Department of Medicine

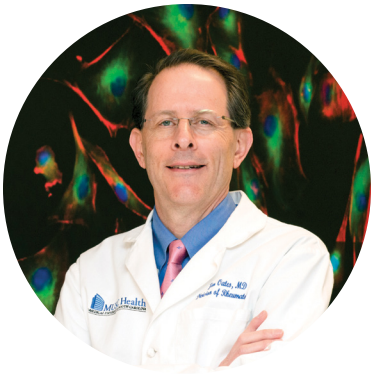
2025 RESEARCH SYMPOSIUM

Friday, March 28, 2025 | 8:00 am - 2:00 pm

Drug Discovery Lobby | Colbert Education Center
Library Lobby | Bioengineering 112 Classroom

FOR MORE INFORMATION VISIT
musc.edu/researchsymposium

MESSAGE FROM THE
VICE CHAIR FOR RESEARCH



Jim Oates, M.D.
Vice Chair for Research
Department of Medicine
MUSC

Thank you to all who contributed to this year's Department of Medicine Research Symposium. We are grateful to the investigators—faculty, residents, fellows, research staff, and students—who shared their innovative work, and to all who attended and supported the event.

Special thanks to the judges for their time and thoughtful evaluation of the presentations, and to the planning team whose efforts made this symposium possible. Your continued commitment to advancing our research mission is deeply appreciated.

Catalin Baicu, Ph.D.
Galina Bogatkevich, M.D., Ph.D.
Anna Brady, M.D.
Elisha Brownfield, M.D.
Melissa Cunningham, M.D., Ph.D.
Zain Gowani, M.D.
Young Im Lee, M.D.
Josh Lipschutz, M.D.
Harriet Mather, M.D.
Paul McDermott, Ph.D.
Blaithin McMahon, Ph.D., MBBChr
Eric Meissner, M.D., Ph.D.
Tammy Nowling, Ph.D.
Toktam Sahranavard, M.D.
Cassy Salgado, M.D., MS
Marharyta Semenikhina, Ph.D.
Amol Sharma, M.D., MSc, FACG, AGAF
Meghan Thomas, M.D., MS, MPH
Justin Van Beusecum, Ph.D.

INNOVATION | IMPACT | INFLUENCE

Meeting Agenda and Schedule

Friday, March 28, 2025

WELCOME AND POSTER SESSIONS: Colbert Library Lobby & Drug Discovery Lobby

8:00 am: **Registration, Poster Hanging, Coffee**

8:20 am: **Welcome and Introduction**
Ben Clyburn, M.D., Chair, Department of Medicine
Jim Oates, M.D., Vice Chair for Research, Department of Medicine

8:30 - 11:00 am: **Poster Presentations**

11:30 am - 12:00 pm: LUNCH - Drug Discovery Lobby

ORAL PRESENTATIONS, KEYNOTE, AWARDS: Bioengineering 112 Classroom

12:00 - 1:00 pm: **Oral Abstract Presentations**

1:00 - 1:45 pm: **Keynote: "MUSC's CAR-T Voyage: From Bench to Bedside"**

Shikhar Mehrotra, Ph.D.
Professor, Department of Surgery
Co-Leader, Cancer Biology & Immunology Program, Hollings Cancer Center Associate Scientific Director, Center for Cellular Therapy
Medical University of South Carolina

1:45 - 2:00 pm: **Research Day Poster Award Ceremony**
Awards recognizing the best research day presentations
Jim Oates, M.D., Vice Chair for Research, Department of Medicine
Ben Clyburn, M.D., Chair, Department of Medicine

Keynote: Shikhar Mehrotra, Ph.D.

Shikhar Mehrotra, Ph.D.
Professor of Surgery
Robert K. Stuart, M.D. Endowed Chair in Hematology/Oncology
Department of Surgery
Medical University of South Carolina

"MUSC's CAR-T Voyage: From Bench to Bedside"

Shikhar Mehrotra, Ph.D. is a Professor of Surgery at the Medical University of South Carolina (MUSC) and holds the Robert K. Stuart Distinguished SC SmartState Endowed Chair in Hematology/Oncology. He serves as the Co-Leader of the Cancer Biology and Immunology Research Program at MUSC's Hollings Cancer Center and is the Scientific Director of the FACT-accredited Clean Cell Therapy Unit, where he leads transformative research in cancer immunotherapy.

Dr. Mehrotra's work focuses on T cell biology and metabolic reprogramming to enhance adoptive cell therapies, including CAR-T cells and tumor-infiltrating lymphocytes (TILs) for melanoma, breast, and prostate cancers. His laboratory has made significant contributions to understanding the metabolic and signaling pathways that regulate T cell function, tumor control, and immunotherapy response, including thiol regulation, p53-mediated glycolysis, and CD38-targeting.

His research has led to an FDA-approved clinical trial utilizing metabolically optimized CD19 CAR T-cell therapy for relapsed/refractory non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL) (ClinicalTrials.gov Identifier: NCT05702853). A principal investigator on multiple NIH R01-funded projects, Dr. Mehrotra has been instrumental in advancing cellular immunotherapy from preclinical studies to clinical applications.

Beyond his research, Dr. Mehrotra is an active reviewer for the National Cancer Institute (NCI) and the National Institutes of Health (NIH), contributing to the evaluation of cutting-edge cancer immunotherapy proposals. His work has been recognized with numerous accolades, including the 2024 Zucker Institute Technology Breakthrough Award and the MUSC Research Excellence Award.

Dr. Mehrotra's expertise continues to shape the landscape of cancer immunotherapy, bridging fundamental discoveries with clinical innovations to improve patient outcomes.

Oral Abstract Presenters

Alec Biscopink, M.D.

PGY-3 Internal Medicine Resident, Department of Medicine

Category: Resident/Fellow
Mentor: Vishal Rao, M.D., MPH
Title: "Implications of Exercise Wedge Pressure in HFpEF Identified by Pressure-Flow Slope"

Aravind Menon, M.D.

Assistant Professor, Pulmonary, Critical Care, Allergy and Sleep Medicine

Category: Junior Faculty
Mentor: Carol Feghali-Bostwick, Ph.D.
Title: "Sex-related Transcriptomic Differences in Idiopathic Pulmonary Fibrosis"

Kush Patel, M.D.

PGY-3 Internal Medicine Resident, Department of Medicine

Category: Resident/Fellow
Mentor: Andrew Schreiner, M.D., MSCR
Title: "MASLD Fibrosis Risk in Primary Care Patients with Diabetes and Prediabetes"

Brennan Winkler

Graduate Student, MUSC College of Graduate Studies

Category: Graduate Student
Mentor: Josh Lipschutz, M.D.
Title: "Tryptophan is a Link Between Cilia and Mitochondria in Renal Tubule Cells"

Poster Participants | Colbert Library Lobby

Poster No.	Presenter	Abstract Title
EL1	Kathryn Counts	Autoantibodies to Extracellular Antigens in Patients with Lupus
EL2	Elaine Park	Infectious Outcomes in Heart Transplantation Patients Receiving Empiric Vancomycin/ Piperacillin-Tazobactam Compared to Vancomycin/ Cefepime
EL3	Mary Elyse	Characterizing Chemotherapy-Associated Drug-Induced Liver Injury
EL4	Will Shugart	Analyzing Racial Disparities in Stroke at a Community Sized Hospital
EL5	Benjamin Teruel	Comparison of performance of Cystatin C to Creatinine in estimating GFR for Melphalan Dosing in Multiple Myeloma Patients Undergoing Autologous Stem Cell Transplant: A Retrospective Analysis
EL6	Dhriti Shah	Outcomes of Kidney Transplant Recipients among Persons with HIV at the Medical University of South Carolina
EL7	Nicolas Ancona	Characterization of E2-Induced Dermal Inflammation
EL8	C. Alex Colvert	Estrogen Receptor Alpha Localization Affects Cytokine Expression After TLR7 Agonism In Lupus Prone Males
EL9	Alexa Corker	Single cell characterization in a murine model of post-traumatic stress disorder
EL10	Ryan Lacey	Sex Differences in Renal Endothelial Inflammation in the Development of Salt-Sensitive Hypertension.
EL11	Zhilan Li	Exploring the Role of Two Estrogen Receptor Alpha Variants in TLR7-induced Macrophage Activation in Lupus
EL12	Marice McCrorey	Sex Dependent Regulation of Endothelin in Humans with Systemic Lupus Erythematosus and A Murine Model of Systemic Lupus Erythematosus-Like Cardiovascular Disease
EL13	Laura Novotny	Characterization of the unique functions of interferon lambda receptor-1 isoforms

Poster Participants | Drug Discovery Lobby

Poster No.	Presenter	Abstract Title
DD1	Jered Schenk	Heart Failure and Transplant-Free Survival After Transjugular Intrahepatic Portosystemic Shunt (TIPS)
DD2	Vincent Bolus	Glucagon-like Peptide-1 Receptor Agonists and Advanced Fibrosis Risk in MASLD
DD3	Robert Easterling	Off Target: Characterizing Post-COVID Sedation Practices in Medical Intensive Care Units
DD4	Sara Hatoum	Histological fibrosis stage and portal hypertension in patients with acute alcohol-associated hepatitis
DD5	Amy Hockman	Atypical Hemolytic Uremic Syndrome: Can anti-complement Rx be discontinued?
DD6	Kathryn Long	New and growing nodules are strongly associated with malignancy in follow-up screens for lung cancer
DD7	Erin Nichols	The burden of receiving vancomycin as part of an OPAT regimen: Time for change?
DD8	Palak Rath	Cross sectional analysis of U1RNP positive Mixed Connective Tissue Disease ILD-A Single center experience
DD9	Evan Rivere	Combined Injectable Regimens in Treatment-Experienced HIV/AIDS Patients at a Southern Academic Medical Center
DD10	Maria Roell	Advances in Adalimumab biosimilar usage in a statewide health system
DD11	Michael Vinzani	Feasibility of Intravenous to Oral Prostacyclin Therapy Outpatient Transition in Patients with Pulmonary Arterial Hypertension
DD12	Danielle Weinberg	Identifying Acute Respiratory Distress Syndrome with Structured Clinical Data Using Machine Learning
DD13	Samantha Wray	Smoking and Progression to Cirrhosis

Poster Participants | Drug Discovery Lobby

Poster No.	Presenter	Abstract Title
DD14	Yosra Alkabab	Diagnostic Accuracy Of The Cepheid Host Response Cartridge For Detection Of Pulmonary Tuberculosis
DD15	Helen Butler	Vascular Activation and Dysfunction in SLE: The Impact of Anti-Endothelial Autoantibodies
DD16	Ellen Esposito	Associations between Tobacco Use and Tobacco Cessation Pharmacotherapy on Rehospitalization
DD17	Anne Maitland	Features of mast cell activation in patients with mannose binding lectin deficien cghand Ehlers- Danlos Syndrome
DD18	Soroush Moradi	Sepiapterin Treatment Improves Survival and Renal Outcomes in a Murine Model of Lupus Nephritis by Restoring Endothelial Integrity
DD19	Leonidas Walthall	Interprofessional Education to Advance Patient Mobility at an Academic Medical Center
DD20	Rachael Werner	Evaluating the Anti-Inflammatory Effects of a Selective Estrogen Receptor Modulator in Systemic Lupus Erythematosus

View the abstracts listed above beginning on page 9 below.

Autoantibodies to Extracellular Antigens in Patients with Lupus **Poster: EL1**

Kathryn Counts, Dulaney Wilson, Leon Furchgott, Gary Gilkeson

Introduction: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by multi-organ involvement and dysregulation of the immune system. Central to its pathophysiology are cytokine dysregulation, complement activation, and immune complex deposition. Prior autoantibody testing in lupus was limited to intracellular antigens like DNA, Ro, La and Sm. A novel technique Rapid Extracellular Antigen Profiling (REAP) allows detection of autoantibodies to extracellular antigens in their 3D confirmation. Over 4000 serum samples from lupus patients, controls and first degree relatives followed over time were assayed. The initial results compared autoantibodies in normals versus lupus patients. Our initial aim was to assess antibodies to Type I interferons (1INF) given their role in lupus and in COVID. In a prior study, patients and controls post COVID infection/vaccine developed auto-antibodies (AAbs) to type I interferons. These autoantibodies increased one's risk for severe viral infections but had a potential beneficial effect in SLE. This study aims to determine the presence of Extracellular AAbs in SLE patients, particularly type I INF AAbs, and determine their association with clinical disease parameters.

Methods: We retrospectively analyzed a longitudinal cohort of 635 subjects with lupus and 485 healthy controls and unaffected family members. Serum antibodies were quantified through a REAP assay. REAP score reproducibility was assessed by running samples in duplicate with a resulting high REAP score correlation (median correlation 0.87). Results are a readout of increased antibody binding to an antigen on a scale of 0-4.

Results: There was a significantly higher prevalence of Type I INF AAbs in patients with SLE than controls. There are 11 different Type I INFs in the library with over 25% of lupus patients testing positive for AAb to a Type I interferon with almost half of the responders having AAb to all 11. Inhibition assays revealed that there is no crossreactivity between the 11 different INF antigens. A prior publication noted that only a small percentage of AAb to Type I interferon are blocking antibodies. Blocking antibodies are the only ones with clinical relevance. Such an assay is in process. Other AAbs detected almost exclusively in lupus patients were antibodies to CD249 (expressed on mesenchymal cells and enhance fibrosis), TThy1 which is a neuronal antigen, and chemokines CCL3L3, CCL4 and CCL3. Of note these reactivities are in clusters with very little overlap. Most patients with anti-CD246 did not have Type I IFN Abs for example. Regarding the entire AAb panel, patients with SLE have on average 4.9 AAbs more than controls. Black patients had 5.9 additional AAbs compared to non-black patients. On average, successive samples had an increase in AAbs over time.

Conclusion: Our study demonstrates a significantly higher prevalence of type I interferon autoantibodies in patients with SLE compared to healthy controls, though these antibodies overall were not strongly associated with lupus nephritis or overall disease activity. Defining blocking antibodies may provide additional insights into their role in disease pathogenesis. Additionally, SLE patients show a broader autoantibody profile, with black patients displaying a greater number of autoantibodies on average. Other clusters of patients had antibodies to CD246, chemokines, and neuronal antigens which were present only in patients with lupus. The clinical association and pathogenicity of each of these antibody clusters is under investigation.

Type of Project: Basic science

Mentor: Gary Gilkeson, MD, Distinguished University Professor

Infectious Outcomes in Heart Transplantation Patients Receiving Empiric Vancomycin/ Piperacillin-Tazobactam Compared to Vancomycin/ Cefepime

Poster: EL2

Ashley L. Golbus[1]*, Elaine Park[1], Courtney E. Harris[2], Rupak Mukherjee[3], Syed Quadri[4], Arman Killic[3], Ryan J. Tedford[5], Patrick T. Murray[6], Blaithin A. McMahon[7]

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5. Division of Cardiology, Department of Medicine, Medical University of South Carolina
6. School of Medicine, University College Dublin, Ireland
7. Department of Medicine, Division of Nephrology, Medical University of South Carolina

Introduction: Empiric antimicrobial selection in orthotopic heart transplantation (OHT) is of critical importance as post-operative infections are a significant cause of morbidity and mortality. While variability of empiric intraoperative antimicrobial selection for OHT exists between centers, both vancomycin and piperacillin-tazobactam (VPT) and vancomycin and cefepime (VC) are acceptable examples. Infectious outcomes in OHT patients have not been prospectively compared between these two antimicrobial regimens. The purpose of this study was to investigate the rates and locations of positive cultures, causative organisms, and time to infection in patients undergoing OHT and receiving empiric VPT compared to VC.

Methods: This was a single-center prospective study in patients undergoing OHT at MUSC between 4/12/2015 and 4/17/2021 (n=120). The empiric intraoperative antimicrobial regimen was transitioned from VPT (n=48) to VC (n=72) as part of a quality improvement to improve AKI outcomes on 6/20/2019, providing a prospective setting to investigate infectious outcomes.

Results: 10.4% of patients receiving VPT had a positive culture within 30 days of OHT, compared to 8.3% of patients receiving VC (p=0.698). No statistical difference in site of infection was identified, with the VPT group cultures including 1 blood, 2 urine, 3 wound, and the VC group including 3 blood, 2 urine, 1 wound, and 1 respiratory (p=0.624). Further, pathogens cultured in the VPT group included *MRSA*, *Klebsiella*, *Enterobacter*, *MSSA*, *Fusifarum*, and *Enterobacter* and in the VC group included *Klebsiella*, *Burkholderia cepacia*, *Actinobacter*, *E. coli*, and *Enterobacter*. There was a statistically significant difference in temporal proximity of infection to OHT, with positive cultures at a median of 28 days for patients receiving VPT and a median of 8 days for patients receiving VC (p=0.028). **Conclusion**: Rates and site of infection were similar between OHT patients receiving empiric intraoperative VPT and VC, however time to infection post-OHT was shorter in patients receiving VC.

Type of project: Clinical

Mentor: Dr. Blaithin McMahon, Department of Medicine, Division of Nephrology

Characterizing Chemotherapy-Associated Drug-Induced Liver Injury **Poster: EL3**

Mary Elyse Moore, COM MDPhD Student (M2/G1)

Introduction: Since their introduction in the early 1900s, chemotherapeutic medications have significantly reduced cancer-related mortality. However, longer survival times have increased the prevalence of long-term consequences, including drug-induced liver injury (DILI). Despite progress in understanding DILI, studies specifically addressing its effects in oncology remain limited. This study seeks to examine the incidence and progression of DILI in patients undergoing chemotherapy.

Methods: This analysis utilized deidentified patient data from the TriNetX platform; this includes 2,028,021 patients seen within the MUSC Health system from 1/1/2013 to 1/12024. We included patients with documented chemotherapy treatment and normal liver function test (LFT) results prior to starting therapy. DILI after chemotherapy was defined as an AST/ALT increase by ≥ 5-fold above ULN, or a total bilirubin ≥ 2.5 mg/dL or increase by ≥ 5-fold or an alkaline phosphatase ≥ 2-fold above ULN, occurring at least one or three months post-chemotherapy initiation. Patients with MASH, alcoholic liver disease, primary or secondary liver and biliary neoplasia, viral hepatitis, or any preexisting liver injury or disease prior to chemotherapy were excluded.

Results: Among 26,397 patients who had normal baseline LFTs and then received chemotherapy, 2,227 and 1,952 experienced DILI-qualifying LFT changes as highlighted above at 1 and 3 months post-treatment initiation, respectively. Within this group overall, at either 1 or 3 months following chemotherapy initiation, mean ALT and AST tripled and quadrupled, respectively, while total bilirubin and alkaline phosphatase levels doubled. The most frequently associated chemotherapeutic classes of drugs implicated were as follows: antimetabolites, alkylating agents, platinum compounds, antitumor antibiotics, taxanes, vinca alkaloids, immune modulators, and hormones. Interestingly, in these patients, the drugs associated with highest frequency of abnormal LFTs were pegaspargase, vincristine, tretinoin, and cytarabine**.** Importantly, the average number of chemotherapy agents received per patient was 2.

Conclusions: Using strict liver test abnormality cutoffs, approximately 8% of patients with no previous liver disease developed abnormal LFTs after chemotherapy treatment. These data suggest that the development of abnormal LFTs after treatment with chemotherapeutic agents is common, and given the design of this study, that such abnormalities are due to DILI. The findings also raise the possibility that there is substantial underreporting of DILI in typical clinical settings.

Type of Project: Clinical, hepatology and cancer

Mentor: Dr. Don C Rockey, Professor and Clinician

Analyzing Racial Disparities in Stroke at a Community Sized Hospital **Poster: EL4**

William W Shugart; Michael D Seemuller, MD
College of Medicine, Medical University of South Carolina, Charleston SC

Abstract
We conducted a single-center retrospective cohort of all patients suspected of having stroke at a community hospital during a two-year period. Patient demographics, hypertension status, National Institute of Health Stroke Scale (NIHSS) scores, hospital unit placement and final disposition were recorded. Only Black and White patients were able to be included due to insufficient representation of other racial groups. This data was analyzed to identify racial disparities at a local level and promote health equity. Identifying health disparities allows us to target resources and interventions to areas of greatest need. We found that Black patients had significantly higher rates of uncontrolled hypertension and NIHSS scores, a marker of stroke severity. Black patients were not significantly more likely to be placed in higher acuity hospital units despite their higher NIHSS scores. When analyzing short-term outcomes as measured by final disposition, Black patients were significantly less likely to experience preferred outcomes such as discharge to home and more likely to experience poorer outcomes such as death. We conclude that in our study population higher incidence of uncontrolled hypertension contributes to greater severity of stroke as measured by NIHSS scores in Black patients compared to White patients. Black patients were not significantly more likely to be placed in higher acuity hospital units and ultimately experienced worse short-term outcomes as measured by final disposition. These conclusions agree with findings in previous studies and require greater efforts by healthcare providers and administrators to ensure health equity and better outcomes for all patients, regardless of race.

Comparison of performance of Cystatin C to Creatinine in estimating GFR for Melphalan Dosing in Multiple Myeloma Patients Undergoing Autologous Stem Cell Transplant: A Retrospective Analysis

Poster: EL5

Benjamin Teruel, BS[1], Ashley Golbus, BS[1], Elaine Park, BS[1], Hamza Hashmi, MD,[2] James Davis, PharmD[3], Blaithin A. McMahon, MD/PhD[4*].

[1]Department of Medicine, Medical University of South Carolina, Charleston, SC, USA.
[2]Myeloma & Cell Therapy Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA.
[3]Department of Clinical Pharmacy and Outcome Sciences, Medical University of South Carolina, Charleston, SC, USA.
[4]Department of Medicine, Division of Nephrology, Medical University of South Carolina, Charleston, SC, USA.

Introduction: Accurate renal dosing of high dose melphalan as conditioning chemotherapy is critical for patients with multiple myeloma undergoing autologous stem cell transplant (ASCT). In Practice, serum creatinine (sCr) is used to estimate glomerular filtration rate (eGFR) for dosing calculations. We conducted a retrospective study to evaluate the role of serum Cystatin C, in comparison to sCr, in calculating eGFR for appropriate melphalan dosing in patients undergoing ASCT for multiple myeloma.

Methods: We analyzed 76 patients with multiple myeloma who received melphalan conditioning before ASCT. Melphalan dosing in all patients was based on pre-transplant eGFR calculated from sCr, 200 mg/m2 for eGFR >50 mL/min/1.73m^2, 140 mg/m^2 for eGFR < 50 mL/min/1.73m^2). We estimated eGFR using both sCr and Cystatin C levels prior to transplantation and observed the 30-day hospitalization and incidence of symptoms of melphalan toxicity. We identified patients who may have qualified for a reduced melphalan dose based on eGFR calculated with Cystatin C that was not observed with eGFR using sCr.

Results: Of 76 patients, 13 (17%) were identified as having received a higher than intended dose of melphalan when eGFR was estimated using SCr rather than Cystatin C (200 mg rather than 140 mg). All of these patients had at least one hospitalization within 30 days of melphalan dosing compared to 60% of the remaining patients who received appropriate melphalan dosing ($p = 0.006$).

Conclusion: Cystatin C may be a superior biomarker for estimating eGFR in the context of melphalan dosing for ASCT in multiple myeloma patients. Use of Cystatin C to calculate eGFR could significantly decrease the incidence of hospitalizations within 30 days, potentially improving patient outcomes and reducing treatment-related toxicity.

Type of Project: Clinical science

Mentor's Name: Dr. Blaithin McMahon, MD/PhD

Outcomes of Kidney Transplant Recipients among Persons with HIV at the Medical University of South Carolina

Poster: EL6

Dhriti Shah MS2; Jillian Catalano, MS3; Kyle M. Crawford, MD; Alexandra G. Mills, MD; Yusra Alkabab; Courtney E. Harris; Ruth O. Adekunle, MD, MSCR[1]

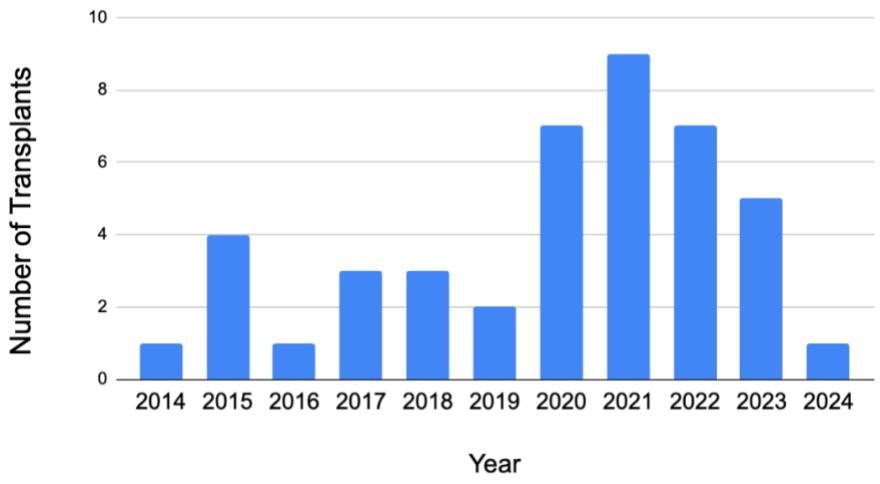
Purpose: Persons with HIV (PWH) are at an increased risk of developing end-stage renal disease (ESRD) compared to individuals without HIV. Kidney transplant is the preferred treatment for ESRD among all patients. Though graft survival between PWH and HIV-negative patients is similar, PWH experience higher rates of rejection. This study describes kidney transplant outcomes among PWH who received post-kidney transplant care at the Medical University of South Carolina (MUSC).

Methods: This was a retrospective review of PWH who received post-kidney transplant care at MUSC Health Care System between May 1st, 2012 and December 31st 2024. Cases were included if sufficient data on their post-transplant care was available in the medical record system. Descriptive statistics were used to analyze clinical characteristics and variables related to post-transplant outcomes.

Results: A total of 44 PWH with kidney transplants were included, of which, 36 (82%) were transplanted at MUSC. Three (7%) received a living-donor kidney and 2 (5%) received multi-organ transplants. Figure 1 represents the number of kidney transplants among PWH performed yearly. All recipients transplanted at MUSC received anti-thymocyte globulin (ATG) for induction therapy. Of the 44 recipients, 12 (27%) experienced delayed graft function, and 4 (9%) developed graft failure. Rejection was treated in 8 (18%) recipients, and the median calculated Panel Reactive Antibody (PRA) was 38%. The median length of time between transplant and rejection was 1.1 years. Regarding infectious complications, 7 recipients (16%) developed Cytomegaloviral (CMV) disease at any point post-transplant, 12 (27%) recipients developed other viral diseases (most commonly BK Viremia), and 6 (14%) had bacterial complications including bacteremia and urinary tract infections. Patient death occurred in 7 patients (16%) with medium time to death being 3.3 years. None of the recipients experienced HIV-related complications.

Conclusion: One-year graft survival among PWH who received post-kidney transplant care at MUSC were comparable to rates described in the literature (approximately 90%). Three-year patient survival was also comparable (approximately 75%). Rejection rates were lower in our study (approximately 30% in the literature), though infectious complications were higher (approximately 25% in the literature). This could be secondary to the universal use of ATG. Ongoing research is needed on managing rejection rates while minimizing risk of infectious complications.

Figure 1. Frequency of PWH receiving a kidney transplant per year



Characterization of E2-Induced Dermal Inflammation **Poster: EL7**

Nicolas Ancona, B.S.[1*], Yucui Li, M.D.[2*], Ludivine Renaud, Ph.D.[1], Carol Feghali-Bostwick, Ph.D.[1] and DeAnna Baker Frost, M.D./Ph.D.[1]

[1]Department of Medicine, Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC
[2]Department of Rheumatology and Immunology, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University Taiyuan, Shanxi, China
[*]Co-1[st] authorship

Background: Scleroderma (SSc) is an autoimmune disease characterized by dermal inflammation and fibrosis. Patients with SSc have high systemic levels of estradiol (E2), a form of estrogen, compared to age-matched controls, and worse mortality. E2 also contributes to dermal fibrosis in SSc, but we are unsure of its role in dermal inflammation. Using bulk RNA sequencing (RNA seq), we investigated inflammatory pathways in E2-treated dermal tissue.

Methods: We isolated total RNA from human skin tissue treated with ethanol (ETOH, vehicle) or E2 for 48 hours for bulk RNA seq. Using bioinformatics software, we identified statistically significant inflammatory genes and pathways. We confirmed transcript and protein levels using qPCR and ELISA, respectively. Primary human skin dermal fibroblasts from healthy donors treated with ETOH or E2, and dermal fibroblasts from patients with SSc were used for mechanistic studies. Statistical significance was defined as $p< 0.05$.

Results: We detected and confirmed that *CXCL5*, *CXCL8*, and *CCL20* chemokines are significantly increased in E2 treated skin tissue compared to ETOH. Additionally, these chemokines are induced by E2 in primary human dermal fibroblasts, with E2-induced CXCL5 and CCL20 transcript and secreted protein levels dependent on the MAPK pathway. We detected an association between E2-induced *IL-6* and *CXCL8* and *CCL20* ex vivo transcripts. Using inhibitors to prevent IL-6 signaling prior to E2 stimulation prevented E2-induced *CXCL8* and *CCL20* transcripts ex vivo and in vitro. SSc dermal fibroblasts that were treated with anastrozole to block E2 produced significantly less *CXCL5* and *CXCL8* transcripts, but not *CCL20* transcripts.

Conclusion: E2 increases CXCL5, CXCL8, and CCL20 chemokines in dermal tissue and fibroblasts. The MAPK pathway and IL-6 signaling are important in their E2-induced expression. Our data suggests E2 production is responsible, in part, for increased *CXCL5* and *CXCL8* transcripts in SSc. Therefore, E2 augments highly active inflammatory pathways in SSc.

Type of Project: Basic science

Mentor's Name: DeAnna Baker Frost, M.D./Ph.D., Assistant Professor

ESTROGEN RECEPTOR ALPHA LOCALIZATION AFFECTS CYTOKINE EXPRESSION AFTER TLR7 AGONISM IN LUPUS PRONE MALES

Poster: EL8

Authors: **C. Alex Colvert**, Jena Wirth, Zhilan Li, and Melissa Cunningham; Medical University of South Carolina, Division of Rheumatology and Immunology, Charleston, South Carolina, United States of America

Background/Purpose:
Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by autoantibody production and immune complex formation, resulting in inflammation and tissue damage. There are gaps in knowledge regarding the pathogenesis of SLE, including female sex as risk. It has also been suggested that male patients diagnosed with SLE have increased disease severity (organ-threatening disease) compared to women. It is known that estrogen contributes to SLE disease expression. Estrogen exerts its effects on the immune system via the nuclear hormone receptor estrogen receptor alpha (ERα), and ERα's function is tissue-, cell-, and localization-specific. Herein, we backcrossed mice with membrane-only ERα (MOER) function and nuclear-only ERα (NOER) function onto the lupus prone B6.Nba2 strain. This allows us to investigate the hypothesis that ERα localization to the membrane may impact disease development.

Methods:
Bone marrow (BM) was isolated from MOER, NOER, and wildtype (WT) male B6.Nba2 mice at 12 weeks of age. On days 0 and 3, BM cells were cultured with GM-CSF and IL-4 (10 ng/uL) to promote dendritic cell (BMDC) differentiation. On day 7, BMDCs were treated with 100 mM of loxoribine (Lox, a Toll-like receptor 7 agonist) or DMSO vehicle for 6 hours. Message levels of pro-inflammatory cytokines IL-1β, IL6, and TNF-α were assessed via qPCR.

Results:
NOER BMDCs had a trend toward increased *Il1β* expression after 6 hours of Lox treatment compared to MOER (p=0.07) but not WT animals (p=0.91). There was a trend toward downregulation of *Il1β* in MOER animals treated with Lox compared to WT animals (p=0.14). MOER BMDCs also had decreased *Il6* compared to WT animals (p=0.02). while BMDCs from NOER mice trended toward increased TNF-α expression compared to MOER (p=0.07) BMDCs.

Conclusions:
These preliminary results suggest that ERα localization to the membrane impactσ IL-1β, IL-6 and TNFα expression in DCs. Non-genomic mechanisms of action by membrane ERα may be involved in anti-inflammatory signaling in the right setting. Further investigation is warranted in female mice to elucidate sex differences in cytokine profiles after TLR7 agonism.

Type of project: Basic science

Mentor's name: Melissa Cunningham, M.D., Ph.D.

Single cell characterization in a murine model of post-traumatic stress disorder **Poster: EL9**

Alexa Corker, PhD candidate, Division of Cardiology, Department of Medicine

Introduction: Post-traumatic stress disorder (PTSD) is a risk factor for cardiovascular disease (CVD). Clinical and basic science research have found strong correlations between PTSD diagnosis and inflammation. Accordingly, we hypothesize fear conditioning increases alterations in immune cell populations compared to controls resulting in adverse cardiac outcomes.

Methods: Male and female C57BL/6 mice were exposed to 5 separate foot-shock incidences (IFS; 1.0 mA, 1 sec duration) in 6 min to mimic trauma induced PTSD. Control mice underwent the same protocol except no foot shocks were experienced. A composite score consisting of behavioral parameters based on DSM-5 clinical standards was generated to separate out mice that do not demonstrate PTSD-like behavioral characteristics and PTSD-like mice. Single cell sequencing of bone marrow cells at 8-weeks post-IFS was performed to determine potential niche cellular phenotypes and pathways associated with PTSD.

Results: Bone marrow single cell analysis revealed male PTSD-like mice had a downregulation of genes associated with cell-cell adhesion (*Clmp*),and inflammatory pathways (*Il31ra*, *Tnfrsf11a*) with upregulation of genes associated with thyroid hormone resistance (*Thrb*), focal adhesions (*Peak1*), and immunity (*Nlrp5*, *Ebf1*, *Bach2*, *Aff3*) in the granulocyte cell cluster. Within the granulocyte cell cluster, female PTSD-like mice had a downregulation of genes associated with environment sensing (*Vmp1*) and immune response (*S100a9*, *Camp*) with upregulation in focal adhesions (*Peak1*), cell proliferation (*Baiap2l1*), and DNA-sensing (*Trim30a*). Gene ontology cellular component analysis showed enrichment ($p<0.5$, FDR<0.05) of immune cell pinocytosis and endocytosis in both male and female PTSD-like mice.

Conclusions: In conclusion, our data suggests that PTSD-associated pathology may be triggering alterations in bone marrow and immune homeostasis.

Type of project: Basic science

Mentor's name: Dr. Kristine Y. DeLeon-Pennell, PhD Associate Professor

Sex Differences in Renal Endothelial Inflammation in the Development of Salt-Sensitive Hypertension.

Poster: EL10

Ryan S. Lacey, PREP Scholar, Division of Nephrology, Department of Medicine

Introduction: Hypertension (HTN), commonly known as high blood pressure, is closely associated with prevalent chronic illnesses, including myocardial infarction, stroke, and kidney disease. According to the World Health Organization, HTN increased from 650 million to 1.28 billion from 1990 to 2019, with males predominating over females. Recent in-vitro experiments have shown the expression of immunological proteins, such as MHC I and MHC II, in a sex-dependent manner in endothelial cells (EC). However, in-vivo MHC I and MHC II sex-dependent expression in ECs remains unknown.

Hypothesis: We hypothesize that the immunological response in mouse renal ECs will be upregulated in males compared to females in salt-sensitive HTN models.

Methods: Male and female wild-type (C57) mice were subject to a nitric oxide synthase inhibitor in the form of N(G)-nitro-L-arginine methyl ester (L-NAME) through their water for two weeks; this diet modification is intended to give the models salt-sensitive HTN. Following this completion, a regular diet ensued for another two weeks. Males and females were randomly selected with one group given a high salt (HS; 4.0%) and the other a normal salt (NS; 0.4%) diet for four weeks. At the terminal time point, mice were euthanized for blood and kidney collection. One cohort's kidneys were evaluated for renal injury protein neutrophil gelatinase-associated lipocalin (NGAL) western blot analysis. At the same time, the blood was spun down for blood plasma soluble intercellular adhesion molecule-1 (sICAM-1) and soluble vascular cell adhesion molecule 1 (VCAM-1) via ELISA analysis. The other cohort's kidneys were separated; one kidney was sent off for future histology immunofluorescence, and the other supplied isolated ECs, which were evaluated via RNA sequencing via CD31 (an EC marker) nanobeads.

Results: NGAL western blot analysis yielded no significant sex difference in either the control or experimental group. ELISA analysis of sICAM-1 showed significant sex differences in expression between control group, but not experimental groups. Elisa's analysis of sVCAM-1 elucidated sex differences in expression between control and experimental groups. Immunofluorescence yielded the presence of MHC I and MHC II in both male and female renal ECs. RNA sequencing showed numerous differences between the sexes. More specifically, immunology-related genes were increased in males compared to females. Males also presented a significant increase in immunology-related genes in HS diet samples compared to NS diet samples. Contrarily, females showed no significant difference in gene response between diet-varied samples.

Conclusion: Our data prove that immunological responses in mouse renal ECs are regulated sex-dependently. Some immediately useful experiments include flow cytometry and EC in-vitro shear stress immunological response. These findings may prove useful in the origination of new HTN therapeutics.

Type of Project: Basic Science

Mentor: Justin P. Van Beusecum, Ph.D.

Exploring the Role of Two Estrogen Receptor Alpha Variants in TLR7-induced Macrophage Activation in Lupus

Poster: EL11

Zhilan Li, visiting PhD student, Division of Rheumatology & Immunology, Department of Medicine

Introduction: Lupus is a classical autoimmune disease affecting mainly women of reproductive age, which has led to investigations into the role of sex hormones and their receptors in its pathogenesis. Our previous research has shown that a functional knockout of estrogen receptor alpha (expressing ERα short, similar to ERα46), but *not* complete ERα deletion (ERα null), is protective for lupus development, suggesting complex effects of ERα variants on lupus pathogenesis. This study aims to investigate the role of two ERα variants, the classic full-length ERα66 and a short variant ERα46, in modulating the inflammatory response in macrophages to Toll-like receptor 7 (TLR7) stimulation, which is involved in the pathogenesis of lupus.

Methods: Raw 264.7 cells (a mouse macrophage cell line) were transfected with a plasmid containing ERα66 or ERα46, with an empty plasmid as a control. After 24h, cells were treated with 0.2 mM loxoribine (Lox), a TLR7 agonist, or an equal volume of DMSO (vehicle) for 1h or 18h. The expression of ERα66 and ERα46 was validated by RT-qPCR and western blot. RNA levels of pro-inflammatory cytokines (IL-6, IL-1β, TNF-α, and MCP-1) were then assessed.

Results: ERa mRNA expression was decreased after Lox treatment for 18h when using primers to exon 4-5 (shared by full-length and short ERα variants), whereas no difference was observed when using primers to exon 1-2 (only exists in ERα66), suggesting the expression of the short ERa variant, which was probably ERa46, decreased in macrophages after TLR7 signal activation. Compared to plasmid control (pc), Raw 264.7 cells transfected with ERα66 or ERα46 plasmids successfully overexpressed ERα66 or ERα46, evidenced by mRNA and protein levels. Unexpectedly, our pilot data showed that both ERα46 and ERα66 overexpression promoted IL-6, IL-1β, TNF-α, and MCP-1 by macrophages in response to TLR7 stimulation, contrary to our hypothesis that ERα46 might antagonize the pro-inflammatory influence of ERα66 in lupus.

Conclusion: Two main ERα variants, ERα66 and ERα46, both promoted the TLR7-induced activation and inflammatory responses of macrophages in the setting of low estrogen. It enriches the understanding of gender effects on lupus pathogenesis by investigating the respective roles of ERa66 and ERa46. Further studies are needed to systemically elucidate the respective roles of ERα66 and ERα46 in different types of immune cells.

Type of Project: Basic science

Mentor's Name: Melissa A. Cunningham, Associate Professor.

Sex Dependent Regulation of Endothelin in Humans with Systemic Lupus Erythematosus and A Murine Model of Systemic Lupus Erythematosus-Like Cardiovascular Disease

Poster: EL12

Marice K. McCrorey, Ph.D Candidate, Department of Medicine, Division of Nephrology

Introduction: Systemic Lupus Erythematosus (SLE) is the most common form of lupus autoimmunity. Interestingly, SLE disproportionately affects women to men (9:1), with a high prevalence in minority women. Clinically, SLE patients have a higher prevalence of hypertension (HTN) and systemic vasculature dysfunction. Chronic HTN is the leading risk factor for the development of cardiovascular disease (CVD). Importantly, women with SLE are at a significantly higher risk of CVD and HTN than their healthy counterparts. However, the causative link between increased CVD prevalence in SLE remains to be elucidated. Interestingly, HTN, CVD, and SLE share a common factor where multiple studies find Endothelin-1 (ET-1), the most potent vasoconstricting peptide, elevated in patients' samples. However, no studies have explored whether sex plays a role in the elevation of ET-1 in SLE patients with and without hypertension.

Methods: To investigate this, we studied both Non-SLE Non-HTN (sex = f/m) (n= 36/14), Non-SLE HTN (n= 30/7), SLE Non-HTN (n = 35/15), and SLE HTN (n=35/15) subjects plasma samples for ET-1 and endothelial activation. In addition, utilizing the female and male Resquimod-induced B6.Nba2 murine model of SLE-associated CVD. We performed a longitudinal study measuring cardiac dysfunction with echocardiography and analysis of the ET-1 levels at the terminal timepoint.

Results: Plasma ET-1 levels were significantly elevated in SLE females ($p=0.0003$) and not in males ($p=0.9956$) compared to sex matched Non-SLE controls. HTN status only contributed to ET-1 elevated in SLE HTN females compared to SLE Non-HTN ($p=0.0150$) and Non-SLE HTN ($p=0.0065$). No differences in male ET-1 by HTN status were observed. Plasma ET-1 had a significant positive correlation with systolic blood pressure (SBP) in females ($r = 0.3316$; $p=0.0009$) while no correlation was observed in males. Plasma sVCAM-1, a marker of endothelial activation, was significantly elevated in female SLE ($p <0.0001$) and trended in elevation in male SLE ($p=0.0616$) compared to sex matched controls. Furthermore, sVCAM-1 levels positively correlated with ET-1 in females ($r =0.2663$; $p =0.0099$) and did not in males. Analysis of female B6.Nba2 hearts demonstrated a significant increase in cardiac ET-1 ($p=0.0027$) and VCAM-1 ($p=0.0268$) compared to controls that was not observed in males.

Conclusions: The current findings of this study warrant further exploration into the sex dependent pathological role of ET-1 signaling in SLE-associated CVD. Moreover, we demonstrate that female B6.Nba2 mice have elevated ET-1 levels and endothelial activation compared to sex matched controls. Furthermore, this study may have broad impacts on the development of ET system targeting medications in the treatment of HTN and CVD in SLE patients.

Type of Project: Clinical and Basic

Mentor's Name: Dr. Justin Van Beusecum, Ph.D., Assistant Professor COM DOM Nephrology

Characterization of the unique functions of interferon lambda receptor-1 isoforms

Poster: EL13

Laura A. Novotny, Ph.D., Staff Scientist, Division of Infectious Diseases, Department of Medicine

Introduction: Lambda interferons(IFNLs) are cytokines that bind a receptor comprised of interferon lambda receptor-1(IFNLR1) and IL10RB. Three transcriptional isoforms of *IFNLR1* are expressed: isoform1 is signaling capable, isoform2 has a truncated intracellular JAK1-binding domain and isoform3 is secreted. In hepatocytes, isoform1 enables IFNL-induced antiviral and proinflammatory gene expression with inhibition of hepatitis B virus replication, while isoforms2&3 only permit antiviral gene expression with minimal viral inhibition. Here we explored the mechanisms imparting these responses to better understand how relative expression of each receptor variant influences the cellular response to IFNL exposure.

Methods: HEK293T and iPSC-derived hepatocytes with or without endogenous IFNLR1 expression were engineered to express doxycycline(dox)-inducible, FLAG-tagged IFNLR1 isoform1,2,3 or empty vector(EV) constructs. Cells were treated +/-dox, then stimulated with IFNL3. The kinetics of IFNLR1 trafficking by imaging cytometry, JAK-STAT signaling mediator phosphorylation by flow cytometry and susceptibility to clinically-relevant inhibitors by qRT-PCR were examined.

Results: IFNLR1 isoform1 was internalized 5min after binding IFNL, leading to rapid STAT1 phosphorylation. Isoform1-expressing cells also showed enhanced phosphorylation of signaling mediators JAK1 and TYK2 15min after engaging IFNL, compared to EV. Further, isoform1-expression imparted reduced susceptibility to JAK1 inhibitor, but enhanced susceptibility to TYK2 inhibitor, compared to EV. In contrast, IFNLR1 isoform2 had slower internalization and STAT1 phosphorylation kinetics, compared to isoform1. Isoform2-expressing cells did support phosphorylation of JAK1 and TYK2, however were more susceptible to JAK1 and TYK2 inhibitors compared to isoform1-expressing cells. Ongoing work includes global transcriptomic and phosphoproteomic analyses.

Conclusions: We are beginning to dissect the mechanisms that impart unique functions observed for each IFNLR1 isoform. As inhibitors that target JAK-STAT signaling are used to treat autoimmune diseases and cancers, it will be important to understand how these therapies may also impact IFNL-IFNLR1 signaling which are critical in innate immune responses against a wide variety of pathogens.

Type of Project: Basic science

Mentor's Name: Eric G. Meissner, MD PhD

Heart Failure and Transplant-Free Survival After Transjugular Intrahepatic Portosystemic Shunt (TIPS)

Poster: DD1

Jered Schenk, MD, Department of Internal Medicine, Resident

Co-Author: Hampton Sasser, MD, Department of Gastroenterology and Hepatology, Fellow

Introduction: Cirrhosis has a widespread impact on the cardiovascular system. Cirrhotic cardiomyopathy (CCM) has been defined, but the influence of cardiac dysfunction on patient outcomes following TIPS is not clear. The aim of this study was to determine the association between CCM and the development of symptomatic heart failure (HF), as well as its effect on 1-year transplant-free survival (TFS) following TIPS placement in patients with cirrhosis at MUSC.

Methods: Retrospective cohort study of 235 TIPS cases between January 2016 and March 2023. Exclusion criteria: age <18 years, no underlying cirrhosis, absence of pre-TIPS echocardiogram, or lack of post-TIPS follow-up. Demographic and comorbid variables were collected as well as measures of cirrhosis severity and echocardiographic parameters. Primary outcomes were post-TIPS HF and 1-year TFS. Univariate analyses were done using chi-square or Fisher's exact test for categorical data and Mann-Whitney U test for continuous data. SPSS was used for all statistical analyses.

Results: Of 235 TIPS cases, 159 met the inclusion criteria. Post-TIPS HF occurred in 25/159 (15.7%). Patients who developed post-TIPS HF were more likely to be obese (BMI >30 kg/m2, 23.1% vs 10.6%, p=0.046) and have coronary artery disease (40.0% vs 12.2%, p=0.004). Obesity also negatively impacted TFS (55.4% vs 31.9%, p=0.003%). The presence of CCM did not predict HF but was associated with worse TFS (21.4% vs 62.1%, p=0.003). The echocardiographic parameters most associated with reduced TFS were measures of diastolic dysfunction, including A wave, septal e' wave, and E/e' ratio. Compared to subjects with alcoholic cirrhosis, those with MASH had worse diastolic function and TFS (44.2% vs 70%, p=0.015). A higher pre-TIPS MELD score negatively impacted TFS.

Conclusion: Post-TIPS HF is not uncommon but difficult to predict using pre-TIPS echocardiography data alone. However, the presence of CCM (particularly diastolic dysfunction) and metabolic risk factors are associated with worse post-TIPS survival.

Type of Project: Clinical Research

Mentor's Name: David Koch, MD

Glucagon-like Peptide-1 Receptor Agonists and Advanced Fibrosis Risk in MASLD

Poster: DD2

Vincent Bolus MD, Internal Medicine PGY-2, Department of Medicine

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common cause of chronic liver disease in the United States and is a leading cause of liver-associated morbidity and mortality. Advanced fibrosis is the critical link between MASLD and severe liver outcomes, and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have demonstrated benefit in clinical trials to stop and potentially reverse fibrosis progression in MASLD. We examined the association of GLP-1 therapy with advanced fibrosis risk progression in real-world primary care.

Methods: We performed a retrospective cohort study of electronic health record (EHR) data from primary care patients with MASLD to evaluate the association of GLP-1 therapy with advanced liver fibrosis risk. We identified patients with MASLD that were exposed to a therapeutic dose of GLP-1 therapy and had inputs for calculating Fibrosis-4 Index (FIB-4) scores pre- and post-exposure. We identified control patients with MASLD and at least 2 FIB-4 scores 6-36 months apart. We then limited our cohort to patients with T2DM, since virtually all of our exposed patients had T2DM. The primary outcome of interest was a stable to improved FIB-4 advanced fibrosis risk. Our primary exposure was GLP-1 therapy. We performed univariate analyses for the overall cohort and by exposure groups, comparing continuous variables using two sample t tests and categorical variables using Chi square tests. We developed unadjusted and adjusted logistic and linear regression models for the outcomes of stable to improved advanced fibrosis risk and FIB-4 score (as a continuous variable), respectively.

Results: The cohort included 764 patients, of whom 126 (16%) were exposed to GLP-1 therapy. Of the exposure group, 80% of patients had a low-risk FIB-4 at baseline compared to 67% of the control group ($p=0.01$). More patients exposed to GLP-1 lost weight (60% vs. 45%, $p<0.01$) and had a significant decrease in ALT (-7.2 IU/L vs. 0.2 IU/L, $p=0.01$) compared to the control group. For the entire cohort, 615 (80%) of patients had a stable or improved fibrosis risk, which did not significantly differ by GLP-1 exposure ($p=0.11$). There was no significant association between GLP-1 exposure and FIB-4 risk category (aOR 1.28; 95%CI 0.74-2.22) or FIB-4 score (β 0.06; 95%CI –0.39 - 0.51) in the adjusted logistic and linear regression models, respectively.

Conclusions: While there was not a significant decrease in FIB-4 score, there was a significant decrease in ALT in patients exposed to GLP-1 RAs, which correlates to decrease in steatosis compared to the control group. Patients with higher risk FIB-4 scores who would benefit from GLP-1 RAs were not exposed to a therapeutic dose of them, suggesting a potential missed opportunity in prescribing practices.

Type of Project: Clinical Research

Mentor's Name: Andrew Schreiner, MD MSCR, Associate Professor, Department of Medicine

Off Target: Characterizing Post-COVID Sedation Practices in Medical Intensive Care Units

Poster: DD3

Robert Easterling, MD
Pulmonary and Critical Care Fellow
Division of Pulmonary, Critical Care, and Sleep Medicine

Introduction:
Light sedation is associated with comparatively better outcomes than deep sedation among mechanically ventilated patients in the intensive care unit (ICU) and is recommended by society guidelines. However, recent evidence suggests declining adherence to light sedation. We sought to characterize sedation practices in the medical ICUs of our institution as the initial phase of a sedation-focused quality improvement project.

Materials and Methods:
We performed a retrospective data analysis in patients receiving mechanical ventilation in 3 medical ICUs over a 2-month period. Richmond Agitation-Sedation Scale (RASS) scores were extracted and 24-hour means were calculated. RASS scores between -3 and -5 were considered deeply sedated and RASS scores between 0 and -2 were considered lightly sedated. Patients whose mean 24-hour RASS fell in the deeply sedated range were manually reviewed. If the patient was not receiving sedation or if their clinical diagnosis necessitated deep sedation based upon criteria established a priori, the score was deemed “appropriate”. If a patient did not meet these criteria, they were considered “inappropriately deeply sedated.” Descriptive statistics were used to compare the proportion of ventilator days spent lightly sedated versus inappropriately deeply sedated versus appropriately deeply sedated.

Results:
During the study period, 168 unique patients received mechanical ventilation for a median of 4 days leading to a total of 839 ventilator days. Of the total ventilator days, 271 (32%) were associated with an average RASS score corresponding to deep sedation, with 159 (19%) of all ventilator days spent inappropriately deeply sedated. Manual review revealed that 75 (45%) patients experienced at least one ventilator day inappropriately deeply sedated.

Conclusions:
Targeting and maintaining light sedation remains an opportunity for improvement in the ICU. These data will be utilized to inform the next phase of our quality improvement project.

Type of project: Clinical, QI

Mentor:
Andrew Goodwin, MD
Professor of Medicine
Division of Pulmonary, Critical Care, and Sleep Medicine

Histological fibrosis stage and portal hypertension in patients with acute alcohol-associated hepatitis

Poster: DD4

Sara Hatoum, MD, PGY-2, Department of Internal Medicine

Introduction: Alcohol-associated hepatitis (AAH) is an acute form of liver injury resulting from excessive alcohol use. Most patients with AAH have significant hepatic fibrosis and many have associated portal hypertension - even when cirrhosis is not present. Here, we aimed to assess the prevalence of portal hypertension in patients with AAH and examine the correlation between hepatic venous pressure gradient (HVPG) level and histological stage.

Methods: In this cohort analysis, we examined consecutive patients with definite AAH who were admitted to an academic medical center between 2012 and 2022 and underwent HVPG measurement. Patients were considered to have definite AAH if they met clinical and histological criteria based on NIAAA Alcoholic Hepatitis Consortia criteria [1]. They were classified into 3 groups: noncirrhotic (F1-F3), cirrhotic (F4), and chicken-wire fibrosis. One-way ANOVA was used to compare mean HVPG among the three groups.

Results: The cohort included 154 patients with histologically proven acute AAH (age 44, range 22-73; 53% male). Ascites and documented esophageal varices were present in 147 and 54 patients, respectively. The average HVPG overall was 17±7 mmHg. 141 (92%) patients had clinically significant portal hypertension and 90 (58%) patients had histological evidence of cirrhosis. Cirrhotic patients had significantly higher HVPG levels than noncirrhotic patients (18.4±6.5 vs.14.2±7.8 mmHg, p=0.02) and those with chicken-wire fibrosis (18.4±6.5 vs 15.3±4.9 mmHg, p=0.03). There was no significant difference in HVPG among patients with F1 to F3 fibrosis and those with chicken-wire fibrosis (p=0.8) (Figure 1).

Conclusion: Clinically significant portal hypertension is pervasive in patients with AAH, regardless of the degree of fibrosis and patients with cirrhosis had the highest level of portal hypertension. We speculate that the cause of portal hypertension in patients with only F1-F3 fibrosis was related to steatosis and hepatocyte swelling. Finally, we conclude that there is a positive correlation between histological stage and HVPG level in patients with AAH.

Type of project: Clinical

Mentor: Don C. Rockey, MD, Distinguished University Professor, Gastroenterology & Hepatology

[1]Crabb, D.W., et al., *Standard Definitions and Common Data Elements for Clinical Trials in Patients With Alcoholic Hepatitis: Recommendation From the NIAAA Alcoholic Hepatitis Consortia.* Gastroenterology, 2016. **150**(4): p. 785-90.

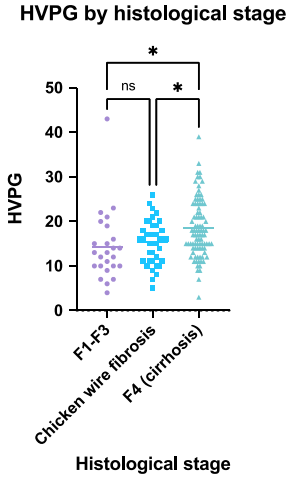


Figure 1. HVPG by histological stage. Shown is a graph comparing the portal pressures between different histological groups.

Atypical Hemolytic Uremic Syndrome: Can anti-complement Rx be discontinued?

Poster: DD5

Amy Hockman, DO, Internal Medicine, Department of Medicine

Introduction: Hemolytic uremic syndrome (HUS) is a severe disorder marked by microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury. Atypical HUS (aHUS), often complement-mediated, has historically carried a high mortality but is now treatable with anti-complement therapies like eculizumab and ravulizumab. Despite the proven efficacy of these therapies, their high cost and risk of adverse events, including an increased susceptibility to meningococcal infections, raise concerns about long-term use. The optimal duration of complement inhibition remains unclear, prompting efforts to explore the possibility of treatment discontinuation. This systematic review and meta-analysis aim to evaluate the benefits and risks of stopping anti-complement therapy in complement-mediated aHUS.

Methods: A comprehensive search of PubMed, Scopus, and CINAHL was conducted for studies on the cessation of anti-complement therapy in aHUS. Studies were eligible if they compared continuing vs. discontinuing eculizumab or ravulizumab in patients diagnosed with complement-mediated aHUS. Data were extracted on relapse rates, relapse-free survival, kidney outcomes, survival, hospital admissions, and adverse events. Quality of studies was assessed using the Newcastle-Ottawa Scale for observational studies. A meta-analysis was conducted to synthesize findings on relapse rates and other clinical outcomes.

Results: Of 3301 identified studies, 13 observational studies (3 case-control, 10 cohort) enrolling 584 patients were included. Discontinuation of therapy was associated with a higher risk of relapse (odds ratio [OR] 4.19, 95% CI: 1.5–11.7, p=0.01). The effects of treatment discontinuation varied by study design, with case-control studies showing significant benefits for continuing therapy, while cohort studies did not consistently favor one approach. Genetic factors, particularly mutational burden, influenced outcomes; patients with multiple genetic mutations had better outcomes with continued therapy. Adverse events, particularly meningococcal infections, were reported, but most were manageable with treatment.

Conclusions: Continuing anti-complement therapy for aHUS reduces the risk of relapse, particularly in patients with high genetic mutation burdens, but the evidence supporting its long-term use is mixed. Discontinuation may be viable in certain patients, especially those with fewer genetic mutations who are at the lower risk of relapse. However, due to the risk of bias in the included studies, and the absence of randomized controlled trials (RCTs), further prospective studies are needed to define the optimal duration of therapy. Until such evidence is available, clinicians should make treatment decisions based on individual patient characteristics, including genetic profile and relapse history.

Type of Project: Systematic Review and Meta-Analysis

Mentor's name: Benjamin Djulbegovic, Alex Coltoff

New and growing nodules are strongly associated with malignancy in follow-up screens for lung cancer

Poster: DD6

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Introduction: Pulmonary nodules are frequently detected on low dose computed tomography (LDCT) screening for lung cancer, though the majority are benign. Nodules detected on follow-up scans may be new or show interval growth since baseline. The purpose of the study was to quantify the risk of malignancy among new or growing nodules detected on follow-up LDCT.

Methods: Persons in the LDCT screening arm of the National Lung Cancer Screening Trial (NLST) with a baseline screen and at least one follow-up screen were included. The primary exposure of interest was nodules that were new or growing on the first (T1) follow-up LDCT. Other covariates included age, sex, family history of lung cancer, presence of emphysema, nodule size, attenuation, lobe location and spiculation. The primary outcome was lung cancer diagnosis within 2 years of T1.

Results: Among 24,604 participants with baseline and T1 follow-up LDCT, 6,952 had nodules present during the first round of follow-up screening from which lung cancer was diagnosed within 2 years in 208 participants. Compared to pre-existing nodules with no growth, new nodules were associated with nearly 4-fold greater odds of lung cancer within 2 years (OR: 3.9, 95% CI: 2.51, 6.05, $p<0.0001$); pre-existing nodules with growth were associated with nearly 20-fold increased odds (OR: 19.7, 95% CI: 13.6, 28.4, $p<0.0001$).

Conclusion: New and growing nodules detected on follow-up LDCT are strongly associated with the risk of malignancy. The magnitude of these risks is substantially greater than for most other well-established risk factors.

Type of project: Clinical research

Mentor's Name: Gerard Silvestri, MD MS, Hillenbrand Professor of Thoracic Oncology, Division of Pulmonary, Critical Care, Allergy and Sleep Medicine, Department of Medicine

The burden of receiving vancomycin as part of an OPAT regimen: Time for change?

Poster: DD7

Erin Nichols, DO, Zach Gruss, PharmD, Chloe Jackson, PA-C, Charles Teixeira, DO, Cassy Salgado, MD, MS (mentor)
Division of Infectious Diseases, Department of Medicine

Introduction: Outpatient parenteral antimicrobial therapy (OPAT) allows timely discharge of patients who require extended regimens. This requires close monitoring via labs, imaging, and communication with multiple services by our OPAT team. Vancomycin (vanco) is a highly utilized antibiotic for OPAT, however, can be associated with significant toxicity. We sought to quantify the OPAT burden associated with vanco and whether use of daptomycin (dapto) would have less while maintaining good outcomes.

Methods: We retrospectively reviewed patients enrolled in OPAT between 10/2023 and 2/2025. We compared demographics, OPAT characteristics, interventions, and outcomes for patients who received vanco as part of their OPAT regimen to those who received dapto. The t-test was used to compare continuous variables, and the z-test was used for proportions.

Results: 1,739 patients were enrolled in OPAT over the study period, 370 received vanco and 201 received dapto. There were no differences in age or sex between the groups. The most common reason for OPAT was osteoarticular infection (58.9% in the vanco group and 50.7% in the dapto group). Fewer patients who received vanco had an endovascular or intra-abdominal infection compared to those who received dapto (10% vs 15.9%, $p=0.04$ and 1.6% vs 8.5%, $p<0.001$, respectively). Receiving vanco was associated with 34-fold higher odds of having an OPAT team directed intervention (353 interventions for vanco vs 76 for dapto $p<0.001$). The majority (62%) of interventions among the vanco group were due to therapeutic drug monitoring and most (57.9%) among the dapto group were related to abnormalities in CMP/BMP with LFTs. Assuming an intervention takes 5 to 20 minutes to complete, the time cost for the OPAT team for the vanco group ranged from 29.4 to 88.3 hours compared to 6.3 to 25.3 hours for the dapto group, a 3.5-to-4.7-fold higher time investment for the vanco group ($p<0.001$). Among patients who received vanco, 182 encounters (interactions outside a regularly scheduled visit) occurred, and 36 patients required hospitalization for an average of 8.5 days (estimated cost $594,000). Among patients who received dapto, 72 encounters occurred, and 29 patients required hospitalization for an average of 6.7 days (estimated cost $384,000). Completion of therapy was high in both groups (86.9% for vanco and 86.3% for dapto) and reasons for not completing therapy were similar (patient stopped or transitioned to hospice, lost to follow up). All-cause mortality and treatment failure rates were also similar (3.2% for vanco vs 2.4% for dapto, and 2.4% for vanco vs 4.5% for dapto, respectively).

Conclusion: The burden associated with the use of vancomycin for OPAT was significantly greater compared to that of daptomycin without differences in outcome. Use of daptomycin instead of vancomycin should be considered among our OPAT cohort, especially for osteoarticular infections.

Type of Project: Clinical

Mentor: Cassy Salgado, M.D., MS

Cross sectional analysis of U1RNP positive Mixed Connective Tissue Disease ILD-A Single center experience

Poster: DD8

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[1]Medical University of South Carolina, Charleston, SC, USA

Introduction: This study seeks to analyze the demographic characteristics, radiographic patterns, clinical and the immunosuppression status of patients with interstitial lung disease (ILD) associated with anti-U1RNP antibody positivity.

Methods: We performed a retrospective chart review of patients with positive U1RNP antibody serology between 2019 to 2023. We abstracted demographic data, presenting symptoms, and immunosuppressive agents employed in the cohort, along with clinically relevant baseline variables including Forced vital capacity (FVC) and Diffusion capacity (DLCO).

Results: We identified 140 individuals in the cohort. Mean age of presentation was 44 yrs (SD 17.6), majority female (76.4%). 65.7% (n=92) were white, 29.3% African American and 5% belonged to other groups. Most common presenting symptom was arthralgias (n=52, 37.1%) followed by pulmonary symptoms (n=32, 22.9%). 40% did not have any lung pathology on CT chest; those with ILD most commonly had NSIP ,(n=32, 22.9%) followed by unclassifiable (n=14, 10%), UIP (n=8, 5.7%), and OP (n=7, 5%). Chest.

The minority of patients (n=12, 8.5%) not on immunosuppression were older than the rest of the cohort (Mean age 68.4 vs 42.1). Interestingly, 6 patients who had lung involvement were not on immunosuppression. The baseline disease characteristics between the two groups showed similar FVC (64% predicted vs 66% predicted) but lower DLCO (45% predicted vs 53% predicted) for those not on immunosuppression Amongst the patients on immunosuppression, 67 (47.8%) were found to have ILD, with NSIP being the most common followed by unclassifiable, UIP and OP. 9 patients died during the study period.

Conclusion: Interstitial lung disease (ILD) was identified in 43.6% of the cohort with positive anti-U1RNP antibodies, with the majority exhibiting a non-specific interstitial pneumonia (NSIP) radiographic pattern. Additionally, 90% of these patients were receiving immunosuppressive therapy.

Combined Injectable Regimens in Treatment-Experienced HIV/AIDS Patients at a Southern Academic Medical Center **Poster: DD9**

Evan Rivere, MD; Chief Fellow, Division of Infectious Diseases; Department of Medicine

Introduction: Long-acting injectable antiretroviral therapy (ART) regimens represent a potential solution to many problems facing people living with HIV. These include intermittent adherence leading to drug resistance, difficulty with absorption, high pill burden, and stigma. To date, there are few publications describing the efficacy of all-injectable ART regimens other than cabotegravir/rilpivirine (CAB/RPV-LA), which is limited to those without resistance to this regimen.

Methods: In this case series, we describe eight patients who required a fully injectable ART regimen but were not candidates for cabotegravir/rilpivirine (CAB/RPV-LA). Data abstracted from the electronic medical record included baseline medical history, demographics, ART history and reason for ART switch, genotypic resistance markers, viral load trends, and CD4 count pre- and post- injectable ART regimen.

Results: Adherence issues represented the most common indication for an injectable regimen, in 5 of 8 (62.5%). Other reasons included poor enteral absorption in a patient with short gut syndrome, cobicistat interacting with inhaled corticosteroids, and chronic esophagitis limiting oral intake. All patients had some level of drug resistance precluding CAB/RPV-LA as a single agent. Two patients were on CAB-LA + lenacapavir (LEN), four on CAB/RPV-LA + LEN, and the remaining two on CAB + LEN + ibalizumab. Seven patients remained on a completely injectable regimen. Four patients had a detectable viral load at the start of their all-injectable regimen, and three of these achieved viral suppression. One patient's viral load remained above 300 while on an all-injectable regimen. Therefore, an oral protease inhibitor was added to her regimen, with subsequent undetectable viral load. The remaining four patients were virally suppressed at the time of switch to an all-injectable regimen and remained suppressed.

Conclusion: These cases demonstrate that an all-injectable regimen may be a safe and effective option for PLWH, barring logistic issues of maintaining such a regimen. Given limitations in size, further long-term prospective studies would be beneficial.

Type of Project: Clinical

Mentor's Name: H. Jensie Burton, MD, Assistant Professor, Division of Infectious Disease, MUSC

Advances in Adalimumab biosimilar usage in a statewide health system **Poster: DD10**

Maria Roell, MD, Department of Internal Medicine, Medical University of South Carolina, Charleston, SC

Background: Biologic therapies have revolutionized the management of Crohn's disease and ulcerative colitis (UC) by reducing disease burden, improving quality of life, and minimizing steroid dependence. However, high costs and limited accessibility of biologics have impeded widespread adoption. Biosimilars have emerged as a cost-effective alternative to address these challenges. This case series examines how a statewide health system has incorporated Adalimumab biosimilars into clinical practice. By assessing relative efficacy and time-to-treatment initiation, our goal is to optimize workflows and maximize potential benefits of biosimilars for inflammatory bowel disease (IBD) management.

Methods: Following IRB exemption, a comprehensive report was extracted from the electronic medical record of all Adalimumab biosimilar orders from January 1, 2023, through May 1, 2024, including patient identifiers. Patient charts were reviewed for IBD characteristics and biosimilar tolerability. Data was analyzed to evaluate treatment outcomes.

Results: A total of 22 IBD patients managed by a tertiary care center's specialty pharmacist were prescribed Adalimumab biosimilars, specifically Hadlima, Amjevita, Hyrimoz, and Yuflyma. The cohort was 88% female, 59% Caucasian, and 32% African American, with an average age of 37 years. Crohn's disease was present in 64% and UC in 36%. Medicaid was the predominant insurance provider. Data on prior biologic, immunomodulator, and steroid use were collected. Nine percent of patients received concomitant immunomodulators, and 9% used steroids while on the biosimilar.

Laboratory results showed the following averages: ESR 18.4 mm/hr, CRP 2.2 mg/dL, fecal calprotectin 394 mcg/g, hemoglobin 12.9 gm/dL, iron 68.7 mcg/dL, TIBC 341 mcg/dL, and albumin 3.97 g/dL. Two patients were tested for HLADQA1*05, one of whom was positive.

Adverse events occurred in 18% of patients. One serious event required hospitalization for small bowel obstruction, likely due to disease worsening. Injection site reactions were the most common adverse effect, reported in 13% of patients, while 5% experienced a disease flare. Patients who could not tolerate the biosimilar were switched back to the originator. Majority of patients (82%) continued to respond to TNF-α therapy and remained on the biosimilar without difficulty.

Time-to-treatment initiation averaged 2-4 business days from insurance approval to medication dispensation via specialty pharmacy, compared to 7-10 business days when dispensed through retail pharmacies. On average, patients received their medication 3.5 days after order entry.

Conclusions: Adalimumab biosimilars demonstrate comparable efficacy to the originator drug and are generally well-tolerated. The most common adverse effect is injection site reactions. Time-to-treatment initiation for biosimilars is comparable to that of the originator drug. Challenges included delays in dispensing medication due to prior authorizations, retail pharmacy availability issues, and a 30-business day appeal process for switching back to the originator. Although insurance mandates largely drive the switch from originator to biosimilar, shared decision-making between providers and patients is essential for a smooth transition in biologic therapy.

Type of Project: Case series

Mentor: Erin Forster, MD, MPH, Division of Gastroenterology and Hepatology

Feasibility of Intravenous to Oral Prostacyclin Therapy Outpatient Transition in Patients with Pulmonary Arterial Hypertension **Poster: DD11**

Dhriti Shah, BS[a], **Michael Vinzani, MD[b]**, Maria Muehrcke, PharmD, MBA, BCPS[b], Meghan Morrisette, PharmD[c], Kristine Ritenour, RN[c], Denise Sese, MD[c], Rahul G. Argula MBBS, MPH[c]
Affiliations: a. MUSC College of Medicine, b. MUSC Department of Internal Medicine, c. MUSC Division of Pulmonary, Critical Care, Allergy, and Sleep Medicine.

Introduction
Pulmonary arterial hypertension (PAH) is a disease characterized by aberrant remodeling of the pulmonary arterial vasculature, causing elevated pulmonary vascular resistance (PVR), progressive right ventricular (RV) failure, and death. Pulmonary vasodilators, including intravenous (IV) prostacyclin analogs (PCAs) and oral (PO) prostacyclin receptor agonists (PRAs) are a cornerstone of PAH therapy. Patients often transition from PCA to PRA therapy, requiring careful titration and monitoring. While current literature describes this being performed while inpatient, there is a dearth of data on outpatient transition. This retrospective case series describes four patients undergoing outpatient IV-to-PO transition.

Methods
Four patients with PAH were carefully selected for this study. Inclusion criteria were stability on IV PCA, compliance with medications and appointments, well controlled PAH on right heart catheterization (RHC), and no significant RV dysfunction on echocardiography. Patients underwent outpatient cross-titration from the parenteral PCA, epoprostenol, to oral PRA, selexipag. Medication doses were recorded throughout transition, while patients' hemodynamic and functional parameters including RHC values, echocardiographic measurements, and 6-minute walk distance (6MWD) were measured before and after transition.

Results
Four patients were identified with ages ranging 26-54. Three had idiopathic PAH and one had PAH secondary to systemic sclerosis. Reasons for transition included patient preference and adverse reactions/complications from PCA therapy. Length of transition was determined by patient tolerance and ranged from 17-57 days. Average IV epoprostenol decrease was 0.62 ng/kg/day while selexipag was increased by 49.9 mcg/day. Mean difference in RV systolic pressure before and after transition was +16.6 mmHg, while tricuspid annular plane systolic excursion was stable with an average change of -0.2mm. Average mean PA pressure prior to transition was 34 mmHg which increased to 42, with a similar change in average PVR from 3.24 to 4.51 Wood units. 6MWD was largely stable, with mean change of –62.5 ft.

Conclusions
Here we describe four patients' successful transition from IV PCA therapy to PO PRA in the outpatient setting. In the correct patients, this transition can be completed safely and efficiently at home while closely followed-up by a multidisciplinary team.

Type of Project: Clinical Research

Mentor: Rahul Argula

Identifying Acute Respiratory Distress Syndrome with Structured Clinical Data Using Machine Learning

Poster: DD12

Authors

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Introduction

Acute respiratory distress syndrome (ARDS) remains underdiagnosed with substantial interobserver disagreement with radiographic interpretation. In this study, we trained and tested different machine learning models to predict cases of ARDS using available data from the electronic health record (EHR) from the first 48 hours following intubation.

Methods

In an observational retrospective cohort study, we trained logistic regression (LR), elastic net (EN), and extreme gradient boosting (GB) models to identify clinician-identified ARDS and where ARDS was present but missed, according to administrative billing codes. We reviewed 444 hospital admissions of patients requiring mechanical ventilation for 48 hours to 30 days. ARDS was identified using the Berlin criteria by the research team. The data was randomly divided into a 70% training and 30% test set. Our primary outcomes were areas under the receiver operating curves (AUROC) for identifying ARDS and missed cases of ARDS, sensitivity, specificity, and accuracy of models with the lowest mean test set error.

Results

AUROC values for identifying ARDS and missed ARDS with LR, EN, and GB models were 0.779 and 0.739; 0.793 and 0.697; and, 0.814 and 0.685, respectively. The best performing sensitivities and specificities for each model are recorded in the following table.

Test Performance for Machine Learning Models Identifying ARDS and Missed ARDS

	ARDS		Missed ARDS	
Model	Sensitivity	Specificity	Sensitivity	Specificity
Logistic Regression	47.5%	95.5%	36.7%	84.3%
Elastic Net Regression	46.0%	95.5%	4.3%	96.6%
Extreme Gradient Boosting	38.5%	97.2%	34.8%	92.7%

Conclusion

The GB model was the most accurate for identifying ARDS, while the LR model was the most accurate for identifying missed ARDS. These models could improve the accuracy of ARDS diagnosis for labelling clinical data for research and clinical quality review.

Type of Project: Research, Technology in Medicine

Mentor: Charles Terry, MD

Smoking and Progression to Cirrhosis

Poster: DD13

Samantha Wray MD, Andrew D. Schreiner MD MSCR, David G. Koch MD MSCR

Affiliation: Department of Medicine, Medical University of South Carolina

Background: About 40% of patients with liver disease have a smoking history. In this study, we aim to determine the association of tobacco use with progression to advanced fibrosis in primary care patients.

Methods: We performed a retrospective cohort study of primary care patients with chronic liver disease and inputs for at least two separate Fibrosis-4 Index (FIB-4) calculations. Patients with index FIB-4 values $\geq$ 3.25 or with diagnoses of cirrhosis, hepatocellular carcinoma, or liver transplant prior to their first FIB-4 score were excluded. Our primary outcome of interest was the time to a FIB-4 $\geq$ 3.25 (high-risk for advanced fibrosis). The primary exposure was tobacco use, categorized as ever or never smoked. Other cardiometabolic risk exposures (diagnoses of metabolic dysfunction, statin prescriptions) and demographic variables (age, sex, race) were collected. We performed univariate and bivariate analyses to describe the cohort overall and by tobacco use status. We developed unadjusted and adjusted Cox regression models to evaluate the association of tobacco use with time to high-risk for advanced fibrosis. We tested for interactions between tobacco use and other cardiometabolic risk exposures. SAS 9.4 (Cary, NC) was used for all statistical analyses. This study was approved by the IRB at MUSC.

Results: The study cohort included 2,547 primary care patients with chronic liver disease and a mean age of 49 years. 55% were female, 46% were identified as Black, and 59.5% (1,515) were former or current tobacco users. After a mean follow-up of 5.4 ($\pm$ 2.6) years, 23.5% (600) of the cohort progressed to a FIB-4 $\geq$ 3.25. Of patients that smoked, 26% progressed to a high-risk FIB-4 compared to 19% of those that did not smoke ($p < 0.001$). In the unadjusted Cox regression model, tobacco use was associated with an increased risk of progressing to a FIB-4 $\geq$ 3.25 (HR 1.40; 95% CI 1.18-1.66). After adjusting for other cardiometabolic risk exposures, statin prescriptions, and demographics, smoking was still associated with an increased hazard of progressing to a FIB-4 at high-risk for advanced fibrosis (HR 1.25; 95% CI 1.05-1.49).

Conclusion: A history of smoking is associated with progression to a high-risk FIB-4 even when adjusted for metabolic and demographic factors.

Type: Clinical

Mentors: Andrew D. Schreiner MD MSCR and David G. Koch MD MSCR

Diagnostic Accuracy Of The Cepheid Host Response Cartridge For Detection Of Pulmonary Tuberculosis

Poster: DD14

Yosra Alkabab, Assistant Professor, Division of Infectious Diseases, Department of Medicine

Introduction: Existing sputum-based diagnostic methods fail to identify many active TB cases, highlighting the need for non-sputum-based rapid and accurate triage tests. This study evaluated the Xpert MTB Host Response (Xpert HR) assay for detecting host responses to pulmonary TB across diverse settings.

Methods: We conducted a prospective study in Peru, South Africa, Uganda, and Vietnam. Adults with TB symptoms underwent Xpert MTB HR testing using capillary and venous blood samples. Diagnostic accuracy was assessed against a microbiological reference standard (culture and/or Xpert Ultra over two consecutive days enrolment).

Results: Among 813 participants, 52% were female, median age 38 years, and 92 (24%) were HIV-positive. For capillary blood, the overall sensitivity was 92%, specificity was 45%, AUC was 0.86, NPV was 94%, and PPV was 35%. In Vietnam, the AUC was 0.61, with a sensitivity of 83% and a specificity of 27%. Capillary testing had a higher AUC of 0.86 compared to venous testing within one hour of collection (AUC 0.66). Participants with diabetes had a sensitivity of 92% and specificity of 44%; specificity was 19% in patients living with HIV.

Conclusions: The Xpert HR assay demonstrated high sensitivity and NPV in diverse settings. While specificity remains a challenge, the assay's simplicity, rapid turnaround, and scalability make it valuable for TB triage in resource-limited settings.

Type of Project: Clinical science

Mentor's name: Susan Dorman, M.D.

Vascular Activation and Dysfunction in SLE: The Impact of Anti-Endothelial Autoantibodies

Poster: DD15

Helen Butler, PhD, Division of Nephrology, Department of Medicine

Introduction: Systemic lupus erythematosus (SLE) is a chronic and common autoimmune disease that profoundly affects the cardiovascular system, including the vessels of the kidney, heart, and brain. Patients with an SLE diagnosis have a higher clinical incidence of hypertension, cardiovascular disease, and vascular inflammation compared to patients with no SLE diagnosis. There is a significant need to understand the pathophysiological mechanisms underlying SLE-associated cardiovascular disease. Importantly, novel anti-endothelial autoantibodies may contribute to the development of numerous autoimmune disease states. For example, anti-endothelin receptor autoantibodies (ETAR-AAs) are significantly increased in patients with SLE-associated pulmonary arterial hypertension. However, there is a knowledge gap regarding the clinical relevance of anti-endothelial autoantibodies as serum biomarkers and the functional signaling mechanism of these autoantibodies on endothelial activation and dysfunction in SLE. We hypothesize that elevated patient anti-endothelial autoantibodies positively correlate with vascular activation and promote endothelial cell dysfunction.

Methods: We recruited a small cohort pilot study to evaluate endothelin receptor autoantibodies and markers of endothelial activation and inflammation in healthy control (non-SLE) (n=18) and SLE patients (n=13) female human subjects (ages 23-64). Isolated primary human renal endothelial cells (HRECs) were used to study the direct effects of isolated serum IgG from healthy control and SLE individuals on renal endothelial cell activation and calcium signaling with and without endothelin receptor blockade.

Results: Patient plasma ETAR-AAs and anti-ETBR autoantibodies (ETBR-AAs) levels were elevated in subjects with SLE ($p<0.0001$; $p=0.0266$). Further, plasma anti-ETAR-AAs were positively correlated with soluble vascular adhesion molecule-1 (sVCAM-1) ($r=0.4288$, $p=0.0114$) and soluble intracellular adhesion molecule-1 (sICAM-1) ($r=0.3812$, $p=0.0286$), emphasizing the link between these autoantibodies and endothelial activation. In a scratch assay, blockade of ETBR reduced HREC migration when incubated with SLE but not healthy control (HC) IgG ($p=0.032$). *In vitro* preliminary molecular data on endothelin receptor expression is unchanged between HC and SLE IgG incubation. However, preliminary calcium imaging data shows a chronic and prolonged increase in intracellular calcium in HRECs exposed to SLE IgG relative to HC.

Conclusion: Our clinical data links pathological endothelial autoantibody production and related cardiovascular complications in SLE patients. Future experiments will include *in vitro* mechanistic testing of HRECs with exposure to anti-endothelial autoantibodies under physiological and pathological stretch. Isolation of ETAR-AA and ETBR-AAs will be performed for receptor specific stimulation.

Type of Project: Clinical and Basic Science

Mentor: Justin P. Van Beusecum

Associations between Tobacco Use and Tobacco Cessation Pharmacotherapy on Rehospitalization

Poster: DD16

Ellen Esposito, MD
Division of Hospital Medicine
Department of Internal Medicine

Introduction

Tobacco use remains a major public health issue in the United States as it is linked to a broad spectrum of serious diseases. Although intensive inpatient tobacco treatment programs have shown success, the impact of prescription of smoking cessation medications alone on hospital readmissions has not been thoroughly studied. This study aims to assess the associations of smoking status and prescription of smoking cessation medication on rehospitalizations.

Methods

We conducted a retrospective cohort study of patients from a primary care clinic hospitalized between July 1, 2013 and December 31, 2020. The primary outcomes of interest were rehospitalization rates by smoking status and by smoking cessation medication prescription among current smokers.

Results

Of the 11,164 patients studied, rehospitalization rates at all timepoints were higher among current and former smokers compared to never smokers. After adjusting for covariates, former and current smokers had higher odds of rehospitalization within 365 days compared to never smokers (OR1.14, 95%CI 1.03-1.25; OR1.15, 95%CI 1.01-1.31, respectively). Among current smokers, those prescribed tobacco cessation medications had a lower likelihood of rehospitalization within 365 days after adjusting for confounders (OR0.75, 95%CI 0.56-0.99).

Conclusions

This study confirms that both current and former smokers are at an increased risk for rehospitalization compared to never smokers. Notably, the prescription of tobacco cessation medications is associated with a decreased risk of rehospitalization among current smokers. However, the low prescription rate of these therapies highlights a significant gap in care. Improved treatment of tobacco use during hospitalizations could potentially lower rehospitalization rates.

Type of Project

Clinical Research

Mentor's Name

Marc Heincelman, MD

Additional Mentors

Andrew Schreiner, MD, MSCR
Benjamin Toll, PhD

Features of mast cell activation in patients with mannose binding lectin deficien cghand Ehlers- Danlos Syndrome

Poster: DD17

Anne Maitland, M.D.

Background
Several studies have implicated an association between hypermobile Ehlers Danlos Syndrome/hypermobile spectrum disorder (HEDS/HSD), a group of heritable connective tissue disorders, and mast cell activation disease (MCAD), but clinical studies, which elaborate the basis of these co-segregating disorders, are lacking. Here we show that two disorders: an immunodeficiency disorder and a connective tissue disorder, associated with chronic disruption of the epithelial borders and mast cell dysfunction, associated with multi-organ system pathology.

Objective: Assess the prevalence of MCAD in patients with mannose binding lectin deficiency (MBL) and hypermobile Ehlers Danlos Syndrome (hEDS)/ hypermobile spectrum disorder (HSD).

Methods: We retrospectively studied 987 patients seen in our allergy/immunology clinic, with suspected MCAD, from 2017-2020. We identified 56 patients with MBL deficiency, presenting with infectious and non-infectious multi-organ system involvement, including mucocutaneous, articular and systemic features. consistent with the hypermobile Ehlers Danlos Syndrome/hypermobile spectrum disorder (HEDS/HSD).

Results: Of the MBL deficient patients, 40 (71%) had been diagnosed with HEDS/HSD. Symptom distribution for all cases was as follows: Rhino-conjunctivitis (94%), Neurocognitive impairment (85%), Gastrointestinal symptoms (83%), Skin manifestations (Urticaria, angioedema) (76%), musculoskeletal complaints (75%), Asthma (51%), psychiatric disorders (50%), Cardiovascular manifestations (42%), Orthostatic intolerance, POTS (38%), Anaphylaxis (32%), Dysuria (20%). A significant difference between EDS and non-EDS subgroups could be seen in cardiovascular and neuropsychiatric manifestations.

Conclusion: Among this cohort of patients with MBL deficiency, MCAD and HEDS/HSD are common. These observations implicate bi-directional influences of epithelial derived factors and mast cell activation in barrier function and tissue homeostasis and prompt the recommendation to screening of hEDS/HSD patients, including secondary mast cell dysfunction due to deficiencies in other immune compartments and abnormal connective tissue metabolism.

Sepiapterin Treatment Improves Survival and Renal Outcomes in a Murine Model of Lupus Nephritis by Restoring Endothelial Integrity

Poster: DD18

Soroush Moradi, MD, Postdoctoral scholar, Rheumatology

Introduction:
Lupus nephritis (LN), a severe complication of systemic lupus erythematosus (SLE), is characterized by persistent endothelial dysfunction, partly due to endothelial nitric oxide synthase (eNOS) uncoupling. Sepiapterin (L-Sep) has been shown to restore eNOS coupling and production of nitric oxide, potentially alleviating endothelial damage and improving renal outcomes. This study investigates L-Sep's therapeutic effects in a murine LN model, evaluating the impact on survival and renal pathology. Additionally, we analyzed gene expression in murine LN renal cortices to further clarify L-Sep's mechanistic role in various renal cell types, providing a basis for its potential as a targeted therapeutic intervention in LN.

Methods:
We treated female NZM2410/J mice (lupus nephritis model) with vehicle or 20 mg/kg/day L-Sep beginning at 18 weeks of age. After 6 weeks of treatment with placebo or L-Sep (or when mice met endpoint criteria), kidney cortex samples were collected, flash-frozen, and stored at -80°C. Nuclei were isolated and sorted, then single-nuclear RNA sequencing (snRNA-seq) was performed on renal cortical nuclei from placebo (n=5) and 20 mg/kg/day L-Sep treated mice (n=5) to assess transcriptional changes. Differentially expressed genes (DEGs) padj < 0.05 were analyzed. Survival and renal activity and chronicity were also assessed.

Results:
NZM2410 mice had improved survival when treated with 20 mg/kg/day L-Sep (p=0.018), along with improved renal outcomes evidenced by lower total activity and chronicity scores (p=0.017). snRNA-seq of renal cortices showed L-Sep-treated mice had increased proportions of normal endothelial cells with a decrease in injured endothelial cells compared to vehicle. L-Sep also increased the proportion of podocytes and decreased injured proximal tubule cells. Analysis of DEGs revealed a decrease in Cxcl10 (IFN-regulated) and genes associated with lupus and redox in normal endothelial cells treated with L-Sep, while injured endothelial cells had decreased expression of the inflammatory markers FoxO3, Jun, Tnf, and Nfkb1.

Conclusion:
LSep treatment of lupus nephritis-prone mice improved survival and renal outcomes. snRNAseq further revealed the protective mechanism of LSep on renal endothelial cells and podocytes. This data suggests LSep may be beneficial in the treatment of renal endothelial damage from lupus.

Type of Project: Basic science

Mentor's Name: Jim Oates, MD

Interprofessional Education to Advance Patient Mobility **Poster: DD19**

Leonidas Walthall, MD
Assistant Professor
Division of Hospital Medicine
Department of Medicine

Introduction:
Hospitalized patients have been shown to spend an average of 83% of their stay in bed, leading to a myriad of harms related to immobility. Given staff shortages within the hospital setting and our desire to inspire prioritization of mobility in future healthcare providers, we hypothesized that health profession students could safely advance inpatient mobility.

Methods:
Our innovative mobility course was offered to all health profession students across campus. The course consisted of one lecture by a physician reviewing literature on mobility, followed by a demonstration of interprofessional communication and appropriate mobilization techniques for ambulatory inpatients by a physical therapist (PT). PT evaluated the students to ensure correct performance of patient mobilization. Thereafter, students independently mobilized hospitalized patients who were evaluated as ambulatory by nursing or PT.

Results:
Twelve students completed the course in its first iteration (3 PT students, 9 OT students). 503 ambulation events were recorded with no reported falls. Students demonstrated improved confidence both communicating interprofessionally (pre 33.3%, post 91.7% strongly agree) and safely ambulating patients (pre 33.3%, post 75% strongly agree). Furthermore, 91.7% of the students strongly agreed the course increased awareness of the importance of mobilizing patients. An 8-item hands-on evaluation of mobilization demonstrated improvement of skills (average score: pre 2.17/5, post 4.25/5 - a rating of 4/5 indicated “completes skill well, in a timely manner”).

Conclusions:
Our pilot study of health profession students who completed a mobility curriculum showed improvement in mobilization skills and an increase in confidence communicating interprofessionally and mobilizing patients. Results from this pilot study has the potential to be replicated at other academic medical centers to improve mobility in hospitalized patients.

Type of Project:
Quality Improvement

Mentor’s Name:
Meghan Thomas, MD, MPH, MSCR
Marc Heincelman, MD, MPH

Evaluating the Anti-Inflammatory Effects of a Selective Estrogen Receptor Modulator in Systemic Lupus Erythematosus

Poster: DD20

Rachael J. Werner, MD, PhD, Rheumatology Fellow-PGY-5, Division of Rheumatology & Immunology

Introduction: Systemic lupus erythematosus (SLE) is a complex autoimmune disorder primarily affecting women, emphasizing the significant role of sex hormones, particularly estrogen, in its pathogenesis. Estrogen signaling through estrogen receptor alpha (ERα) is implicated in the onset and progression of SLE, yet the therapeutic potential of selective estrogen receptor modulators (SERMs) remains underexplored. Pathway Preferential Estrogen (PaPE) is a low-affinity non-nuclear ERα agonist that may provide a beneficial approach for SLE treatment. By activating ERα, PaPE exerts favorable effects in non-reproductive tissues, such as reducing body weight gain and enhancing endothelial repair, while sparing typical estrogenic actions like promoting cell proliferation in breast cancer. These properties suggest that PaPE could mitigate inflammation and tissue damage in lupus without exacerbating other estrogen-related risks, making it a promising candidate for therapeutic intervention in SLE.

Methods: This study evaluated the anti-inflammatory effects of PaPE in murine immune cells. Optimal dosing was determined in a murine dendritic cell line before progressing to bone marrow-derived dendritic cells (BMDCs) from wild-type and NZM2410 lupus-prone mice. Given that Toll-like receptor 7 (TLR7) is implicated in lupus pathogenesis, TLR7-agonism was used to assess PaPE's ability to minimize TLR7-induced inflammatory responses, with changes in mRNA levels of key inflammatory cytokines serving as the initial output measure.

Results: PaPE downregulated TLR7-induced inflammatory cytokines in a dose-dependent manner in vitro and significantly reduced MCP1 and TNFα in ex vivo BMDCs from both wild-type and lupus-prone mice. Interestingly, IL1β expression showed a clear reduction in wild-type BMDCs but was not observed in lupus-prone cells.

Conclusions: These findings support PaPE as a promising therapeutic approach for SLE. Its selective targeting of ERα and anti-inflammatory effects highlight its potential to modulate immune responses in lupus. Further research is warranted to explore its mechanisms of action and assess its clinical applicability, particularly through studies involving longer timepoints and patient samples to enhance translational relevance.

Type of project: Basic Research

Mentor: Melissa Cunningham, MD, PhD, Associate Professor Division of Rheumatology & Immunology