulase-negative staphylococcus and vancomycin-resistant enterococcus being most common. We then evaluated patients who were receiving broad-spectrum antibiotics. 358 blood cultures were collected while a patient was receiving broad-spectrum antibiotics, and of those only 13 (4%) grew a clinically significant organism. Upon further review of the 13 positive blood cultures, none of the positive blood cultures represented new positive infection.

Conclusions:
In patients receiving broad-spectrum antibiotics, the likelihood of identifying a new clinically significant organism was zero. We speculate that by focusing the utilization of blood cultures, we can improve patient satisfaction, decrease blood usage, and reduce costs without an increase in infectious complications.

Figure 1. The graphs depict the total number of positive blood cultures (n=111, 8%) in the cohort (all cultures, whether or not they were on antibiotics). In (A) is shown a breakdown of gram-positive organisms and in (B) gram-negative and other organisms. Abbreviations: coagulase-negative Staphylococcus (CoNS), methicillin-sensitive Staphylococcus aureus (MSSA), methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus mitis (S.mitis), vancomycin-resistant Enterococcus (VRE), Enterobacter cloacae (E.cloacae), Escherichia coli (E.coli), Klebsiella pneumoniae (K.pneumoniae).
Hands-on Medical Education Tutorial: application of femoral traction splints
Danika Brodak, MD1, Janelle Sourbeer2, Simon Watson, MD1
1 Medical University of South Carolina Department of Emergency Medicine
2 Medical University of South Carolina College of Medicine

Introduction: The annual incidence of femur fractures is approximately 10 per 100,000 person-years. A myriad of complications can result from femur fractures, some of which may be life-threatening. Initially, femur fractures can be treated with femoral traction splints. Splint application is a required competency for pre-hospital medical professionals; however, it is not frequently taught in standard emergency medical education. Our tutorial will attempt to address this deficiency and enable learners to: 1) identify indications and contraindications to splint application, 2) proficiently perform physical exam skills pertinent to femur fractures, and 3) properly apply femoral traction splinting.

Methods: The target audience for this lecture and tutorial is medical students. The initial phase of the tutorial includes a PowerPoint presentation that provides information on femur fractures, on how to conduct the primary physical assessment of femur fractures, and how to properly apply traction splints. The secondary phase of this tutorial will encompass hands-on experience and testing of proper traction splint application. We conducted a pre- and post-tutorial questionnaire assessing participants’ experience and comfort level with femoral traction application. Assessment of the participants’ performance was accomplished via direct observation and completion of a “Critical Action Checklist” which assessed their approach to femur fracture examination and splint application. A post-tutorial debriefing was also conducted to understand areas in which the tutorial could be improved for future sessions.

Results: Overall the tutorial was well-received. Participants felt the context appropriate and pertinent to the emergency medical profession. Learners also felt more confident and proficient in assessing femur injuries and application of traction splints. Our results suggest that students can be quickly and effectively taught proper splint application through a hands-on tutorial.

Discussion: It is important to teach medical professionals on how to properly apply traction splints given the high incidence of femur fractures, the life-threatening complications from fractures, and the implications of improperly placed splints. Traction splint application is not routinely taught to medical students. Our paper suggests that application can be quickly, easily, and effectively taught to medical students through a brief tutorial and hands-on exposure. These findings are important in providing avenues to enhance medical education.

Category: Resident/Fellow, Clinical Science
Mentor: Simon Watson, M.D., Department of Emergency Medicine
Multi-Disciplinary Pulmonary Embolism Response Team (PERT): Initial experience using a PERT at Medical University of South Carolina

Emily Hodskins MD3, Jeffrey Yourshaw MD1, Morgan Randall MD3, Rahul Argula M.B.B.S., MPH2, Dee Ford MD2, Barbara Wiggins, PharmD, BCPS6, Andrew Matuskowitz MD5, Ming Lim, MD4, Alice Boylan MD2, Thomas M. Todoran MD1

1Division of Cardiology, 2Division of Pulmonary and Critical Care Medicine, 3Division of General Medicine, 4Division of Hematology, Department of Medicine, Department of Emergency Medicine5 and Department of Pharmacy6, Medical University of South Carolina, Charleston, SC

Introduction: Acute Pulmonary Embolism (PE) is the third most common cause of cardiovascular death nationwide, resulting in approximately 300,000 annual deaths. Both invasive and non-invasive treatment modalities are available, but a lack of consensus guidelines and randomized trials has led to reliance on expert opinion for treatment. Our PERT was created to serve as a systematic approach to evaluate and risk stratify patients diagnosed with acute PE and provide individualized treatment plans in order to improve patient outcomes.

Process: A PERT page is activated through the hospital operator by a clinician caring for a patient with a PE. Clinical information including vital signs, laboratory data and imaging data are assimilated, after which clinicians from a multi-disciplinary team participate in a conference call or bedside evaluation of the patient. The patient is risk-stratified to massive (defined by the presence of hypotension), submassive (defined as embolus with evidence of right ventricular dysfunction), or low risk PE, according to published guidelines. An individualized treatment plan is then developed for each patient.

Methods: Data from patients treated via the PERT was gathered in a retrospective manner via chart review of electronic medical records. The database was stored on a secure password-protected server (RedCap); results were generated using the RedCap data exporting and reporting system.

Results: From March 2015 to January 2018, there were a total of 150 PERT activations. Of these, 142 patients had a confirmed diagnosis of PE via imaging. Among confirmed PE patients, 21.1% were massive, 69.7% were submassive, and 9.2% were low risk. The most common treatment modality was anticoagulation alone (64.1% of PE patients). Patients with massive PE were more likely to receive systemic thrombolysis (43.3% vs. 4.0% in patients with submassive PE). Treatment with catheter-directed thrombolysis was utilized in 20.0% of patients with massive PE and 24.2% of patients with submassive PE. In-hospital all-cause mortality was 13.4%, with massive PE having the highest mortality at 24.1%. Mortality was lowest amongst patients receiving catheter-directed thrombolysis (0%) and highest among patients receiving anticoagulation alone (16.1%). Among all PERT patients, there were 6.8% in-hospital adverse bleeding events related to treatment. Activations increased over time; in the first 6 months of the PERT implementation period there were 6 activations vs 27 activations in the final 6-month period.

Conclusions: Patients with acute PE are often complex due to comorbid conditions and require careful consideration of multiple available treatment modalities. As our analysis above has demonstrated, patients with massive and submassive PE have a high mortality. A variety of treatment modalities were utilized in our institution using the PERT strategy. We were able to successfully implement a PERT at Medical University of South Carolina and believe that this is an effective and innovative way to treat patients diagnosed with acute PE.

Category: Resident/Fellow, Clinical Science
Mentor: Thomas Todoran, M.D., M.Sc., Division of General Internal Medicine and Geriatrics
Abstract Title: Prevalence of Obstructive Sleep Apnea Among Veterans with Non-Alcoholic Fatty Liver Disease

Author Names
Shetty, Akshay1; Mark Brodie1; Brinton, Daniel1; Syn, Wing-kin1
1 Department of GI & Hepatology, RHJ VAMC, MUSC

Abstract Text
Background:
In the US, prevalence of obstructive sleep apnea (OSA) and non-alcoholic fatty liver disease (NAFLD) is rising in association with obesity and type 2 diabetes mellitus. Recent studies implicate OSA in the pathogenesis of nonalcoholic fatty liver disease (NAFLD) progression.

Objectives:
In this study, we investigated the prevalence of OSA and associated metabolic co-morbidities among Veterans with NAFLD

Methods:
We identified Veterans with OSA or NAFLD between 1/1/2006 to 1/1/2016. Those who carried a concomitant diagnosis of other liver diseases or had excess alcohol use were excluded. Among those with OSA, abdominal cross-sectional imaging was reviewed for evidence of NAFLD. Among those with NAFLD, charts were reviewed to determine if they had undergone a sleep study.

Results:
34/59 patients (57%) with NAFLD had a sleep study. 30/34 (88%, P<0.05) of these had a positive sleep study, and the vast majority were obese (28/30, 93%; p<0.001) and were insulin resistant (24/30, 80%; p<0.05). Conversely, among those with OSA, 83/168 (49%) had cross-sectional imaging. 42/83 (51%) were found to have NAFLD, and the majority of these were obese (94%) and had insulin resistance (61%). Interestingly, only 45/135 (33%) of those with OSA and recent labs had abnormal liver enzymes.

Conclusions:
This pilot demonstrates that there is a high prevalence of OSA among Veterans with NAFLD, and vice versa. Insulin resistance and obesity are associated with OSA and NAFLD. Further studies are needed to determine if those with OSA should be electively screened for NAFLD as most individuals with OSA had normal liver enzymes.

Category: Resident/Fellow, Clinical Science
Mentor: Wing Syn, M.B.Ch.B., Division of Gastroenterology and Hepatology
Can the PHAROS predict the future? – Identifying high risk phenotypes among patients with Systemic Sclerosis associated Pulmonary Arterial Hypertension (SSc-PAH)

Nicholas Fox MD1, Madison Hyer MS2, Viswanathan Ramakrishnan PhD2, Matthew R. Lammi MD, MSCR3, Virginia D Steen MD4, Rahul G Argula MBBS, MPH1
1. Division of Pulmonary, Critical Care, Allergy and Sleep Medicine, 2. Division of Biostatistics, Medical University of South Carolina 3. Louisiana State University Health Sciences Center 4. Georgetown University Medical Center

Introduction:
SSc-PAH patients continue to have a significantly high mortality despite the availability of vasodilator therapies. We attempted to understand the clinical features associated with increased mortality in SSc-PAH patients from the PHAROS database. The PHAROS registry is a prospective, longitudinal multi-center observational study of SSc patients at risk for or with incident pulmonary hypertension (< 6 months from diagnosis).

Methods:
We identified 98 patients with SSc-PAH who had at least two values available for six-minute walk distance (6MWD), B-type natriuretic peptide (BNP), 36-item Short Form survey (SF-36) and World Health Organization functional class (WHO FC). Using linear trajectories for SF-36 and 6MWD changes over time, we performed a cluster analysis on SSc-PAH patients with the primary outcome of all-cause mortality. We then characterized differences between the clusters.

Results:
We identified four clusters with distinct mortality trends over a ten-year period. Clusters (labeled 1, 2, 3 and 4) had a cumulative mortality of 26%, 36%, 39%, and 60% respectively. The median survival times for the four clusters were >9, 5, 7 and 3 years respectively. Cluster 4 was significantly older and had the longest 6MWD when compared to the other clusters. There were no significant between-group differences with regard to disease duration, WHO FC, immunosuppression or vasodilator use. Cluster 4, which had the highest mortality, also had the greatest decline in 6MWD and a higher BNP trend over time. Cluster 1, which had the lowest mortality, exhibited a stable 6MWD over time and a BNP that showed a trend of stability.

Conclusion:
From our analysis of the PHAROS cohort, we were able to identify an SSc-PAH cohort at high risk for disease progression and mortality. This is the first such analysis attempting to identify a high risk “endo-phenotype” within the SSc-PAH population. Our results suggest that a closer follow up of SSc-PAH patients could further help identify such patients. We speculate that these high risk patients may benefit from an aggressive up-titration of therapies and quite possibly an early referral to lung transplantation.

Category: Resident/Fellow, Clinical Science
Mentor: Charlie Strange, M.D., and Rahul Argula, M.D., Division of Pulmonary and Critical Care
Impact of Biomarker Testing on Pulmonary Nodule Management

Paul Bradley Brasher Jr., M.D., Division of Pulmonary and Critical Care Medicine

Introduction
The management of pulmonary nodules depends on the presumed risk of malignancy (pCA). Immune biomarker testing is an emerging modality to aid in differentiating benign from malignant nodules and may be applied to aid in risk stratification. It is unclear at this time, however, how clinicians would integrate the results of a rule-in biomarker test to aid in decision making.

Methods
A survey was designed to assess pulmonary nodule management before and after exposure to a rule-in immune biomarker test. Four clinical cases of intermediate risk pulmonary nodules (low-intermediate pCA 6-33%, high-intermediate pCA 34-64%) were presented and participants indicated pre-test probability for malignancy and management alternatives considered appropriate. Additional data including calculated pCA, PET scan imaging, and blood biomarker test results were presented sequentially, and participants reassessed their management in response.

Results
416 physicians (332 pulmonologists and 84 thoracic surgeons) were included. In the case of a baseline low-intermediate risk nodule followed by a “high level” blood biomarker result, surgical excision increased by 42% (from 31 to 73%), while surveillance dropped by 78% (from 83 to 5%). In a low-intermediate risk nodule with a blood biomarker result of “moderate level of antibody detected” half of participants continued to surveil while the remainder shifted toward more invasive diagnostics. When a high-intermediate risk nodule was evaluated in a patient high-risk for surgery, and a “moderate level of antibodies” biomarker result given, respondents were more comfortable in referring to radiation oncology without a tissue diagnosis.

Conclusions
This study demonstrates the potential impact of a rule-in blood biomarker test on physician management of pulmonary nodules. Absent an actionable test result, physicians rightly follow their initial assessment and management strategy. When presented with a biomarker test result with high specificity, physicians tend to follow the suggested action of the result. This led to a shift toward intervention thereby avoiding a delay in diagnosis. Future clinical utility studies are warranted to investigate these potential changes in management strategies.

Category: Resident/Fellow, Clinical Science
Mentor: Nichole Tanner, M.D., MSCR, Division of Pulmonary and Critical Care
Herpes Zoster Infection and Cardiovascular and Cerebrovascular Events among Patients with Systemic Lupus Erythematosus (SLE)

Pooja Kumari, Diane Kamen
Department of Medicine, Division of Rheumatology, Medical University of South Carolina, Charleston, SC

Introduction: Herpes zoster (HZ) has been identified as a cause of increased risk of stroke and myocardial infarction (MI) in the general population. Only one prior study examined stroke risk in patients with autoimmune diseases following HZ but did not include patients with SLE. We conducted this study to test the hypothesis that HZ infection will contribute to the increased prevalence of stroke and MI among patients with SLE.

Methods: A longitudinal observational registry of patients with SLE followed at MUSC was used for this study. Medical chart review was used to confirm SLE diagnosis, HZ status, and outcomes of interest. Descriptive statistics and Chi square tests (or Fisher’s exact when appropriate) were used to compare demographic, cardiovascular, cerebrovascular and disease-specific characteristics among those with and without HZ. Logistic regression was used to compare groups while adjusting for covariates.

Results: 600 participants with definite SLE diagnosis and any past diagnosis of HZ and / or MI and stroke were included in this study. Of those, 105 (17.5%) had confirmed diagnosis of HZ. Those with HZ included 18.1% of the 543 females and 12.3% of the 57 males (p=0.36) and 15.2% of the 448 black patients and 24.3% of the 152 non-black patients (p=0.01). Overall, patients with HZ were not more likely to have MI (9.5%) or stroke (14.3%) compared to patients without HZ (8.5%, p=0.73) and (17.0%, p=0.50) respectively. In logistic regression models, significant predictors of HZ infection include history of lupus nephritis (OR 2.3, p<0.01) and non-black race (OR 2.6, p<0.01), adjusting for gender, age and SLE disease duration.

Conclusion: Several significant associations between SLE subset and HZ infection risk were observed. However, HZ history did not appear to influence the risk of MI or stroke among patients with SLE in this study.

Category: Resident/Fellow, Clinical Science
Mentor: Diane Kamen, M.D., MSCR, Division of Rheumatology and Immunology
**Predictors of Early Graft Loss in Older Kidney Transplant Recipients**  
P Amaechi, D Rodriguez, V Rao, DJ Taber, A Posadas Salas

**Introduction:** Older transplant recipients greater than 65 years old are vulnerable to early graft loss likely due to burden of comorbidities. Other factors not inherent to the recipient may also contribute to early graft loss. The goal of this study was to conduct a detailed assessment of risk factors for early graft loss in elderly transplant recipients.

**Methods:** Retrospective longitudinal cohort study of 500 kidney transplant recipients (KTR) age ≥ 60, from 2005-2015. Detailed baseline demographic and transplant characteristics were abstracted from medical records. Univariate statistics and multivariable logistic modeling were used for analysis.

**Results:** 39 out of the 500 older kidney transplant recipients (7.8%) had graft loss within 1 year post-transplant. Univariate analysis showed that HTN as etiology of CKD (OR=2.0 [0.9-4.8]), longer dialysis duration (OR=1.2 [1-1.4]), previous transplant (OR=6.2 [1.6-23.4]), higher KDPI (OR=3.3 [1-13]), DGF (OR=3.8 [1.7-8.7]), and acute rejection (OR=3.2 [1.4-7.3]) were significantly associated with early graft loss among older kidney transplant recipients. Multivariate analysis showed that higher KDPI (OR=6.5 [1.2-33]), DGF (OR=4.3 [1.8-10.4]), GFR variability (OR=1.05 [1.03-1.08], PRA (OR=1.02 [1-1.03]) predicted early graft loss. On the other hand, female recipient gender (OR=0.14 [0.04-0.45]) was a protective factor. The same factors seem to predict graft loss within 2 years post-transplant. The final logistic model had excellent discernibility in predicting those at risk for early graft loss among those older than 65 years old.

**Conclusion:** Several recipient and clinical characteristics significantly predict early graft loss in older kidney transplant recipients. Risk stratification of donors and recipients, judicious organ allocation, as well as close clinical monitoring of at-risk patients may help to preempt rapid GFR decline and early graft loss in older kidney transplant recipients. This study strongly suggests that a more rigorous selection and follow-up process especially for high risk older kidney transplant recipients may help improve graft outcomes in this group.

**Category:** Resident/Fellow, Clinical Science  
**Mentor:** Maria Aurora Posadas, M.D., Division of Nephrology
ACEI/ARB Use within One Year of Kidney Transplant is Associated with Less AKI and Graft Loss in Older Recipients
R Rodriguez, P Amaechi, D Taber, A Posadas Salas

Body: As short-term outcomes have improved, optimizing long-term graft survival remains a major focus of transplant programs. Older kidney transplant recipients are particularly vulnerable to acute kidney injury (AKI) and graft loss. This study assessed the safety and efficacy of ACEI/ARB use in older kidney transplant recipients and impact on graft outcomes.

Methods: Retrospective, longitudinal, cohort study of 500 patients age ≥60, who underwent kidney transplantation between 2005-2015. Demographic data, transplant characteristics, and outcomes data were collected. Manual chart abstraction was conducted to determine cardiovascular medication use at discharge, 1 year, 3 years, and 5 years' post-transplant. Univariate and multivariable Cox regression modeling were used to analyze outcomes based on medication utilization.

Results: Mean age of older kidney transplant recipients was 66 years (range 60-81). 59% were males and 50% were African-American. 49% had CKD due to DM. A total of 38, 134, 167, and 112 kidney transplant recipients were on ACEI/ARB at discharge, 1 year, 3 years, and 5 years' post-transplant respectively. ACEI/ARB initiated within 1 year of transplant was strongly associated with lower risk of graft loss (HR=0.62, CI 0.38-0.99, p=0.047). This was driven mainly by a lower risk of death (HR=0.41, CI 0.24-0.71, p=0.002) in the older kidney transplant recipients. ACEI/ARB use was also associated with lower risk of AKI events after 1 year (HR 0.70, CI 0.52-0.95, p=0.02). Moreover, ACEI/ARB was not associated with increased risk of acute rejection or hospitalization. Statin or ASA use did not significantly impact graft outcomes.

Conclusion: Initiation of ACEI/ARB therapy within 1 year of transplant is strongly associated with lower risk of AKI events and graft loss, driven predominantly by lower risk of death in older kidney transplant recipients. Given the relatively low use of these agents, as compared to statins and ASA, transplant clinicians should work to maximize the initiation of ACEI/ARB therapy early on after kidney transplant.

Category: Resident/Fellow, Clinical Science
Mentor: Maria Aurora Posadas, M.D., Division of Nephrology
Risk factors for fungal prosthetic joint infections
Talha Riaz MD1; Cassandra Salgado MD1; Camelia Marculescu MD1; Aaron Tande MD2
Medical University of South Carolina, Charleston, SC1
Mayo Clinic College of Medicine, Rochester, MN2

Introduction: Over the course of last decade, there has been an increase in the size of patient population with implanted, artificial joints. Prosthetic joint infection is a well-documented adverse outcome. While there are IDSA consensus guidelines with regards to treatment of bacterial infections of prosthetic joints, periprosthetic infections due to fungi are rare. Candida species account for less than 1 % of all cases of infections of joint prosthesis whereas mold infections including Aspergillus have also been infrequently reported. To our knowledge, no well-designed multicenter study to identify all the potential risk factors for fungal PJIs

Methods:
• The study design is a retrospective case control study matched 1: 1 of all the patients with fungal (yeast and mold prosthetic joint infections of hip, elbow, knee and shoulder between January 1st, 2006 and December 31st, 2016 at Mayo Clinic Rochester, MN and Medical University of South Carolina, Charleston, SC.
• The cases were identified as all yeast and molds grown in a monomicrobial culture, and the controls were represented by cases of bacterial PJIs within the same period. The matching will be done by joint location and year of infection.
• Data will be analyzed by using univariable and multivariable logistic regression models. Risk factors with a p value of less than 0.1 in univariable analysis will then be entered in a multivariable logistic regression model. We will use SAS and EPI info for statistical analysis
• At the Mayo clinic, PJI database was used to identify cases with fungal infections. Mayo clinic medical record search tool, ACE, was also be used to identify cases of fungal PJI as well as clinical microbiology laboratory data.
• We extracted data including demographic characteristics, comorbid conditions and other relevant risk factors from patient’s chart.

Results:
Preliminary results from Mayo Clinic Rochester:
• Total of 30 cases of fungal prosthetic joint infections (PJIs) were identified over a 10 year study period.
• Gender: 14 were male and 16 females.
• We had 8 right knee PJIs, 6 left knee PJIs, 6 right hip and 10 left hip PJI’s.
• Reason for implantation:
  - degenerative osteoarthritis: 20
  - rheumatoid arthritis: 4
  - avascular necrosis of femur: 3
  - post-traumatic arthritis: 1
  - malignancy: 2
• Duration of onset of symptoms before presentation ranged from 1 to 613 days with an average of 106.5 days.
• Majority of patients(29) presented with pain, followed by swelling of the involved joint(24), purulent drainage(9), sinus tract (7), blister formation(9) and erythema(11).
• Total of 8 patients were on immunosuppression including 4 patients who had rheumatoid arthritis.
• 27 patient have had prior operation at the index joint.
• 21 patients had prior antibiotics in the last 3 months.
• 22 patients had prior joint aspiration.
• Average sedimentation rare was 54.8 mm/hr and average C reactive protein level was 48 mg/L.
• Fungal organisms:
  - candida albicans 18
  - candida parapsilosis 6
  - candida guilliermondii 1
  - candida glabrata 3
  - candida tropicalis 2

Conclusion: Data collected so far from single center (Mayo Clinic) suggests that having history of prior operation is a risk factor that can predispose to fungal prosthetic joint infection. Also exposure to antibiotics in the last 3 months can be considered a risk factor predisposing to fungal PJI. All of the implicated fungi are candida species.
Bilateral Transradial Approach to Alcohol Septal Ablation for Symptomatic Hypertrophic Obstructive Cardiomyopathy

Thomas Miller¹, Justin Heizer¹, John M Neathawk¹, Shawn Shaji², Alexandria Panuccio², Stewart M Benton³, Jeremy D Rier³, Valerian Fernandes³, Christopher D Nielsen³

Background:
Alcohol septal ablation (ASA) for hypertrophic obstructive cardiomyopathy (HOCM) has conventionally been performed via transfemoral (TF) approach. TF procedures historically have higher bleeding and vascular complications while transradial (TR) approach for PCI has led to reduction in bleeding and vascular complications with better patient satisfaction and with similar outcomes. The purpose of this study was to evaluate feasibility, safety, and results of bilateral TR access approach for ASA.

Methods:
Bilateral TR ASA was attempted in 60 consecutive patients (24M, 36 F) with average age 61.75 ± 12.84 years, compared to 65 consecutive patients (27M, 38F) with average age 61.69 ± 13.92 via TF approach. 2 patients in TR group required crossover to TF and thus excluded from this study. Prism 7 software was used to analyze procedural success, fluoroscopy time, contrast use, and vascular complications using two tailed t-test comparison of means and contingency tables with Chi-squared tests assessing statistical significance of categorical data.

Results:
Procedural success defined as ≥50% reduction in resting gradient was similar at 98.33% in TR group (average post-ASA gradient of 7.51) and 95.38% in TF group (average post-ASA gradient of 5.56). There were no strokes or deaths in either group. The TR group had 0 vascular complications, whereas the TF group had 2. Length of stay and average contrast use were equivalent. Average fluoroscopy time was statistically higher in the TR group (19.9±14.2 min vs. 13.8±7.5 min, p-value of 0.004).

Conclusions:
Bilateral TR approach ASA for symptomatic HOCM is feasible, equally effective, with less vascular complications, and a low rate of crossover to TF. TR procedures had equivalent contrast usage, but higher fluoroscopy times when compared to the TF approach.

Category: Resident/Fellow, Clinical Science
Mentor: Valerian Fernandes, M.D., and Christopher Nielsen, M.D., Division of Cardiology