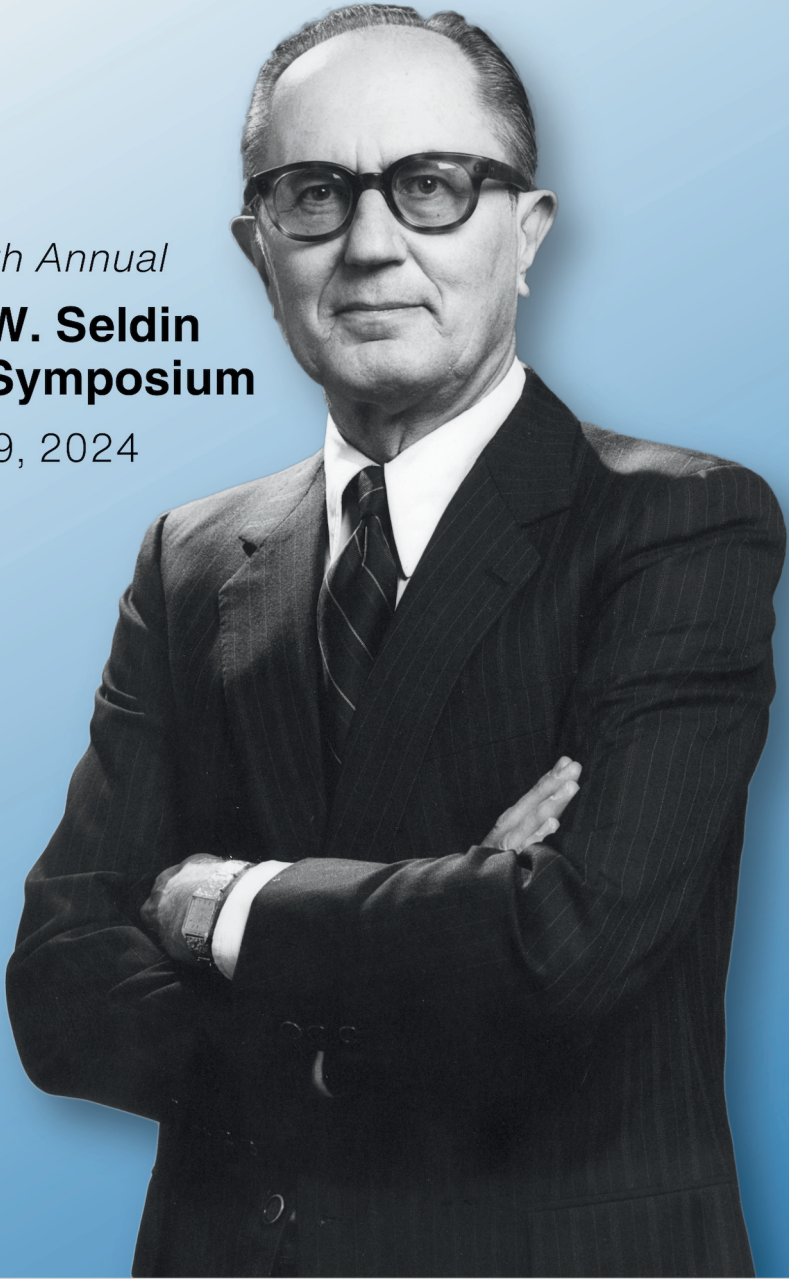


*The Ninth Annual*

**Donald W. Seldin  
Research Symposium**

April 19, 2024



**UTSouthwestern**  
Medical Center  
Internal Medicine

WELCOME

**Thomas J. Wang, MD**

Professor & Chair of Internal Medicine  
UT Southwestern Medical Center



**THANK YOU FOR YOUR INTEREST** in the Ninth Annual Donald W. Seldin Research Symposium. Since 2016, this conference has been a showcase of the Department’s strengths in research, education, and patient care, through a celebration of our trainees’ mentored research accomplishments. As in previous years, the

symposium features poster presentations spanning the entire range of research, from fundamental biology to quality improvement.

Throughout his 36-year tenure as Chair, Dr. Seldin was an unwavering advocate for the clinical scholar. As academic medicine evolved with increasing clinical demands, Dr. Seldin ensured that research remained a cornerstone of the core mission of the Department. He emphasized the intertwined relationship between research and clinical medicine, noting that “the critical observation and analysis of disease contributes both to good medical care and new knowledge.” The Department remains strongly committed to carrying on this tradition.

We are thrilled to welcome you to the Seldin Symposium. We are excited to continue Dr. Seldin’s legacy and celebrate the incredible work and mentorship in the Department. ■

*Dr. Wang holds the Donald W. Seldin Distinguished Chair in Internal Medicine*



TRIBUTE

**Donald W. Seldin, MD**

1920-2018

**THE BIOMEDICAL RESEARCH PEDIGREE** of UT Southwestern Medical Center is as storied and accomplished as that of other prominent institutions more than twice its age. Those who lead UT Southwestern today can point to one figure who, more than anyone, was the guiding force and architect of one of the preeminent academic medical institutions in the United States: Dr. Donald W. Seldin.

The beginning of Dr. Seldin's tenure at UT Southwestern is a tale that has been told many times throughout the years, but bears repeating. In 1951, Dr. Seldin arrived in Dallas from Yale University to find a set of military barracks and a brick building in disrepair: the entire campus of UT Southwestern. By the middle of 1951, Dr. Seldin was the sole remaining full-time faculty member at UT Southwestern, and thus Chair of the Department of Medicine by default. Through community engagement and collaboration with local physicians, he built the Department of Medicine upon a foundation that still underpins the strength of UT Southwestern today: its trainees. By personally selecting the most promising talent, sending them across the nation to study with the best scientific minds of their time with the promise to return, Dr. Seldin's faculty tree bloomed with distinction and accomplishment. Daniel Foster. Michael Brown. Jean Wilson. Floyd Rector. Norm Kaplan. His personal encouragement of Joseph Goldstein to study genetics instead of neurosurgery, and his

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## NINTH ANNUAL DONALD W. SELDIN RESEARCH SYMPOSIUM

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suggestion that Dr. Goldstein partner with Michael Brown, culminated in their Nobel Prize in Physiology or Medicine.

Throughout his 37-year tenure as Chair, Dr. Seldin never wavered in his advocacy that anchored the Department to the mission of the clinical scholar – advancing a fundamental understanding of human health, disease, and its treatment via research. During the evolution of academic medicine and its increasing clinical demands, Dr. Seldin’s leadership ensured that research flourished as a key emphasis in the university’s tripartite mission. He emphasized the definition of a medicine faculty as clinicians who pursued innovation, discovery of new knowledge and its transmission to others. He emphasized the intertwined relationship between research and clinical medicine, noting that “the critical observation and analysis of disease contributes both to good medical care and new knowledge.”

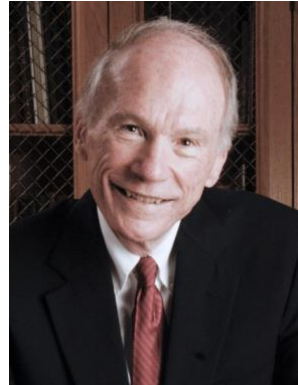
The list of honors achieved by Dr. Seldin during and after his chairmanship is as varied as it is long. Seven societies lay claim to him as past president: the American Society of Nephrology, the Association of Professors of Medicine, the Association of American Physicians, the International Society of Nephrology, the Central Society for Clinical Research, the American Society for Clinical Investigation, the Southern Society of Clinical Investigation. Too numerous to list, his awards include the John P. Peters award from the American Society of Nephrology, the Kober Medal from the Association of American Physicians, and the Distinguished Teacher Award from the American College of Physicians.

Dr. Seldin’s belief in the moral responsibilities shouldered by those in medicine continues to reverberate and be imprinted upon our trainees. His postwar encounters with Nazi medicine, seeing medicine used to create suffering, taught him to emphasize the importance of practicing humane medicine with integrity. To this day, Dr. Seldin’s passion for discovery, his standards of professionalism and humanity, and his enthusiasm for training the next generation of physicians remain the bedrock upon which the Department of Internal Medicine and UT Southwestern continue to build and expand.

Without his guiding hand, it is hard to imagine that UT Southwestern would have achieved its stature in world-renowned research or trained so many gifted and successful physicians still serving in Texas and across the United States. Simply put, it is hard to imagine UT Southwestern Medical Center without Donald W. Seldin. ■

IN MEMORIAM

**Daniel W. Foster, MD**  
1930-2018



**THE THIRD OF FIVE CHAIRS** of the Department of Internal Medicine at UT Southwestern, Dr. Daniel W. Foster was a pioneering force in patient care, education, and research throughout his entire career, including his time at UT Southwestern.

After graduating from UT Southwestern medical school at the top of his class, Dr. Foster followed his residency at Parkland Memorial Hospital with a research fellowship at the National Institutes of Health. He returned to UT Southwestern at the behest of Drs. Donald Seldin, Michael Brown, and Joseph Goldstein. In a spectacular three-decade collaboration with his scientific partner, Dr. J. Denis McGarry, Dr. Foster discovered the malonyl-CoA regulatory system—detailing its fundamental role in fuel metabolism, fatty acid oxidation and ketone body formation.

As Department Chair from 1987 to 2003, Dr. Foster spearheaded Internal Medicine’s remarkable academic growth, recruiting numerous outstanding faculty who went on to establish their own successful careers at UT Southwestern. His bold vision for the Department enabled the launch of the transformative Dallas Heart Study. Dr. Foster’s seminal contributions to academic Internal Medicine were widely recognized. His many honors included election to the National Academy of Medicine, the American Society for Clinical Investigation, and the Association of American Physicians, as well as the Banting Medal for Scientific Achievement from the American Diabetes Association.

He was equally committed to the education and training of students and residents, serving as Headmaster of the Academic Colleges at UT Southwestern, President of the Academy of Medicine, Engineering, and Science of Texas, and being named an Outstanding Physician Educator in Diabetes by the American Diabetes Association.

Dr. Foster’s patients greatly appreciated his counsel, kindness, and personal warmth—and to this day reflect upon him fondly as they return to UT Southwestern for their care. Dr. Foster’s legacy of integrity, education, research, and patient care remains etched into the mission of the Department of Internal Medicine, and his leadership by example continues to serve as a guiding light to UT Southwestern. ■

KEYNOTE ADDRESS

**William G. Kaelin Jr., MD**

Sidney Farber Professor of Medicine  
Dana-Farber Cancer Institute  
& Harvard Medical School

*“New Treatments for Anemia, Ischemia,  
and Cancer Emerging from Studies of  
von Hippel-Lindau Disease”*

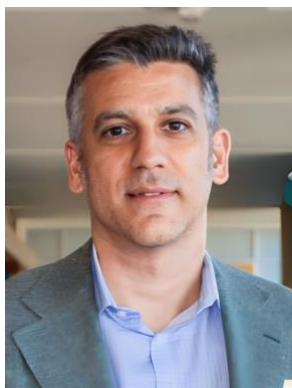


**ORIGINALLY FROM NEW YORK**, Dr. Kaelin studied chemistry and mathematics at Duke University in Durham, North Carolina, and received his medical

degree there in 1982. He then completed internal medicine residency training at Johns Hopkins Hospital in Baltimore, Maryland, where he served as Chief Resident. He received advanced training in medical oncology at Dana-Farber, where he began his studies of tumor suppressor proteins. He became an independent investigator at Dana-Farber in 1992, and a Howard Hughes Medical Institute Investigator and Professor of Medicine at Harvard Medical School in 2002.

In 2019, the Nobel Prize in Physiology or Medicine was awarded jointly to Dr. Kaelin, Sir Peter J. Ratcliffe, and Gregg L. Semenza for their discoveries of how cells can sense and adapt to changing oxygen availability. During the 1990s they identified a molecular machinery that regulates the activity of genes in response to varying levels of oxygen. The discoveries may lead to new treatments for anemia, cancer, and other diseases.

Among Dr. Kaelin’s other honors, he was elected to the National Academy of Medicine (formerly the Institute of Medicine) in 2007, and the National Academy of Sciences in 2010. ■



SELDIN-SMITH PHYSICIAN SCIENTIST  
LECTURE

**Stephen E. Mansoor, MD, PhD**

Assistant Professor of Internal Medicine  
Division of Cardiovascular Medicine  
Oregon Health & Science University

*“From Molecular Structure to Drug Development:  
How Structural Biology Can Impact  
Cardiovascular Medicine”*

**DR. MANSOOR HOLDS** a bachelor’s degree in biochemistry and molecular biology from Reed College in Portland, Oregon. He then received a combined M.D./Ph.D. degree from Oregon Health & Science University, before fast-tracking through internal medicine residency into a combined clinical cardiology/research fellowship at OHSU. In addition to running a basic science research program, Dr. Mansoor is an active clinical cardiologist treating patients with cardiovascular disease.

The Mansoor Lab uses structure/function studies to explore and define the molecular pharmacology of ligand-gated ion channels and G-protein coupled receptors in order to then use in silico, structure-based drug design to develop novel small-molecules capable of selectively modulating the function of these receptors. His research vision spans from studying molecular ligand/receptor interactions at the laboratory bench, to development of novel small-molecule pharmacologic therapies, and to ultimately treating patients with cardiovascular diseases at the bedside.

In 2023, Dr. Mansoor received the Donald Seldin-Holly Smith Award for Pioneering Research from the American Society for Clinical Investigation, from which he had previously received a Young Physician-Scientist Award. He was elected for membership in 2024. He also is a 2022 recipient of the NIH Director’s New Innovator Award. ■



Poster #1

**Presenter:** Amanda Clark, MD

Basic Science

**Authors:** Amanda J Clark, MD; Kyle Q Vu, BS; Samir M Parikh, MD

**Title:** Maternal NAD<sup>+</sup> Deficiency Contributes to Reduced Fetal Nephron Endowment

**Abstract:**

**Background:** Maternal disease and nutrition are known to affect the long-term health of offspring. For the human kidney, this is particularly impactful because lifetime nephron endowment is determined in utero. Low nephron endowment increases the risk of chronic kidney disease (CKD) and hypertension in adulthood. Therefore, nutritionally modifiable gestational events in nephrogenesis may impact long-term health. Genetic deletions of nicotinamide adenine dinucleotide (NAD<sup>+</sup>) biosynthetic enzymes lead to severely reduced NAD<sup>+</sup> and frank renal malformation. It is not known if less severe maternal NAD<sup>+</sup> fluctuations affect fetal renal development. Developing fetuses are increasingly exposed to maternal conditions associated with reduced NAD<sup>+</sup> like diabetes and malnutrition. Those same conditions are associated with reduced fetal nephron endowment. PARP1 is an NAD<sup>+</sup> consuming enzyme that has been implicated in cellular differentiation. I hypothesize that maternal NAD<sup>+</sup> deficiency is a nutritionally modifiable cause of reduced fetal nephron endowment.

**Methods:** Maternal NAD<sup>+</sup> deficiency was generated by depriving QPRT +/- mice of niacin. QPRT is the bottleneck enzyme of the Tryptophan --> NAD<sup>+</sup> pathway. With niacin deprivation, NAD<sup>+</sup> biosynthesis depends on this haploinsufficient pathway. For rescue experiments, alternative NAD<sup>+</sup> precursor nicotinamide (NAM) was added to maternal water. Nephrons were counted via acid maceration. Blood pressure was measured with tail cuff. GFR was measured with subcutaneous clearance of FITC-sinistrin. Proliferating nephron progenitor cells (NPCs) were stained (Six2) using immunofluorescence, and primary NPCs were isolated and differentiated in vitro. A novel NPC-Parp1 deletion mouse was generated by crossing Six2Cre and Parp1 fl/fl mice.

**Results:** A novel mouse model of maternal NAD<sup>+</sup> deficiency leads to oligonephronia associated with hypertension and CKD in adulthood. Nephron count can be rescued by maternal NAM supplementation, which prolongs the "stem state" of NPCs in vivo and in vitro. NAM supplementation also increases activity of fetal kidney PARP1. A novel mouse with targeted NPC PARP1 deficiency, has reduced nephron endowment.

**Conclusion:** Maternal NAD<sup>+</sup> abundance is a nutritionally modifiable determinate of fetal nephron endowment. This may take place in a Parp1 dependent fashion. Ongoing studies are needed to fully elucidate this mechanism as there may be broad implications for population CKD and hypertension reduction.



Poster #2

**Presenter:** Jake Lichterman, DO

Basic Science

**Authors:** Jake N. Lichterman, DO; Tarun Srinivasan, BS; Chaitanya Dende, PhD; Mitchell Von Itzstein, MD; Wenling Li, PhD; Parastoo Sabaeifard, PhD; Laura Coughlin, MS; Nicole Poulides, MS; Suzette Palmer MS; John Shelton BS; Xiaowei Zhan, PhD; Bret Evers, MD, PhD; Xin Li, PhD; David E. Gerber, MD; Lora V. Hooper, PhD; Andrew Y. Koh, MD

**Title:** The Circadian Clock Modulates Cancer Immune Checkpoint Therapy Through Immune Cell Trafficking

**Abstract:**

**Background:** Immune checkpoint inhibitor therapy (ICT) can provide durable remissions for cancer patients with previously incurable malignancies. However, ICT is ineffective for many cancer types, and even those who initially respond may develop ICT resistance and succumb to their cancer. Tumor cell extrinsic factors, termed host factors, have recently emerged as key mediators and biomarkers of ICT response. One intriguing host factor that may influence ICT response is the circadian clock, an evolutionarily conserved transcriptional-translational feedback loop that allows mammalian organisms to adapt to environmental exposures (e.g. light). However, whether “the clock” modulates the ICT anti-tumor immune response is unknown.

**Methods:** We utilized multiple preclinical mouse models of cancer immunotherapy (e.g. MC38) to investigate whether the efficacy of immunotherapy (e.g. anti-PD-1) was time-of-day-dependent. We utilized circadian light cabinets to harvest tumors/blood from mice at ZT2 and ZT18 for flow cytometry, bulk cytokine analysis and single cell RNA sequencing. To interrogate the role of the clock we generated DC/T-cell conditional clock knockout mice (BMAL1<sup>fl/fl</sup> crossed with CD11c-cre or CD8a-Cre).

**Results:** Utilizing preclinical mouse models of cancer immunotherapy, we found that ICT efficacy is time-of-day dependent. ICT was most efficacious if ICT was administered at two hours after first light exposure (Zeitgeber time 2, ZT2) and least efficacious at ZT18. We found an increase in effector granzyme B- and interferon- $\gamma$  producing CD8+ T-cells in the tumor at ZT2 versus ZT18. This was accompanied by an increase in CD11c+ dendritic cells (DCs) and intratumoral chemokines (e.g. , CXCL9, CXCL10) that promote DC/T-cell migration into the tumor, and leads to enhanced DC-T-cell priming and anti-tumor immunity. Interestingly, these time-of-day dependent differences in tumor immune cell infiltration were present prior to the administration of ICT. To interrogate the role of the clock in mediating these time-of-day dependent differences, we characterized the response to ICT in mice that lack the core clock gene, BMAL1. Loss of BMAL1 in DCs attenuated ICT efficacy, abrogated time-of-day dependent differences in ICT efficacy and dampened anti-tumor immunity.

**Conclusions:** Our findings highlight a role for a novel host factor, the circadian clock, in mediating the efficacy of cancer immune checkpoint therapy.

Poster #3

**Presenter:** Jianyi Yin, MD, PhD

Basic Science

**Authors:** Jianyi Yin, MD, PhD; Ezra Burstein, MD, PhD

**Title:** Upregulated Type I Interferon Response is Associated with Active Inflammation in Ulcerative Colitis and Causes Increased Susceptibility to Dextran Sulfate Sodium-Induced Colitis in Mice

**Abstract:**

**Background:** Type I interferon (IFN-I) signaling has diverse effects on the host immune response via receptor-mediated JAK/STAT activation. Inflammatory bowel disease (IBD) has been associated with several genetic conditions that lead to upregulated IFN-I responses in human. However, in animal studies, the role of IFN-I in intestinal inflammation remains controversial. We hypothesized that constitutive upregulation of IFN-I response may promote the development of clinical and experimental colitis.

**Methods:** We performed bulk RNA sequencing and analyzed the publicly available single cell RNA sequencing data of colonic biopsies from the inflamed sites of patients with active ulcerative colitis (UC) and the non-inflamed sites of healthy controls. We investigated the changes in type I interferon-stimulated genes (ISGs) in the murine model of dextran sulfate sodium (DSS)-induced colitis. We determined the susceptibility of *Ifnar1SA* knock-in mice, which carry a mutant receptor of IFN-Is that causes constitutively upregulated IFN-I responses, to DSS-induced colitis.

**Results:** The IFN-I response was one of the most significantly enriched biologic processes among the differentially expressed genes upregulated in active UC biopsies. Type I ISGs appeared to have various expression patterns in immune and non-immune cell compartments. Several type I ISGs were similarly up-regulated at the transcript level in mouse colonic tissues after DSS treatment. Compared to wild-type littermates, *Ifnar1SA* mice had higher mRNA levels of type I ISGs in tissues at baseline. Moreover, *Ifnar1SA* mice were more susceptible to DSS-induced colitis than their wild-type littermates, with greater weight loss, colon shortening, and disease activity.

**Conclusions:** An increased type I ISG signature is associated with active inflammation in patients with UC and in mice with DSS-induced colitis. Constitutive upregulation of IFN-I response may contribute to increased susceptibility to DSS-induced colitis. Further studies are needed to determine the cell compartment(s) and specific type I ISGs that are responsible for the phenotype. This pathway may provide opportunities to understand the therapeutic response to JAK inhibitors and discover new therapeutic targets.

Poster #4

**Presenter:** Kurt Reichermeier, MD, PhD

Basic Science

**Authors:** Jerry Li, BS; Nicholas Purser, BS; Joanna Liwocha, PhD; Daniel C. Scott, PhD; Holly A. Byers, BS; Barbara Steigenberger, PhD; Spencer Hill, PhD; Ishita Tripathi-Giesgen, PhD; Trent Hinkle, MS; Fynn M. Hansen, PhD; J. Rajan Prabu, PhD; Senthil K. Radhakrishnan, PhD; Donald S. Kirkpatrick, PhD; Kurt M. Reichermeier, MD, PhD; Brenda A. Schulman, PhD; Gary Kleiger, PhD

**Title:** Cullin-RING Ligases Employ Geometrically Optimized Catalytic Partners for Substrate Targeting

**Abstract:**

**Background:** Over 90% of potential drug targets are considered undruggable via conventional pharmacology. Via degradation instead of inhibition of protein targets, Proteolysis Targeting Chimeras (PROTACs) have become a promising novel strategy to overcome this unmet need. PROTACs co-opt Cullin-RING ligases (CRLs) to ubiquitylate protein neo-substrates, thereby inducing targeted protein degradation of disease-driving proteins. Understanding of mechanisms governing CRL activity is paramount to PROTAC drug development. Substrate discrimination and ubiquitin transferase activity of CRLs were thought to be strictly separated. Substrates are recognized by substrate receptors, such as Fbox or BCbox proteins. Meanwhile, CRLs employ assorted ubiquitin-carrying enzymes (UCEs, which are a collection of E2 and ARIH-family E3s) specialized for either initial substrate ubiquitylation (priming) or forging poly-ubiquitin chains. We discovered specific human CRL-UCE pairings governing substrate priming.

**Methods:** Using a combination of mass-spectrometry, biochemical, cell biological, and structural approaches, we investigate molecular mechanisms governing endogenous and PROTAC-induced neo-substrate ubiquitination via CRLs.

**Results:** The results reveal the pairing of CUL2-based CRLs and UBE2R-family UCEs in cells, essential for efficient PROTAC-induced neo-substrate degradation. Despite UBE2R2's intrinsic programming to catalyze poly-ubiquitylation, CUL2 employs this UCE for geometrically precise PROTAC-dependent ubiquitylation of a neo-substrate and rapid priming of substrates recruited to diverse receptors. Cryo-EM structures illuminate how CUL2-based CRLs engage UBE2R2 to activate substrate ubiquitylation. Thus, pairing with a specific UCE overcomes E2 catalytic limitations to drive substrate ubiquitylation and targeted protein degradation.

**Conclusions:** We discover that endogenous and PROTAC-induced neo-substrate targeting by CRLs is not solely determined by substrate receptors but also depends on CRL-UCE pairing. The results demonstrate that specific UCEs function with subgroups of CRLs and the efficiency of PROTAC-induced neo-substrate degradation depends on UCE protein levels. These findings have important implications for not only endogenous regulation but also for developing targeted protein degradation therapeutics. We propose that design elements of PROTACs should focus not only on co-tethering the E3 and neo-substrate but also on catalytic geometric activation that may facilitate therapeutic efficacy.

Poster #5

**Presenter:** MariaSanta Mangione, MD, PhD

Basic Science

**Authors:** MariaSanta C. Mangione, MD, PhD; Dian J. Cao, MD, PhD

**Title:** Innate Immune Pathway cGAS-STING in Macrophage Function in Atherosclerosis

**Abstract:**

**Background:** Macrophages are key cells in atherosclerotic cardiovascular disease, mediating the progression from sub-intimal lipid deposits to fatty streak to advanced plaques and regulating plaque stability. Macrophages within a plaque are heterogeneous: some are lipid-laden “foam cells” while others secrete traditional “pro-inflammatory” signals. Macrophages’ ability to recycle lipoproteins and clear dead cells can allow for plaque regression. On the other hand, pro-inflammatory macrophages are associated with plaque rupture and subsequent thrombosis. Determining what signals bias macrophages to one phenotype versus another could identify a therapeutic target.

Our lab showed that in the setting of acute myocardial infarction, macrophages are skewed to a protective, reparative phenotype by loss of cGAS-STING signaling. cGAS-STING are a pattern recognition receptor-adaptor pair that are activated by double stranded DNA in a sequence-independent manner. We hypothesize that myeloid-specific loss of Cgas in a mouse model of atherosclerosis will reduce plaque burden by biasing macrophages to a less inflammatory phenotype and upregulating pro-resolving functions.

**Methods:** Ldlr<sup>-/-</sup> mice underwent total body irradiation followed by bone marrow transplant from Cgas<sup>-/-</sup> or wildtype donor mice. After bone marrow reconstitution, Ldlr<sup>-/-</sup> recipient mice were started on a Western diet (i.e. high in saturated fats and sucrose). Baseline complete blood cell counts (CBC), triglyceride (Tg), and total cholesterol (TC) levels were obtained. Mice will be continued on Western diet for 12 weeks (through April 24, 2024). After 12 weeks, aortas, peripheral blood, spleen, and bone marrow will be collected for further analysis including plaque burden, fibrous cap thickness, and macrophage phenotype. To complement in vivo studies, we will perform in vitro studies to determine how Cgas<sup>-/-</sup> affects macrophage effector functions critical for atherosclerosis.

**Results:** Cgas<sup>-/-</sup> donor bone marrow did not affect the baseline CBC, Tg, and TC levels. Bone marrow derived macrophages (BMDM) from Cgas<sup>-/-</sup> mice have increased expression of fibronectin.

**Conclusions:** At baseline, Cgas<sup>-/-</sup> BMDM express high level of a marker associated with pro-reparative or pro-resolving macrophages. More studies are needed to confirm this and determine the consequence for in vivo atherosclerosis.

Poster #6

**Presenter:** Roger Fan, MD

Basic Science

**Authors:** Roger Fan, MD; Surbhi Gahlot, PhD; Kathy Mountjoy, PhD; Teppei Fujikawa, PhD; Sarah Huen, MD, PhD; Joel K. Elmquist, DVM, PhD

**Title:** Immune Regulation by Alpha-Melanocyte-Stimulating Hormone: A Potential Target for Sepsis Therapy

**Abstract:**

**Background:** Sepsis, a dysregulated host response to infection, is associated with multiorgan failure and death. Despite being the most common cause of in-hospital mortality worldwide, the pathophysiology of sepsis remains poorly understood. The melanocortin system consists of several pro-opiomelanocortin (POMC)-derived peptides which signal through 5 melanocortin receptors. Among these peptides are three structurally related melanocortin-stimulating hormones (MSH):  $\alpha$ -,  $\beta$ -, and  $\gamma$ -MSH. Intriguingly, previous studies have indicated that  $\alpha$ -MSH contributes to anti-inflammatory effects. However, the mechanism by which  $\alpha$ -MSH regulates inflammation remains unclear due to the lack of genetic models enabling the manipulation of specific MSH peptides. We hypothesize that  $\alpha$ -MSH critically regulates energy metabolism and mitigates inflammation during sepsis. To test our hypothesis, we developed an  $\alpha$ -MSH null model ( $\alpha$ MSHKO mice) to assess whether  $\alpha$ -MSH is required for anti-inflammatory responses.

**Methods:** We administered single intraperitoneal (i.p.) injections of either saline or low-dose lipopolysaccharide (LPS, 100  $\mu$ g/kg) to 10–14-week-old male  $\alpha$ MSHKO and WT mice. Additionally, we co-injected mice with saline or melanotan II (MTII, 100  $\mu$ g/kg), a melanocortin agonist. We used telemetry to measure core body temperature and ELISA to measure circulating cytokines. For survival studies, male  $\alpha$ MSHKO and WT mice received a single i.p. injection of high-dose LPS (8 mg/kg).

**Results:** LPS administration led to elevated plasma cytokines in  $\alpha$ MSHKO mice, including IL-1 $\beta$ , IL-6, MCP-1 and MIP-1 $\alpha$ . Notably, LPS induced a prolonged hypothermic response in  $\alpha$ MSHKO mice that could be prevented by MTII. MTII also reduced expression of MCP-1 and MIP-1 $\alpha$  in wild type mice after LPS. Surprisingly, MTII had no significant effect on cytokine expression in  $\alpha$ MSHKO mice. High-dose LPS resulted in 50% survival in  $\alpha$ MSHKO mice at 96 hours compared with 100% survival in WT mice ( $p=0.0092$ ).

**Conclusions:** Our findings highlight the pivotal role of endogenous  $\alpha$ -MSH in modulating inflammatory responses triggered by LPS, ultimately influencing survival outcomes. Treatment with MTII improved the hypothermic response to LPS in  $\alpha$ MSHKO mice and reduced macrophage-derived cytokines in WT mice. Targeting of the melanocortin system may offer new approaches for sepsis management.

Poster #7

**Presenter:** Roger Fan, MD

Basic Science

**Authors:** Surbhi Gahlot, PhD; Roger Fan, MD; Kathy Mountjoy, PhD; Teppei Fujikawa, PhD; Sarah Huen, MD, PhD; Joel K. Elmquist, DVM, PhD

**Title:** The Role of Gamma-Melanocyte-Stimulating Hormone in Energy Metabolism

**Abstract:**

**Background:** The melanocortin system is critical for the regulation of energy balance and glucose homeostasis. The system consists of several pro-opiomelanocortin (POMC)-derived peptide hormones/neurotransmitters which signal through 5 melanocortin receptors. Among these, three structurally related melanocortin stimulating hormones are  $\alpha$ -,  $\beta$ -, and  $\gamma$ -MSH.  $\gamma$ -MSH is expressed in the brain and binds exclusively to the melanocortin receptor 3 (MC3R). Genetic deletion of MC3R in mice increases fat mass, reduces lean mass, and blunts response to fasting. Further, selective MC3R agonist, D-Trp<sup>8</sup>- $\gamma$ -MSH significantly decreases fat mass/lean mass ratio in mice. While these findings suggest an important role of MC3R and  $\gamma$ -MSH in regulating body energy balance, physiological roles of  $\gamma$ -MSH in regulation of metabolism remain unknown due to the lack of genetic models enabling us to manipulate  $\gamma$ -MSH specifically. We recently generated a  $\gamma$ -MSH null mouse by introducing a targeted mutation in exon 4 of the Pomc gene that prevents the cleavage of N-POMC into  $\gamma$ -MSH.

**Methods:** Both male and female mice were challenged with 60 % high fat diet (HFD) beginning at 5 weeks of age. A series of metabolic phenotyping experiments were performed to determine the role of  $\gamma$ -MSH in the control of energy and glucose balance.

**Results:** Male adult mice lacking  $\gamma$ -MSH showed mild increase in body weight, with increased fat mass and increased fat mass/lean mass ratio. We then challenged these mice with glucose and insulin tolerance tests (GTT and ITT, respectively). GTT revealed no differences in glucose clearance following an i.p. injection of 1.5 g/kg glucose. Further, ITT revealed no glucose counterregulatory measures when mice received an i.p. injection of 1.25 units/kg insulin (Humulin R).

**Conclusions:** Our findings suggest that  $\gamma$ -MSH null mice recapitulate the phenotype seen in MC3R null mice. Future studies will address the contributions of  $\gamma$ -MSH in regulating feeding behavior and inflammation.

Poster #8

**Presenter:** Athena Huang, MD

Clinical Science

**Authors:** Athena Huang, MD; Rohit Nathani, MD; Manasa Dutta, MD; Colby Ayers, MS; Ann Marie Navar, MD, PhD; Fiona Strasserking, MD

**Title:** Characteristics and Outcomes of Peripartum Cardiomyopathy Patients at a Large Metropolitan Safety Net Hospital

**Abstract:**

**Background:** Peripartum cardiomyopathy (PPCM) incidence and outcomes vary across the country. Parkland Hospital serves a diverse, primarily indigent urban population and is one of the busiest maternity wards in the country. The primary objective of this study is to describe the characteristics and outcomes of PPCM patients at Parkland.

**Methods:** This is a retrospective cohort study of women >18 years diagnosed or treated for new onset PPCM between April 1, 2009 – December 31, 2022 at Parkland. Patients who delivered during the study period and had a transthoracic echocardiogram (TTE) with a left ventricular ejection fraction (LVEF) of <0.45 in the late third trimester or months following delivery were screened via chart review for study inclusion.

**Results:** 46 of 83 screened patients were included in the final cohort. Over the study period, the overall incidence of new onset PPCM per delivery at Parkland was 0.03%. Median age was 31 (IQR 27-37) years. The cohort was 57% Black and 35% Hispanic. Most (76%) were Medicaid-insured. Over half (54%) had hypertensive disorders of pregnancy. At the time of PPCM diagnosis, median LVEF was 0.32 (IQR 0.25-0.40) and median LV end diastolic diameter was 5.6 (IQR 5.2-6.2) cm. The majority of patients were diagnosed postpartum (85%), with a median time to diagnosis of 7 (IQR 1-94) days after delivery. 3 patients required inotrope support. Beta blockers (80%) and ACEi/ARB/ARNI (63%) were the most commonly prescribed therapies on discharge. 26% were lost to cardiology follow-up after their index hospitalization or PPCM diagnosis, and another 47% were lost after 6 months. Among the 30 patients who had any follow-up TTE, only 12 (40%) had LVEF recovery >0.50 within a median of 223 (IQR 149-787) days. On follow-up, 2 died, 8 received implantable cardioverter-defibrillators, and 1 received a ventricular assist device and subsequent heart transplant.

**Conclusions:** In this single-center study of an underserved patient population diagnosed with new onset PPCM, follow-up was poor, and LVEF recovery was delayed and achieved at lower rates compared to previously reported data. PPCM remains a morbid condition in this studied cohort. Quality improvement measures to close management gaps are desperately needed.



Poster #9

**Presenter:** Baqir Jafry, MD

Clinical Science

**Authors:** Baqir Jafry, MD; Allante Milsap, MS; Syed Kazmi, MD

**Title:** Effect of Racial and Gender Disparities, Tumor site and Treatment utilization on Clinical Outcomes of Neuroendocrine Tumor (NET): A Retrospective Study Using a Single Institutional Database

**Abstract:**

**Background:** Neuroendocrine tumors (NETs) present unique clinical challenges due to their diverse origins and variable prognoses. This retrospective study explores the impact of socioeconomic disparities, tumor site, and treatment on clinical outcomes of NET.

**Methods:** We identified patients diagnosed with stage 1-4 NET (ICD-O-3/WHO 2008 histology recode: "8150-8157; 8240-8249") of colorectal, small intestine, pancreatic, and lung primary from 2009 to 2017 using tumor registry of NCI-designated Comprehensive Cancer Center. We described baseline patient characteristics. Overall survival (OS) was estimated using the Kaplan-Meier method and Cox proportional hazards model with an index date of tumor diagnosis until death.

**Results:** We identified 294 patients - 96 (33%) had lung, 90 (31%) had pancreatic, 77 (26%) had small intestinal, and 31 (11%) had colorectal primary; the median age of diagnosis = 60 yr (IQR: 50-69). Most patients were females (51%), non-Hispanic whites (73%), had stage 4 disease (42%) and had well-differentiated tumors (70%). Among patients with known T stage, most had pT3 (n= 66/207; 32%). The liver was the most common site of metastasis (26%). 222 (74%) patients underwent surgical resection among whom 111 (50%) had positive lymph nodes, 95 (43%) had lymphovascular invasion, and 26 (12%) had positive surgical margins. Patients with small intestinal primary had a better 5-year OS (88%) compared to those with colorectal (80%), pancreatic (70%) and lung primary (65%). In Cox regression analysis, female gender (HR: 0.5; 95CI: 0.3-0.8) and surgical treatment (HR: 0.3; 95CI: 0.2-0.5) were associated with better OS while stage 4 disease (HR: 4; 95CI: 2-9) was associated with poor OS. Compared with small intestinal NET, lung NET (HR: 3; 95CI: 2-7) and pancreatic NET patients (HR: 2; 95CI: 1-5) had poor OS while there was no significant difference in OS in colorectal NET (HR: 2; 95CI: 0.7-6).

**Conclusion:** In this single institution cohort, most patients with NET were females and had stage 4 disease. NET of the small intestinal primary had better OS compared to NET originating from other sites. Female gender and surgical treatment were associated with better OS while higher stage was associated with worse OS.

Poster #10

**Presenter:** Christopher Grubb, MD

Clinical Science

**Authors:** Grant Tucker, BS; Christopher Grubb, MD; Neda Bionghi, MD, MPH; Colby R. Ayers, MS; Nicholas S. Hendren, MD; Justin L. Grodin, MD, MPH; Jennifer T. Thibodeau, MD, MScS; Ann Marie Navar, MD, PhD; Maryjane A. Farr, MD, MSc; Sandeep R. Das, MD, MPH; James A. de Lemos, MD; Eric J. Hall, MD

**Title:** Intubation Practices and Peri-intubation Complications Among Patients with Cardiogenic Shock

**Abstract:**

**Background:** Acute cardiogenic shock (CS) is often complicated by respiratory failure requiring invasive mechanical ventilation. The risk of intubation is increased in patients with hemodynamic derangements, yet little is known regarding practices and outcomes surrounding intubation in patients with CS.

**Methods:** Single center retrospective analysis at a public safety net hospital of patients with CS requiring invasive mechanical ventilation. Choice of induction agent, paralytic agent, and peri-intubation complications were assessed.

**Results:** A total of 112 patients were identified (median age 59yo, 72% male, 38% of Black race, 39% of Hispanic ethnicity), of whom 67% experienced CS due to heart failure exacerbation and 33% due to acute MI. Of these 112 patients, 34 have currently been reviewed, with the remainder to be reviewed within the following month. Thus far, the majority of patients were intubated for hypoxic respiratory failure (38%) or active cardiac arrest (35%). The most common induction and paralytic agents were etomidate (46%) and rocuronium (69%), respectively. Peri-intubation complications occurred in 29% of patients, with new/increased vasoactive medications within 10 minutes and cardiac arrest within 1-6 hours of intubation the most common complications.

**Conclusions:** Intubation in patients with cardiogenic shock is high risk, with approximately one-third of patients experiencing peri-intubation complications, primarily related to worsening hemodynamic instability or post-procedural cardiac arrest.

Poster #11

**Presenter:** Douglas Kyrouac

Clinical Science

**Authors:** Douglas Kyrouac, Nicholas Talbot, James MacNamara, Michinari Hieda, Christopher Hearon, Tiffany Brazile, Benjamin D. Levine, MD; Satayam Sarma

**Title:** Effects of year Long Aerobic Exercise on Left Atrial Size in Patients with Stage B HFpEF

**Abstract:**

**Background:** Habitual aerobic exercise is associated with left atrial (LA) enlargement and risk of atrial fibrillation. This risk may be accentuated in patients with increased left ventricular (LV) stiffness due to high LA pressure during exercise. We tested the hypothesis that 1 year long aerobic endurance exercise would increase LA size to a greater extent in patients with left ventricular hypertrophy (LVH) at risk for heart failure with preserved ejection fraction (HFpEF) than previously published age-appropriate controls.

**Methods:** Middle-aged adults (age 45-64 yrs) with LVH (n=53) enriched for increased HFpEF risk (N-terminal pro-B-type natriuretic peptide >40 pg/mL or high-sensitivity cardiac troponin T >0.6 pg/mL) and healthy subjects (n=58) were randomized to one year of high intensity aerobic exercise or yoga control. LA and LV volumes were measured using 3D echo.

**Results:** Of 111 participants, 83 had complete data available (LVH cohort: 18 exercisers, 10 yoga; healthy cohort: 29 exercisers, 26 yoga). Baseline left atrial volume index was similar in those at risk for heart failure as compared to healthy subjects (19.75 +/- 4.4 mL/m<sup>2</sup> vs 18.8 +/- 4.1 mL/m<sup>2</sup>; p=0.33). There was a nominal increase in LA volume index in LVH exercisers compared to LVH yoga (4.6 ± 4.8 vs 2.4 ± 2.2 mL/m<sup>2</sup>; p=0.18) which was proportional to LV volume (LA:LV ratio 0.06 ± 0.05 vs 0.06 ± 0.1; p=0.92). Healthy subject exercisers increased LA size compared to healthy yoga controls (2.0 ± 2.8 vs -0.02 ± 3.3 mL/m<sup>2</sup>; p=0.02) with no increase in LA:LV ratio (-0.02 ± 0.06 vs -0.02 ± 0.08; p=0.62). When combining the four groups, exercise (p=0.003) and LVH (p=0.001) were each associated with an increase LA volume index, while LVH (p<0.001) and not exercise (p=0.59) was associated with an increased LA:LV ratio.

**Conclusions:** One year of aerobic training resulted in higher LA volume index in patients with at risk LVH compared to healthy subjects. The increase in LA size was greater than changes in LV size suggesting chronic aerobic training in these people may preferentially affect LA remodeling.

Poster #12

**Presenter:** Eric Hall, MD

Clinical Science

**Authors:** Eric J. Hall, MD; Colby R. Ayers, MS; Nicholas S. Hendren, MD; Christopher Clark, BS; Amit Saha, MD; Hadi Beaini, MD; Isabella L. Alexander, BS; Evan P. Gee, BS; Ian R. McConnell, BA; Emily S. Samson, BSA; Roslyn J. Saplicki, BA; Justin L. Grodin, MD, MPH; Jennifer T. Thibodeau, MD, MSCS; Mark H. Drazner, MD, MSc; Mujeeb Basit, MD, MMSc; Maryjane A. Farr, MD, MSc; Ann Marie Navar, MD, PhD; Sandeep R. Das, MD, MPH; James A. de Lemos, MD

**Title:** Long-term Outcomes and Medical Therapy Among Patients with Cardiogenic Shock Treated in a Safety Net Hospital

**Abstract:**

**Background:** While in-hospital mortality in patients with cardiogenic shock (CS) remains high, the majority of patients survive to hospital discharge. Little is known regarding strategies for medical therapy (GDMT) or long-term outcomes in survivors of CS. In addition, most data regarding CS outcomes are from large tertiary referral centers with limited data from community hospitals, particularly those caring for underserved patient populations.

**Methods:** Single center retrospective analysis of patients treated at a public safety net hospital who had undergone a right heart catheterization (RHC) and met criteria for Society for Coronary Angiography and Intervention (SCAI) Stage C, D, or E CS, defined as requiring mechanical circulatory support (MCS) or vasoactive medications. GDMT use, total hospitalizations and healthcare charges through 1 year were assessed among those who survived the initial hospitalization.

**Results:** A total of 378 patients with Stage C or greater CS were identified (median age 57 years, 44% Black race, 35% Hispanic ethnicity), of whom 81% experienced CS due to decompensated heart failure (HF-CS) and 19% due to an acute myocardial infarction (AMI-CS). MCS was used in 23% of all patients. Overall, 82% of patients survived to discharge, with 66% discharged to home or rehabilitation, 4% to hospice, and 12% transferred to another hospital for higher level care. Mortality within 30 days of admission was lower among patients with HF-CS than those with AMI-CS (26% vs 33%,  $p=0.005$ ). Of those discharged to home/rehab, beta blockers (BB) were prescribed in 38%, with lower use in those with HF-CS than AMI-CS (34% vs 58%,  $p=0.01$ ). In contrast to early mortality, long-term mortality was higher in patients with HF-CS (hazard ratio 2.0, 95% CI 1.1-3.9,  $p=0.03$  at 2 years follow up). BB and ACE/ARB/ARNIs were used in 53% and 59% of survivors at 1 year, respectively, with similar rates between survivors of HF-CS and AMI-CS.

**Conclusions:** In a safety net hospital system, most patients with CS survived to discharge. Early mortality was higher among patients with AMI-CS, while late mortality was higher among patients with HF-CS. GDMT was not used in a substantial minority of patients; future research should aim to evaluate the role of GDMT in CS survivors.

Poster #13

**Presenter:** Eric Hall, MD

Clinical Science

**Authors:** Eric J. Hall, MD; Qiang Li, MS; Paul S. Chan, MD, MSc; Bryan McNally, MD, MPH; Rabab Al-Araji, MPH; James de Lemos, MD; Saket Girotra, MD, SM

**Title:** Survival from Out-of-hospital Cardiac Arrest: Persistence of the COVID-19 Effect?

**Abstract:**

**Background:** The COVID-19 pandemic in 2020 was marked by a sharp decrease in out-of-hospital cardiac arrest (OHCA) survival. It is not known whether OHCA survival has recovered to pre-pandemic levels, and whether changes in OHCA survival have been similar across communities of different racial and ethnic composition.

**Methods:** We included adult patients with non-traumatic OHCA from 2015-2022 in the Cardiac Arrest Registry to Enhance Survival (CARES) registry. Using hierarchical multivariable regression models, we calculated risk-adjusted rates of survival to hospital discharge during 2015-2019 (reference period) and compared this to survival rates during 2020, 2021, and 2022, respectively. We also examined whether the trajectory of survival outcomes over this period differed based on the racial/ethnic composition of the community served by the EMS agency (predominantly White [>80% of residents], majority Black or Hispanic [>50% of residents], and integrated [neither]).

**Results:** Of 501,045 patients with OHCA, mean age was 61.9 years; 64% were male, and 22% were of Black race and 7% of Hispanic ethnicity. Overall, risk-adjusted survival rates to hospital discharge for OHCA decreased from 10.1% in 2015-2019 to 8.4% in 2020 ( $P<0.0001$ ). The relative decrease in OHCA survival was similar in EMS agencies serving predominantly Black and Hispanic communities (-17.4%) as compared to integrated (-16.8%) or White communities (-17.6%). Risk-adjusted survival recovered partially in 2021 (8.7%) and 2022 (8.9%) but remained below the pre-pandemic period. Although there was a large relative improvement in survival at EMS agencies serving predominantly Black and Hispanic communities relative to predominantly White communities, overall survival in Black and Hispanic communities remained lower than predominantly White and integrated communities at all time periods.

**Conclusions:** The initial decrease in OHCA survival that accompanied the onset of the COVID-19 pandemic continues to persist across the United States. Although survival rates have continued to recover, the pattern of recovery differs across EMS agencies. Our findings highlight the urgent need to strengthen the chain of survival for OHCA in the post-COVID era.

Poster #14

**Presenter:** Eric Hall, MD

Clinical Science

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**Title:** Ambulatory Shock?: Management and Long-term Outcomes Among Outpatients with Severely Reduced Cardiac Index

**Abstract:**

**Background:** A subset of ambulatory patients with heart failure have reduced cardiac index (CI) similar to patients in acute cardiogenic shock. Little is known regarding management and outcomes of these patients, particularly those with limited access to advanced therapies.

**Methods:** Single center retrospective analysis of patients with reduced ejection fraction (EF) who underwent outpatient right heart cath (RHC) at a safety net hospital. Patients were categorized based on CI: very low index (VLI,  $CI \leq 1.7$  L/min/m<sup>2</sup>), mildly low index (MLI,  $CI 1.71-2.2$ ), and normal index (NI,  $CI > 2.2$ ).

**Results:** A total of 231 patients were included. Median age was 59yo; 72% of the patients were male, 41% of Black race, and 36% of Hispanic ethnicity. A large proportion (48%) were uninsured or receiving charity care. Patients in the VLI (N=60) and MLI groups (N=87) had lower LVEF than the NI group (N=84; 28% vs 33% vs 36%,  $p_{trend}=0.004$ ). Patients in the VLI and MLI groups also had higher filling pressures (right atrial pressure 11mmHg vs 9 vs 8,  $p_{trend}=0.047$ ). Despite hemodynamic differences, all 3 groups were prescribed beta blockers (BB) at similar rates after the RHC (VLI 77%, MLI 83%, NI 83%,  $p=0.34$ ). Two-year mortality was similar across all 3 groups (VLI 12% vs MLI 16% vs NI 10%,  $p=0.33$ ). Long-term BB use was similar across groups (82% overall,  $p=0.72$ ), as was ACE/ARB/ARNI use (80%,  $p=0.41$ ).

**Conclusions:** Among ambulatory patients with very low cardiac index, long-term survival was similar to patients with mildly reduced or normal cardiac index. Beta blockers were used at high rates regardless of cardiac index.

Poster #15

**Presenter:** Huzair Ali, MBBS

Clinical Science

**Authors:** Huzair Ali, MBBS; Jaspreet Sian, MD; Michael Harms; Steven Brown; Jiten Patel, MD; Ramesh Saxena, MD, PhD

**Title:** Comparison of Kidney Transplantation Evaluation Between Patients on Hemodialysis and Peritoneal Dialysis

**Abstract:**

**Background:** While in-center hemodialysis (HD) is delivered by trained healthcare providers, peritoneal dialysis (PD) involves active patient-engagement in the dialysis treatment. This process of self-care can be associated with a range of potential collateral health benefits, that can positively impact clinical and patient-centered outcomes. Kidney transplantation (KT) is the major outcome goal among kidney failure (KF) patients who initiate dialysis. Several studies have shown that PD patients are more likely to receive KT, compared to HD patients. However, differences among HD and PD patient populations such as age, race, socioeconomic status, may confound the results. In this retrospective study, we compared transplant evaluation and listing status among propensity matched incident HD and PD patients initiating dialysis at Parkland Hospital, a safety net hospital caring for underserved population in Dallas County.

**Methods:** We included patients 18 years of age or older, who were newly initiated on HD or PD at Parkland Hospital. Patients initiated on PD were propensity matched 1:1 based on language, ethnicity/race, age, and comorbidities. The primary outcome was proportion of patients evaluated for transplantation, while key secondary outcomes included proportion of patients listed for transplantation, reasons for not listing, proportion transplanted, time to transplant, hospitalization rates and mortality.

**Results:** During the study period 155 patients were initiated on PD, and were propensity matched with 155 patients initiating on HD. Of patients initiated on PD, 132 (85.2%) were evaluated for transplantation, compared to 106 (68.4%) patients on HD ( $p<0.001$ ). Among patients evaluated for KT, 50 (35.5%) patients on HD vs 78 (50.3%) PD patients were eventually listed for transplantation. Of the patients evaluated but not listed, medical ineligibility was the predominant reason in PD group (70.3%), while in HD group 65% were not listed due to lack of interest and non-adherence.

**Conclusion:** In our study we observed higher transplant evaluation and eventually higher KT rates among PD patients compared to HD patients, suggesting that active patient engagement in dialysis management can improve health care outcomes even in patients coming from underserved areas.



Poster #16

**Presenter:** Jane Lee, MD

Clinical Science

**Authors:** Jane Lee, MD; Oksana Hamidi, DO; Sasan Mirfakhraee, MD

**Title:** Continuous Subcutaneous Hydrocortisone Infusion is Practical and Effective in Select Patients with Adrenal Insufficiency

**Abstract:**

**Background:** Continuous subcutaneous hydrocortisone infusion (CSHI) via insulin pump is an alternative therapy for treating patients with adrenal insufficiency (AI) and allows for adjustable hydrocortisone delivery to provide more physiologic glucocorticoid replacement. Due to a scarcity of data, CSHI is likely underutilized. Our research objectives were to analyze the change in total daily glucocorticoid dose, number of adrenal crises events and hospitalization days, glucocorticoid-related comorbidities, and quality of life of patients transitioned from oral glucocorticoids to CSHI.

**Methods:** We performed a single-center, retrospective longitudinal follow-up study in 23 consecutive patients (87% women, median age 40 years) treated with CSHI between 2015 and 2023. Types of adrenal insufficiency were 48% secondary AI, 35% glucocorticoid induced AI, and 17% primary AI. CSHI delivery settings were generated by a formula we derived using each patient's daily oral glucocorticoid dose and preferred waking time. Median time from AI diagnosis to CSHI implementation was 41 months; median duration of CSHI was 25 months.

**Results:** Total daily dose of glucocorticoid (in hydrocortisone equivalent) before CSHI vs during CSHI decreased from 30.0mg (15.0-80.0 mg) to 26.6mg (14.4-200.5mg) ( $p=0.45$ ). Median number of adrenal crisis events decreased from 1 (0-13) to 0 (0-38) ( $p=0.25$ ), and hospitalization days due to adrenal crisis decreased from 2 (0-46) to 0 (0-58) ( $p=0.53$ ). No significant differences were noted for change in weight, blood pressure, diabetes, cardiovascular and cerebrovascular events, total cholesterol, LDL, and triglyceride concentrations. Median HDL decreased from 59 to 51 ( $p=0.01$ ). In terms of subjective health status, 10 patients completed SF-36 survey while on CSHI. Significant impairments were noted in physical health, vitality, and general health (median score < 40).

**Conclusion:** At the conclusion of the study, 20 patients (87%) preferred CSHI therapy. Only 3 patients stopped CSHI for reasons of inconvenience, skin irritation at pump site, and better symptom control on oral therapy. No significant CSHI-related safety concerns were noted. In conclusion, CSHI is a safe and effective way to deliver individualized therapy to patients with difficult to control AI. CSHI led to reduction in glucocorticoid exposure and fewer adrenal crisis events and hospitalization days due to adrenal crisis.

Poster #17

**Presenter:** Karim Seif El Dahan, MD

Clinical Science

**Authors:** Karim Seif El Dahan, MD; Takeshi Yokoo, MD, PhD; Mishal Mendiratta-Lala, MD; David T. Fetzer, MD; Matthew S. Davenport, MD; Darine Daher, MD; Nicole E. Rich, MD, MSCS; Edward Yang, MD; Neehar D. Parikh, MD, MS; Amit G. Singal, MD, MS

**Title:** Exam Quality of Liver Ultrasound and Dynamic Contrast-Enhanced MRI and Impact on Early-Stage HCC Detection in Patients with Cirrhosis

**Abstract:**

**Background:** Magnetic resonance imaging (MRI) is a potential alternative to ultrasound for hepatocellular carcinoma (HCC) surveillance among patients in whom ultrasound exam quality is limited. However, it remains unclear how the two modalities complement each other in surveillance programs. We characterized ultrasound and dynamic contrast-enhanced (DCE)-MRI exam quality and evaluated its association with early-stage HCC detection.

**Methods:** We conducted a retrospective case-control study at three US health centers among patients with cirrhosis (cases with early-stage HCC per Milan Criteria; controls without HCC) who underwent ultrasound and DCE-MRI within 6 months in 2012-2019. Two radiologists performed independent, blinded interpretations of both exams for HCC detection using LI-RADS algorithms and scored exam quality as no/mild, moderate, or severe limitations. Detection of high-risk liver observations on ultrasound (i.e., US LR-3) and DCE-MRI (i.e., MRI LR-4, LR-5, LR-M) were categorized as positive. Associations between exam quality, patient characteristics, and HCC detection were assessed by odds ratios (OR).

**Results:** Of 216 cases and 432 controls, severe limitations were reported in 7% and 8% of ultrasounds and DCE-MRIs, respectively. Child-Pugh C cirrhosis was associated with severe limitations on both ultrasound (OR 2.54 [1.37-4.58]) and DCE-MRI (OR 3.96 [2.36-6.58]). Severe limitations on ultrasound were also associated with obesity (OR 2.08 [1.32-3.32]) and metabolic dysfunction-associated steatotic liver disease (MASLD) (OR 1.98 [1.12-3.44]), but neither were associated with DCE-MRI visualization. Compared to exams with no/mild limitations, exams with severe limitations had lower sensitivity for HCC detection on ultrasound (79.6% vs. 21.7%,  $P < 0.001$ ) and DCE-MRI (86.1% vs. 50.0%,  $P = 0.001$ ). Most patients (84%) with severely limited ultrasound (ie. score C) had quality scores A (no/mild limitation) or B (moderate limitation) on DCE-MRI. For patients in whom ultrasound was severely limited, DCE-MRI had significantly higher odds of early-stage HCC detection than ultrasound (OR 8.23 [1.25-54.02]).

**Conclusions:** Exam quality limitations at ultrasound and DCE-MRI impair sensitivity for early-stage HCC detection. MRI may be preferable in patient subgroups in whom ultrasound is likely to be limited, such as those with obesity or MASLD. Both modalities have quality limitations in patients with decompensated cirrhosis, underscoring a need for more effective surveillance strategies in this population.

Poster #18

**Presenter:** Katarina Yaros, MD

Clinical Science

**Authors:** Katarina Yaros, MD; Matthew Segar, MD; Vinayak Subramanian, MD; Alvin Chandra, MD; Thomas Koshy, MD; Ross Upton, PhD; Ashley Ackerman, PhD; Ambarish Pandey, MD, MSCS

**Title:** Diagnostic and Prognostic Evaluation of an Echocardiography-based Artificial Intelligence Algorithm for Detecting HFpEF: A Case-Control Analysis

**Abstract:**

**Background:** Heart failure (HF) with preserved Ejection Fraction (HFpEF) is common among older adults and is associated with a high burden of morbidity and mortality. Despite its increasing prevalence, the diagnosis of HFpEF remains challenging and often requires the assessment of left ventricular filling pressure by invasive or non-invasive approaches. Recently, the FDA cleared an echocardiography-based AI HFpEF model that utilizes a 3-dimensional convolutional neural network to detect HFpEF using a single 4-chamber clip from a resting echocardiogram. However, the external validation of this algorithm against clinically adjudicated and confirmed HFpEF cases is limited.

**Methods:** The study included patients referred for HFpEF work-up to the UTSW HFpEF clinic and age, sex, and BMI-matched control participants without HF and a normal echocardiogram. The HFpEF cases were clinically adjudicated based on the clinical history, signs and symptoms of HF, normal ejection fraction (>45%), and objective evidence of elevated filling pressures by resting (PCWP > 15 mm Hg) or exercise invasive hemodynamics (PCWP > 25 mm Hg) or echocardiogram ( $E/e' > 14$ ) in a subset. The performance of the AI HFpEF model was evaluated using receiver operator curves. Among patients with clinically adjudicated HFpEF, the association of the AI-HFpEF phenotype with elevated resting/exercise PCWP and peak exercise oxygen uptake ( $VO_{2peak}$ ) was assessed using multivariable logistic and linear regression models adjusting for age, sex, race, BMI, and comorbidities (diabetes, hypertension, kidney disease, atrial fibrillation)

**Results:** Of the 166 patients referred for evaluation of HFpEF, 82% had clinically adjudicated HFpEF, and 69.8% had elevated LV filling pressure at rest or exercise. In the matched cohorts of patients with clinically adjudicated HFpEF and matched control individuals (N = 122 each), the AI algorithm-based probability of HFpEF demonstrated good performance in identifying clinically adjudicated and hemodynamically confirmed HFpEF (AUROC: 0.75 for each) that was greater than the widely used H2FpEF score (0.69 and 0.70, Figure). In the HFpEF referral cohort, a higher probability of HFpEF based on the AI-algorithm phenotype was significantly associated with lower  $VO_{2peak}$  ( $\beta$  [95% CI] per 5% higher probability: -0.11 [-0.21 to -0.01, P-value: 0.03] and greater odds of elevated PCWP (Odds ratio [95% CI] per 5% higher probability: 1.07 [1.01 – 1.15, P-value: 0.04] at rest or exercise after accounting for other confounders. Based on Youden's index, the AI algorithm-based probability threshold of >0.75 was identified as the optimal cutoff for detecting HFpEF by the AI algorithm, with high sensitivity (0.85) and accuracy (0.74) and, adequate specificity (0.66).

**Conclusion:** The echocardiography-based AI HFpEF model demonstrated excellent sensitivity and discrimination in identifying patients with vs. without clinical HFpEF. Furthermore, the AI HFpEF model also had prognostic utility such that individuals with a higher probability of AI-HFpEF phenotype had more severe HFpEF.

Poster #19

**Presenter:** Mason Marcus, MD

Clinical Science

**Authors:** Mason Marcus MD; Paul S. Chan MD, MSc; Anping Chang MS, MPH; Rob Merritt MA; Bryan McNally MD; Mark S. Link MD; Saket Girotra MD, SM

**Title:** Implantable Cardioverter Defibrillators Among Elderly Survivors of Out-of-Hospital Cardiac Arrest

**Abstract:**

**Background:** Survivors of out-of-hospital cardiac arrest (OHCA) with a shockable rhythm are at increased risk of cardiac arrest, and clinical practice guidelines recommend placement of an implantable cardioverter defibrillator (ICD) in the absence of a reversible cause and an expected meaningful survival of at least one-year.

**Purpose:** Examine patterns of secondary prevention ICD implantation in survivors of OHCA due to a shockable rhythm in a large national registry.

**Methods:** Using 2013-2019 data from the Cardiac Arrest Registry to Enhance Survival (CARES) linked to Medicare files, we identified 3,226 patients aged 65 years and older who survived to discharge following OHCA due to an initial shockable rhythm. We calculated the prevalence of ICD implantation at discharge, 90 days, and 6 months post-cardiac arrest, and by age group, sex, race, and ethnicity. Multivariable hierarchical regression models with random hospital effects were used to determine the adjusted association of patient characteristics with ICD implantation and quantify the extent of variation in ICD implantation across sites, using a median odds ratio (OR) and 95% confidence interval (CI).

**Results:** The mean age was 72.2 years; 23.5% were women, 10% were Black and 4% Hispanic. Among 3,226 OHCA patients, 997 (30.9%) received an ICD before discharge, 1,266 (39.2%) received an ICD within 90 days of the cardiac arrest and 1,287 (39.9%) received an ICD within 6 months. After adjusting for differences in demographics and co-morbidities, the odds of receiving an ICD prior to discharge were lower in patients older than 85 years of age (OR 0.59; 95% CI 0.38-0.92) compared to the 65-74 year age group, and in women compared to men (OR 0.80; 95% CI 0.64-0.99). There was large variation in hospital rate of ICD implantation at discharge, with a median OR of 1.65 (95% CI 1.41 to 1.86), after adjusting for patient demographics and co-morbidities.

**Conclusion:** Fewer than 1 in 3 patients with OHCA due to a shockable rhythm are discharged with a secondary prevention ICD. Female sex, older age, and prior history of stroke and diabetes were associated with ICD implantation. Even after adjusting for case-mix, ICD implantation varied markedly across hospital sites.

Poster #20

**Presenter:** Maya Wiessman, MD

Clinical Science

**Authors:** Maya Wiessman, MD; James Wyatt Miller, Med Std; Arzu Canan, MD; Michael Long, MS; Rodderick McColl, PhD; Travis Browning, MD; Ann Marie Navar, MD, PhD; Parag Joshi, MD; Suhny Abbara, MD; Ronald M. Peshock, MD; Fernando Kay, MD, PhD

**Title:** Implementing Dashboards for Quality Control of Deployed AI-enabled Coronary Artery Calcification Assessment and Correlation with Radiologist Assessment

**Abstract:**

**Background:** Coronary artery calcium (CAC) is a key imaging biomarker for predicting atherosclerotic events. Yet, its evaluation in non-ECG-gated chest CT scans remains largely subjective. Our objective was to determine whether artificial intelligence (AI) derived CAC measurements correspond more accurately with those from ECG-gated CAC CT than do subjective radiologist interpretations.

**Methods:** Between 09/22/2022 and 10/31/2023, 25,680 non-contrast chest CTs were processed with an AI software (AI Rad Companion, Siemens Healthineers, Erlangen, Germany) to quantify CAC volume as none ( $0 \text{ mm}^3$ ), mild ( $\leq 100 \text{ mm}^3$ ), moderate ( $\leq 500 \text{ mm}^3$ ) and severe ( $> 500 \text{ mm}^3$ ). Results were compared with radiologists' assessments as per 2016 SCCT/STR guidelines. A dashboard was developed using PowerBI (Microsoft Corp, Redmond, WA, United States) that utilized data collated from clinical applications. Radiologists' reports derived CAC assessments, were then used to construct a confusion matrix, allowing for comparison of AI and human evaluation. A subsample of 44 chest CT scans from 40 patients, who also had ECG-gated cardiac CT within one year, was reviewed to evaluate radiologist-AI concordance against the Agatston score.

**Results:** 11,791 (54%) studies demonstrated perfect radiologist-AI concordance for CAC assessment, with a weighted kappa of 0.44. Figure 1 shows detailed results for discordant studies. A confusion matrix enabled identification of studies requiring further adjudication. AI CAC measurements were significantly more concordant with Agatston score, with a weighted kappa of 0.96 versus 0.86 for subjective scoring ( $P = 0.001$ ).

**Conclusions:** Monitoring AI and radiologist CAC assessment using business intelligence tools enable identification of studies with radiologist-AI discordance requiring further adjudication. Concordance of AI-assigned CAC categories with Agatston score is higher than subjective scoring, suggesting a role for AI-determined CAC as a benchmark for subjective assessment.

Poster #21

**Presenter:** Neil Keshvani, MD

Clinical Science

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**Title:** Sex Disparities in Longitudinal Use and Intensification of Guideline-Directed Medical Therapy Among Patients With Newly Diagnosed Heart Failure With Reduced Ejection Fraction

**Abstract:**

**Background:** Guideline-directed medical therapies (GDMT) are the mainstay of treatment for heart failure with reduced ejection fraction (HFrEF), but they are underutilized. Whether sex differences exist in the initiation and intensification of GDMT for newly diagnosed HFrEF is unknown.

**Methods:** Patients with new HFrEF from the 2016-2020 Optum Claims Database, which includes privately insured patients covered by United Healthcare, were analyzed. The primary outcome was utilization of optimal GDMT within 12 months of HFrEF diagnosis. Consistent with the guideline recommendations during the time period of the study, optimal GDMT was defined as >50% of the target dose of evidence-based beta-blocker plus > 50% of the target dose of ACE inhibitor, ARB, or any dose of ARNI plus any dose of MRA. Cox proportional hazard models were used to evaluate patient-level factors and the probability of achieving optimal GDMT within 12 months.

**Results:** The study cohort included 63,759 patients (mean age: 71.3 years, 15.2% Non-Hispanic Black, and 56.6% male). Optimal GDMT Utilization was achieved by 3.0% at 3 months, 4.3% at 6 months, 5.3% at 9 months, and 6.2% of participants at 12 months post-diagnosis. Compared to male patients with HFrEF, female patients had lower dose across every GDMT class over each three-month interval and lower utilization of optimal GDMT. In a fully adjusted Cox model, female sex was associated with a lower probability of achieving optimal GDMT by 12 months post-diagnosis (HR 0.77 [95% CI 0.72-0.84],  $P<0.001$ ). Non-Hispanic Black race (HR 1.50 [95% CI 1.37-1.64],  $P<0.001$ ), inpatient diagnosis of HF (HR 1.30 [95% CI 1.20-1.40],  $P<0.001$ ), and number of hospitalizations during follow-up (HR, 2.50 [95% CI, 2.04-3.10];  $P<0.001$ ) were associated with a greater probability of achieving optimal GDMT by 12 months. Lower GDMT utilization was most pronounced for females (vs. males) with commercial insurance compared with Medicare (Pinteraction = 0.005) and for younger females (vs. males) compared with older females (vs males) (Pinteraction = 0.01).

**Conclusions:** While overall utilization of optimal GDMT was low, females had lower utilization of optimal GDMT 1-year after HFrEF diagnosis compared to males, highlighting the need for implementation efforts directed at improving GDMT initiation and uptitration.

Poster #22

**Presenter:** Shota Watanabe, MD

Clinical Science

**Authors:** Shota Watanabe, MD; Peter Van Buren, MD

**Title:** The Association Between Syndecan-1, Osteopontin, and Mineral Bone Disease in Chronic Kidney Disease Patients in the Dallas Heart Study

**Abstract:**

**Background:** Chronic kidney disease (CKD) patients have significantly increased cardiovascular (CV) morbidity and mortality risk compared to the general population due to both traditional Framingham CV risk factors and non-traditional risk factors. Mineral bone disease (MBD) referring to disturbances in homeostasis of calcium, phosphorus (Ph) and their regulators is a recognized CV risk factor in CKD patients, and we have previously found some associations between MBD and endothelial cell dysfunction (ECD) in hemodialysis patients and patients with more preserved renal function. The purpose of this study was to explore potential intermediates of this association using the data from the Dallas Heart Study (DHS).

**Methods:** We retrospectively analyzed data from baseline DHS1 visits. We included all participants with CKD, defined by estimated glomerular filtration rate (eGFR) <60 mL/min or a spot urine albumin/creatinine >30 mg/g. Our primary outcome was the baseline level of plasma syndecan-1, a marker of endothelial glycocalyx injury. Our primary predictor variables were baseline values of the MBD markers Ph and parathyroid hormone (PTH), as well as osteopontin. We used correlation analysis and linear regression analysis to analyze associations between these variables with syndecan-1 while also controlling for age, sex, race, diabetes, eGFR, and albuminuria.

**Results:** There were 171 CKD patients with all included variables available with mean age of 48.0 (9.0) years. Of these participants, 82 (47%) were men, 114 were Black (67%), and 56 (32%) had diabetes. They had mean phosphate 3.38 mg/dL [0.7], PTH (55.0 [54]) pg/mL, eGFR 86.0 (34) mL/min/m<sup>2</sup>, albuminuria 223 mg/g (490), syndecan 4.34 (3.8) ng/mL, and osteopontin 69.1 (79) ng/mL.

Syndecan-1 was significantly correlated with osteopontin ( $r=0.8$ ,  $p<.0001$ ) and PTH ( $r=0.2$ ,  $p=.004$ ), but not with eGFR ( $r=-0.1$ ,  $p=.06$ ) age ( $r=0.06$ ,  $p=.4$ ), phosphate ( $r=0.04$ ,  $p=.6$ ) or albuminuria ( $r=0.03$ ,  $p=.9$ ). In multivariate linear regression analysis, osteopontin was associated with syndecan ( $\beta=0.04$ ,  $p<.0001$ ) as well as diabetes.

**Conclusions:** Syndecan is associated with hyperparathyroidism and elevated osteopontin in CKD patients, but it is only independently associated with osteopontin. Osteopontin should be further explored as a significant mediator of endothelial cell dysfunction and CV disease in general in CKD patients.



Poster #23

**Presenter:** Shubham Agarwal, MD

Clinical Science

**Authors:** Shubham Agarwal, MD; Mujeeb A Basit, MD, MMSc; Michael Bowen, MD, MPH; Daniel Heitjan, PhD; Christine Mai, BS; Kelsea Marble, MS; Jonathan Pak, PharmD, MBA; Zichang Xiang, MS; Ildiko Lingvay, MD, MPH, MSCS

**Title:** Predictors of Selection of GLP-1RA Vs. SGLT2i in People with Type 2 Diabetes and Atherosclerotic Cardiovascular Disease

**Abstract:**

**Background:** In people with T2D and pre-existing ASCVD, either SGLT2i or GLP-1RA are indicated to reduce MACE. We evaluated predictors of prescription of SGLT2i vs GLP1RA in a population eligible for either.

**Methods:** An electronic health record (EHR) based registry was created to identify people with T2D and ASCVD who were eligible for either a GLP1RA or SGLT2i for cardiorenal protection within a large, academic health system (UT Southwestern, Dallas, TX). Data pertaining to demographics, lab and imaging results, ICD-9/10 diagnoses, prescriptions, provider and clinic characteristics were extracted. Eligible encounters occurred in a primary care, endocrinology, cardiology, or nephrology clinic between January 1, 2019 (date of first guideline) and August 23, 2023. For each eligible encounter where a drug was prescribed, the first treatment type (GLP-1 RA or SGLT2i) was determined based on medication history. We estimated a logistic regression using stepwise variable selection to identify a best-predicting model and forced the variables of age, sex, and race into the model.

**Results:** A total of 315 patients with T2D and ASCVD were eligible for either treatment, of whom 142 were prescribed a GLP-1 RA and 173 were prescribed SGLT2i. Lower BMI was associated with use of SGLT2i (OR = 0.91, 95% CI 0.87-0.96), as was being an established patient (OR 2.32, 95% CI 1.14-4.72). Compared to treatment in a primary care setting, treatment in a cardiology clinic was strongly associated with prescription of SGLT2i (OR = 7.77, 95% CI 3.18-19.04), whereas treatment in endocrinology clinic was strongly associated with prescription of a GLP-1RA (OR = 0.35, 95% CI 0.18-0.68). Area under the receiver operating characteristic curve (AUC) for the model was 0.82.

**Conclusion:** In a real-world data from a large academic center, the selection of guideline directed therapy for patients with T2D and ASCVD was strongly determined by the provider's specialty, highlighting an important opportunity for education.

Poster #24

**Presenter:** Shubham Agarwal, MD

Clinical Science

**Authors:** Shubham Agarwal, MD; Alan P B Dackiw, MD, PhD, MBA; Fiemu Nwariaku, MD, MBA; Jorge Esteban Mosquera, MD; Liwei Jia, MD, PhD; Mary Grace Roden, MS; Oksana Hamidi, DO

**Title:** Composite Pheochromocytoma/paraganglioma-ganglioneuroma: Biochemical and Radiological Features

**Abstract:**

**Background:** Composite pheochromocytoma/paraganglioma with ganglioneuroma (PHEO-GN or PGL-GN) is a rare tumor consisting of chromaffin cells or ganglia tissue combined with a developmentally related neurogenic tumor. Composite tumors can be present in up to 10% of PHEO and are rare with just over 100 cases reported in published literature. We present a case series of patients with PHEO-GN and PGL-GN seen at our tertiary care center to examine their natural history, clinical, radiological, and biochemical characteristics.

**Methods:** We conducted a retrospective longitudinal follow-up study of consecutive adult patients with histologically-proven PHEO-GN and PGL-GN seen between 2013 and 2023. We collected and summarized data on demographics, laboratory findings, radiological results, and clinical outcomes.

**Results:** The cohort comprised 10 patients (60% women): 8 with PHEO-GN (1 diagnosed on autopsy), 1 with PGL-GN, and 1 with PHEO-ganglioneuroblastoma. The median age at diagnosis was 47 years (interquartile range [IQR], 35-60). Most (80%) tumors were discovered incidentally. The prevalence of a genetic syndrome was 40% and included multiple endocrine neoplasia (MEN) 2A, MEN 4, Neurofibromatosis 1, and hereditary PHEO-PGL syndrome due to succinate dehydrogenase type B gene mutation. Nine patients (90%) had biochemically functional tumors with adrenergic biochemical phenotype in 89% and noradrenergic in 11%. The tumor associated with MEN 4 also had dopamine secretion. The median elevation above the upper normal limit of plasma metanephrine was 7.4 (IQR, 1.6-12), 24-hour urine metanephrine was 7.12 (IQR, 3.7-8.8), plasma normetanephrine was 1.7 (IQR, 1.5-1.9), and 24-hour urine normetanephrine was 2.9 (IQR, 2.4-3.5). The median tumor size at the time of diagnosis was 4.2 cm (IQR, 3.3-5.2). The median pre-contrast HU on CT imaging was 37 HU (IQR, 20-40). The median time to surgical excision from the diagnosis was 2.7 months (IQR, 1.9-4.6). All patients that underwent surgery were alive without recurrence of disease at last follow-up visit with a median follow-up of 14.5 months (IQR, 0.5-18.4).

**Conclusions:** We present a series of 10 consecutive patients with composite PHEO-GN and PGL-GN. The prevalence of genetic syndrome (40%) was much higher than previously reported (up to 25% in prior reports). PHEO or PGL component of these tumors is commonly biochemically functional with metanephrine and normetanephrine elevation commonly seen. Metastatic or recurrent disease was not observed in our cohort, suggesting favorable outcomes after surgical resection.

Poster #25

**Presenter:** Spencer Carter, MD

Clinical Science

**Authors:** Spencer V. Carter, MD; Justin L. Grodin, MD; Vicente Morales Oyarvide, MD; Eric D. Peterson, MD, MPH; Sadiya S. Khan, MD; Dianalee McKnight, PhD; Ana Morales MS; Emily M. Russell, PhD; Yi-Lee Ting, MS; Ann Marie Navar MD, PhD

**Title:** Racial and Ethnic Differences in the Diagnostic Yield of Cardiomyopathy, Aortopathy, and Arrhythmia Genetic Testing and Frequency of Family Variant Testing

**Abstract:**

**Background:** Genetic testing for individuals with heritable cardiovascular conditions can guide treatment and aid in family screening; however, the molecular diagnostic yield may differ by race and ethnicity.

**Methods:** The molecular diagnostic yield (percentage of tests with pathogenic/likely pathogenic [P/LP] variant[s] that explain the patient's phenotype) was evaluated for cardiomyopathy, aortopathy, and arrhythmia among probands undergoing testing at a large commercial laboratory (Invitae®) from 9/2015–7/2022 for the most common clinician-reported patient race and ethnicity groupings: Hispanic, non-Hispanic Black (hereafter, Black), and non-Hispanic White (hereafter, White) individuals. Using multivariable logistic regression, differences in diagnostic yield were evaluated by race and ethnicity adjusting for age, sex, genetic testing payer, and number of genes tested. The ratio of the number of individuals undergoing family variant testing to the number of probands with positive tests was determined with chi-square tests to evaluate for differences by group.

**Results:** A total of 129,565 individuals undergoing diagnostic genetic testing were identified (n=9,157 Hispanic; n=16,287 Black; and n=78,740 White). Compared with White individuals, the adjusted odds of a positive test were higher in Black and Hispanic individuals for cardiomyopathy (odds ratio [OR] 1.2, 95% confidence interval [CI] 1.2–1.3, p<0.001 and OR 1.3, 95% CI 1.2–1.4, p<0.001, respectively) and aortopathy (OR 2.1, 95% CI 1.8–2.5, p<0.001 and OR 1.9, 95% CI 1.7–2.2, p<0.001, respectively), and higher for Hispanic individuals for arrhythmia (OR 1.2, 95% CI 1.1–1.3, p<0.001). The ratio of family variant testing to proband positive tests was lower (p<0.001) for Black and Hispanic individuals than White individuals for cardiomyopathy (0.32, 1.19, and 1.51, respectively), aortopathy (0.77, 1.62, and 2.34, respectively), and arrhythmia (1.47, 2.23, and 3.33, respectively).

**Conclusions:** Despite being underrepresented in population genomic databases, the diagnostic yield of genetic testing for cardiomyopathy and aortopathy was higher in Black and Hispanic individuals compared with White individuals. The relative frequency of family variant testing was lower in Black and Hispanic than White individuals, indicating an opportunity to improve cascade screening in these groups.

Poster #26

**Presenter:** Thuylinh Nguyen, MD

Clinical Science

**Authors:** Thuylinh Nguyen, MD; Andrew Horvit, MD; Peter Van Buren, MD

**Title:** Characterization of Echocardiographic Diastolic Dysfunction Metrics in Patients with Intradialytic Hypertension

**Abstract:**

**Background:** Cardiovascular disease including hypertension and heart failure (HF) are common in end-stage kidney disease (ESKD) patients on maintenance hemodialysis (HD). Hemodialysis treatments, typically occurring thrice weekly, involve both diffusive solute clearance mediated and net fluid removal referred to as ultrafiltration, and there is significant intradialytic blood pressure (BP) variability during these treatments. Various intradialytic BP patterns have been associated with increase mortality, especially large BP decreases (intradialytic hypotension) or any BP increase (intradialytic hypertension). Many patients with systolic HF experience intradialytic hypotension, but the cardiovascular phenotype of intradialytic hypertension is less well known. We hypothesized that echocardiogram evidence of diastolic dysfunction would be common in ESKD patients with intradialytic hypertension.

**Methods:** We conducted a retrospective cross-sectional study including ESKD patients receiving maintenance HD at Dallas VA Medical Center from the past 3 years with available transthoracic echocardiogram data. We calculated the intradialytic BP slope (IBPS) for each of the 3 HD treatments before and 3 treatments after the echocardiogram. We compared the average  $E/E'$  between patients with intradialytic hypertension, defined by a positive IBPS averaged over 6 treatments, and patients with negative IBPS using an unpaired t-test.

**Results:** There were 92 patients with TTE reporting an  $E/A$ , but only 56 had TTE reporting  $E/E'$ . Among these 56 patients, the mean age was 66.3 (9.5) years. 99% were men, 44 were Black (79%), and 39 (70%) had diabetes. 57% of the echocardiograms were inpatient. Mean  $E/E'$  was 16.1 (6.2). There were 19 patients with intradialytic hypertension with mean IBPS of +1.74 (2.1) mmHg/hr compared to 37 patients with mean IBPS -4.29 (3.4) mmHg/hr ( $p < .0001$ ). Mean  $E/E'$  was 19.0 (6.7) in those with intradialytic hypertension compared to 14.7 (5.5) in those without ( $p = .02$ ). There was no difference in the  $E/A$  in the 2 groups (1.18 [0.6] vs. 0.95 [0.3],  $p = .1$ ).

**Conclusions:** Diastolic dysfunction is common in ESKD patients on HD and is more severe in patients with intradialytic hypertension than those with negative IBPS. While a causal relationship cannot be determined from this study, patients with frequent intradialytic hypertension should be evaluated with echocardiograms to determine the presence/severity of diastolic dysfunction.

Poster #27

**Presenter:** Tiffany Brazile, MD

Clinical Science

**Authors:** Tiffany L. Brazile, MD; Courtney Reisman; RN, Margot Morris; RN, Erika Ivey, MS; Mitchel Samels, MS; Christopher M. Hearon Jr., PhD; James P. MacNamara, MD; Benjamin D. Levine, MD; Satyam Sarma, MD

**Title:** The Impact of Shortened Left Ventricular Filling Time on Early Diastole in Healthy Aging and Heart Failure with Preserved Ejection Fraction

**Abstract:**

**Background:** Patients with heart failure with preserved ejection fraction (HFpEF) have impaired diastolic recoil that is thought to contribute to decreased left ventricular (LV) suction and impaired relaxation at high heart rates (HR), but this hypothesis has not been tested in humans.

**Purpose:** The goal of this study was to assess the impact of progressively shortened LV filling time on parameters of early diastolic function in patients with HFpEF versus age-matched controls.

**Methods:** Preliminary analysis of 19 participants (10 HFpEF & 9 controls, age  $70 \pm 7$  years) underwent echocardiography at rest and with incremental doses of isoproterenol (ISO) to stimulate HR and decrease diastolic filling time. ISO dosing was calculated using actual body weight ( $BMI \leq 25$ ) or adjusted to 30% fat mass derived from DEXA ( $BMI > 25$ ). Serial Doppler echocardiography was used to quantify systolic-diastolic (S-D) coupling as the ratio of early diastolic to systolic mitral annular excursion distances from velocity-time integrals ( $e'VTI/s'VTI$ ), peak early mitral inflow velocity ( $e'$ ), propagation velocity ( $V_p$ ), and isovolumic relaxation time normalized to HR (IVRT/VR-R interval). Linear regression models were used to estimate the effects of escalating ISO doses on diastolic function between groups.

**Results:** S-D coupling increased linearly with each ISO dose; however, the effect was blunted in HFpEF patients ( $p < 0.001$ ) and was driven by lower  $e'VTI$ .  $V_p$  increased with increasing S-D coupling in both groups, but with lower velocities in HFpEF ( $p = 0.011$ ). IVRT shortened more than 2-fold with increasing S-D coupling in controls as compared to patients with HFpEF ( $p = 0.047$ ). PCWP was consistently higher in patients with HFpEF ( $p = 0.033$ ), while  $e'$  was not significantly different between groups ( $p = 0.489$ ).

**Conclusions:** In HFpEF, blunted S-D coupling, specifically lower diastolic mitral annular excursion, and diastolic suction may represent the effects of myocardial stiffening. A smaller magnitude of change in IVRT with incrementally decreased filling time in HFpEF may reflect diminished SERCA2a function. Further studies are needed to explore the functional implications of impaired diastolic relaxation and recoil efficiency on filling pressures with exercise in HFpEF.

Poster #28

**Presenter:** Gayane Tumyan, MD

Clinical Vignette

**Authors:** Gayane Tumyan, MD; Iram Hussain, MD

**Title:** A Case of Beta-hCG-Mediated Hyperthyroidism Related to Metastatic Germ Cell Tumor

**Abstract:**

**Case Presentation:** A 25-year-old male was admitted for abdominal pain, fevers, weight loss, night sweats for 3 months, intermittent dyspnea, and hemoptysis. He reported tremors, insomnia, and palpitations, worsening a week before the admission.

Computed tomography revealed metastatic malignancy involving lungs, liver, and retroperitoneal lymph nodes. Ultrasound showed calcification within the right testis (1.1x0.2x0.2 cm), suggestive of a burned-out testicular tumor. Laboratory evaluation was suggestive of a metastatic germ cell tumor with beta human chorionic gonadotrophin ( $\beta$ -hCG) >1,000,000 mIU/ml (<2 mIU/ml), lactate dehydrogenase 6890 Units/L (135-225 U/L), elevated liver function tests, primary hyperthyroidism, TSH <0.01 mIU/L (0.4-4.5 mIU/L), free thyroxine 4.4 ng/dL (0.8-1.8 ng/dL), free triiodothyronine 9.8 pg/ml (2.0-4.4 pg/ml) and thyroglobulin 50.9 ng/ml (1.3-31.8 ng/ml).

Cholestyramine 4 grams, dexamethasone 4mg, atenolol 25mg twice daily were initiated to decrease the circulating thyroid hormone levels and control symptoms. He developed tachycardia, hypertension, worsening tremors over the next week. Methimazole 5 mg daily was started despite the worsening transaminitis. He received 5 days of chemotherapy with etoposide, ifosfamide, cisplatin;  $\beta$ -hCG improved to 606,000 mIU/ml, thyroid function tests normalized, and methimazole was discontinued.

The course was complicated by kidney injury necessitating renal replacement therapy, respiratory failure requiring intubation, and cytopenias, limiting the ability to tolerate chemotherapy. Respiratory failure due to metastatic involvement worsened and he ultimately passed away.

**Discussion:** Hyperthyroidism due to ectopic  $\beta$ -hCG secretion is exceptionally rare, observed with significant elevation in  $\beta$ -hCG levels (>50,000 IU/L). The mechanism is related to the composition of  $\beta$ -hCG. The alpha subunit of  $\beta$ -hCG and TSH are homologous, enabling  $\beta$ -hCG to interact with TSH receptors, leading to increased production and release of thyroxine and triiodothyronine. There is a correlation between the degree of  $\beta$ -hCG elevation and the clinical severity of hyperthyroidism. Management consists of treatment of the underlying disorder and symptomatic treatment of hyperthyroidism, with or without thionamides. The lack of standardized treatment for  $\beta$ -hCG-induced hyperthyroidism makes the management of this condition challenging. Our case illustrates the importance of early recognition of hyperthyroidism in patients with severely elevated  $\beta$ -hCG levels and prompt treatment of the underlying disorder, which can lead to rapid reduction in thyroid levels.

Poster #29

**Presenter:** Ijeoma Eleazu, MD

Clinical Vignette

**Authors:** Ijeoma Eleazu MD; Jacqueline M. Galvan, MD; Kelechi B. Anyaehie, MD

**Title:** Perimortem Cesarean Delivery and Refractory Cardiogenic Shock after Atypical HELLP Syndrome vs Acute Fatty Liver of Pregnancy vs Amniotic Fluid Embolism

**Abstract:**

**Case Presentation:** A 19-year-old G1 at 37w2d presented to her MFM appointment with worsening nausea, jaundice, and icterus. Workup a month prior, at symptom onset was notable for mild transaminitis, positive EBV IgG with elevated viral load, managed with supportive care.

The patient was afebrile with blood pressure of 108/69. Labs revealed normal glucose, mild transaminitis, elevated total bilirubin, elevated alkaline phosphatase and coagulopathy as evidenced by an INR of 1.7, PTT 43.9, PLT 147,000 with no clear etiology. Fibrinogen was low at 233 mg/dL with undetectable haptoglobin, suggesting hemolysis. Urinalysis was negative for proteinuria.

Given coagulopathy, the patient was admitted for IOL. 2 FFP and TXA were given following ROTEM evidence of a slightly prolonged clotting time. Dural puncture epidural was placed uneventfully. Intrapartum, development of non-reassuring fetal heart tracings with seizure activity was noted. Lorazepam and magnesium were given for presumed eclampsia treatment. The patient was transported to the OR for stat cesarean delivery (CD), where she suffered cardiac arrest. She was intubated and perimortem CD was performed with ongoing resuscitation efforts. ROSC was achieved after ten minutes. CD was complicated by uterine atony/PPH with QBL 2L. MTP with appropriate uterotonics were given.

Post op day 0, chest CTA revealed a right lower lobe segmental PE with right ventricular strain. Echocardiography showed dilated RV with large mobile thrombus and globally depressed biventricular function (LVEF 34%). MRI showed multiple ischemic cortical strokes. On post op day 1, she had refractory cardiogenic shock requiring VA ECMO cannulation x 72 hours as a bridge to ventricular function recovery.

**Discussion:** Undetectable haptoglobin levels, transaminitis, thrombocytopenia, and seizure in absence of hallmark preeclampsia features suggest atypical HELLP syndrome. The incidence of HELLP syndrome in pregnancy is 0.5-0.9%, however, incidence of atypical subtypes is unknown and likely underdiagnosed. Resultant DIC (evidenced by hypofibrinogenemia and worsening coagulopathy) promoted multifocal thrombi and massive PPH leading to refractory shock. Alternative diagnoses include AFLP and amniotic fluid embolism. Timely recognition of this morbid condition and delivery with preparation for potential adverse sequelae is paramount.

Poster #30

**Presenter:** James Roberts, MD

Clinical Vignette

**Authors:** James Roberts, MD; Sophia Cosmich, MS4; Nilofar Syed, MD; Haidy Galous, MD

**Title:** Disseminated Cutaneous Tophi as Initial Presentation for Gout

**Abstract:**

**Case Presentation:** A 46-year-old male with no PMHx presented to the ED with acute, severe left wrist pain with associated erythema and edema that began one day prior to admission. He reported rapid progression to left elbow with development of right knee pain and swelling. He reported prior episodes of joint pains but had relief with NSAIDs. Eight months prior to admission, he developed a diffuse nodular rash on his abdomen in which he expressed “whitish crushed up pill like” exudate which spread to bilateral upper and lower extremities. He denied ETOH use or new medications.

In the ER, he was evaluated for gout vs. Septic arthritis with initiation of antibiotics. Labs revealed uric acid of 8.4, CRP of 6.3, elevated ESR of 24, and WBC of 17.17. X-rays were performed without erosions. Arthrocentesis revealed uric acid crystals consistent with gout. Infectious workup was negative. Dermatology was consulted for his rash and confirmed diagnosis of cutaneous tophi with punch biopsy. Prednisone 40mg, NSAIDs, and allopurinol 100mg daily were started. An attempt with increase in steroids was performed but unsuccessful, therefore Anakinra 100mg subQ injection was provided to patient for a total of 5 days. Patient achieved improvement in his pain and range of motion with Anakinra therapy, therefore patient was discharged on Allopurinol 100mg daily and prednisone taper.

**Discussion:** Early development of cutaneous tophi occurs with an incidence of 16% in patients with gout of less than 10 years. Tophaceous gout has a significant negative impact on both quality of life and mortality risk in people living with gout. A qualitative study showed that the impact of tophi can include impairment in physical, psychological, and social function. A prospective study found that presence of tophi at first encounter was associated with a hazard ratio of 2.05 compared to patients without tophi. This case highlights that disseminated cutaneous gout may occur in patients with a short symptomatic gout history underlining the importance of skin exams in these patients no matter the stage of disease. Tophi are important to recognize and manage early in their clinical course due to their known impact on both quality of life and progression of disease.



Poster #31

**Presenter:** Jaspreet Sian, MD

Clinical Vignette

**Authors:** Jaspreet Sian, MD; Ramesh Saxena, MD, PhD

**Title:** IgA Dominant is not Always IgA Nephropathy

**Abstract:**

**Case Presentation:** A 23-year-old female presented for second opinion of her nephrotic syndrome. Diagnosed with minimal change at age 6 after getting flu vaccine and treated with prednisone she had remission, however flared when tapering and was labelled steroid dependent, thus Tacrolimus started. Subsequently, she remained in remission until age 9 and steroids were increased. Mycophenolate was added to reduce steroids, but she continued to flare, so received rituximab that was two weeks apart, and mycophenolate and steroids were weaned off by age 11. However, at age 12, mycophenolate and prednisone were re-started due to flares. She had another dose of Rituximab at the age of 14 and 19 years and since then she had been in remission and her immunosuppression was slowly weaned off by age 23. However, during the weaning she started to notice weight gain. Kidney biopsy was performed showing an immune complex glomerulonephritis with predominant IgA deposits, and C1q. Diagnosed with IgA nephropathy conservative measures were advised. She remained nephrotic and she resumed immunosuppressive medications on her own, with improvement in symptoms but not complete resolution. She came to UT Southwestern for a second opinion and was found to have a protein/creatinine ratio of 7.5 and serum albumin down to 3.2. Physical exam showed bilateral lower extremity edema. Biopsy report was re-analyzed; given predominant IgA and C1q deposits, immune complex disease with predominant IgA deposits causing kidney injury due to classical complement pathway activation was diagnosed.

**Discussion:** Initially, minimal change was diagnosed however with multiple flares, despite being on immunosuppressants, a kidney biopsy was performed years later, but misdiagnosed as IgA nephropathy. IgA nephropathy is characterized by diffuse mesangial deposition of IgA, and usually a codominant C3 in 90% of the cases. However, C1q deposits, that suggest classical complement pathway activation, are typically absent. This biopsy suggests immune complex mediated glomerulonephritis. Rituximab that targets CD20 proteins on B-cells leading to B-cell depletion by apoptosis decreasing immune deposits. The long-term management is to continue rituximab based upon C-19 levels in order to achieve sustained remission, prevent flares and wean her off other immunosuppressive agents including steroids.

Poster #32

**Presenter:** Jaspreet Sian, MD

Clinical Vignette

**Authors:** Jaspreet Sian, MD; Swee-Ling Levea, MD

**Title:** When Rejection, Infection and PTLD Present Simultaneously – How to Treat?

**Abstract:**

**Case Presentation:** A 71 year old male with diabetes and end-stage kidney disease status post kidney transplant one year ago presented for fevers and weakness. Vitals showed fever of 38.9 degrees celcius. Labs significant for Epstein-Barr virus DNA quantitative of 147853 that continued to rise to 226554, elevated Cr 1.55 mg/dL, leukopenia of  $1.72 \times 10^3$ / uL and anemia of 7.2 g/dL. Patient's immunosuppression was switched from belanocept to tacrolimus, and mycophenolate was held. His Cr increased to 3.84 mg/dL and kidney biopsy was completed which showed acute T cell mediated rejection. He was started on high-dose steroids in the setting of concomitant EBV viremia. A bone marrow biopsy was completed in the setting of the continued bicytopenia which had normocellular marrow. He continued to have worsening Cr to 5.83 mg/dL as well as fevers and a CT was completed showing a large hypodense area involving the hilum and lower pole of the transplant kidney. Biopsy showed monomorphic diffuse large B cell lymphoma consistent with PTLD. He became uremic requiring the initiation of dialysis. Tacrolimus was held and started on rituximab but failed treatment and is currently on mini-RCHOP.

**Discussion:** Kidney transplantation had a variety of complications starting from bleeding, blood clots, infections, rejection, immunosuppressant effects, and PTLD. Unfortunately, many of these present similarly but are treated in opposite ways, such as infections treated with lowering immunosuppression and rejection treated by increasing immunosuppression. It is especially difficult when it occurs at the same time such as in this case. PTLD is a rare complication of kidney transplant and is usually found in advanced stages. There are four main types of PTLD, early lesions which can be treated by simply lowering the dose of immunosuppressive drugs, polymormorphic which has a mix of cells, monomorphic which has one cell type and other including Hodgkin's Lymphoma. Depending on the type of PTLD, patients require rituximab, chemotherapy, radiation and sometimes even removal of the transplanted organ. Unfortunately, no guidelines to the treatment are available when rejection, infection and PTLD appear concurrently, and further research needs to be completed.

Poster #33

**Presenter:** Mauricio Ostrosky Frid, MD, PhD

Clinical Vignette

**Authors:** Mauricio Ostrosky Frid, MD, PhD; Alex Jones, MD; Carolina Martinez Fernandez; Shani Shastri, MD; Orson W. Moe, MD; Laila Lakhani, MD; Anderson Lee, MD; Kamalanathan Sambandam, MD

**Title:** Hydroxocobalamin-associated AKI with Calcium Oxalate Crystalluria in Patients Receiving Non-renal Transplants

**Abstract:**

**Case Presentation:** Hydroxocobalamin (Cyanokit®) is an antidote for cyanide intoxication. This drug may increase blood pressure by scavenging nitric oxide and hydrogen sulfide. For this reason, hydroxocobalamin is used off-label to treat peri-operative vasoplegia.

Cyanokit® prescribing information describes calcium oxalate (CaOx) crystalluria in patients treated with this drug. Three published cases from burn patients report acute oxalate nephropathy on renal biopsy after hydroxocobalamin exposure. No such cases have been described among solid organ transplant recipients. At our institution, four solid organ transplant recipients who received hydroxocobalamin peri-operatively developed acute kidney injury (AKI) with CaOx crystaluria. For reference, serum oxalate (SOx) is normally < 2 umol/L and urine oxalate (UOxV) < 40-45 mg/day.

**Case 1:** Orthotopic liver transplant (OLT) for decompensated nonalcoholic steatohepatitis cirrhosis. SOx and UOxV were 14 umol/L and 120 mg/day, respectively. The initial concern of primary hyperoxaluria in the donor was ruled out following genotyping of donor lymphocytes. The patient was started on renal replacement therapy (RRT) 6 days post-transplant and remained dialysis-dependent for 7 weeks.

**Case 2:** OLT for decompensated cirrhosis secondary to congenital biliary atresia. SOx 6.6 umol/L. The patient was started on RRT one day post-transplant and recovered after 7 days.

**Case 3:** OLT for decompensated alcoholic cirrhosis. SOx 21.1 umol/L and UOx 15.54 mg/dL. The patient was started on RRT 24 hours post-transplant and then recovered after 7 days.

**Case 4:** Orthotopic heart transplant due to non-ischemic cardiomyopathy. SOx 19.5 umol/L and UOx 77 mg/d. The patient was started on RRT 6 days post-transplant and remains on intermittent dialysis for the last 5 months.

**Discussion:** This is the first case series of hydroxocobalamin-associated AKI with calcium oxalate crystalluria in patients receiving non-renal transplants. Although these patients lacked histologic confirmation of oxalate nephropathy, this was the most likely diagnosis in each case based on marked increases in SOx/UOx and urine sediment analysis. AKI post-transplant is multifactorial and avoidance of risk factors may help decrease risk for AKI and need for RRT. Further studies are needed to evaluate the association between oxalate nephropathy and hydroxocobalamin use.

Poster #34

**Presenter:** Reynaldo Sanchez, MD

Clinical Vignette

**Authors:** Reynaldo Sanchez, MD; Veena Rajaram, MD; Nicholas Hendren, MD

**Title:** A Tale of Two Maladies

**Abstract:**

**Case Presentation:** A 22-year-old male with no medical history presented with acute decompensated heart failure and cardiogenic shock. Physical exam revealed thin body habitus, reduced muscle bulk, bilateral ptosis, limited extraocular motion, and upper extremity weakness. An echocardiogram showed severe biventricular dilation and systolic dysfunction. Invasive hemodynamics revealed elevated cardiac filling pressures and low cardiac output. Coronary angiography excluded coronary artery disease and anatomical variants. He was initiated on dobutamine and eventually milrinone given persistently low cardiac index and elevated lactate. A broad workup for the etiology of his cardiomyopathy focused on nutritional deficiencies, myocarditis, genetic mutations, infiltrative cardiomyopathies, and mitochondrial and myopathy-related cardiomyopathies. Ultimately, muscle biopsy and mitochondrial genetic testing revealed a pathogenic deletion (m.7416\_14556) with 70% heteroplasmy concerning for Kearns-Sayre Syndrome (KSS). However, KSS does not typically cause a dilated cardiomyopathy suggesting an additional etiology. A genetic cardiomyopathy panel was sent and revealed a pathologic mutation in the plakophilin-2 (PKP2) gene, which encodes a protein crucial in the structure of desmosomes. This PKP2 mutation was the suspected cause of his dilated cardiomyopathy. A heart transplant evaluation was initiated due to refractory cardiogenic shock, and the patient underwent an uncomplicated heart transplantation and is doing well in the outpatient setting.

**Discussion:** We present the case of a 22-year-old male with no previous medical history who presented with frank cardiogenic shock and was subsequently diagnosed with KSS and a pathogenic PKP2 mutation. Factors which proved crucial in making this diagnosis were the patient's physical exam and persistently elevated lactic acidosis despite escalating support. While KSS accounts for some aspects of this patient's clinical presentation, a high index of suspicion for an additional etiology proved crucial in diagnosing him with a concurrent PKP2 mutation. While heart transplantation provides a treatment for his genetic cardiomyopathy, follow up for the extra-cardiac manifestations of KSS will be imperative moving forward. This case not only highlights the interplay between two distinct disease processes, but also underscores the significance of a broad differential diagnosis, multidisciplinary collaboration, and a detailed physical examination in diagnosing and managing complex patients.

Poster #35

**Presenter:** Kayla Riggs, MD

Medical Education

**Authors:** Kayla A. Riggs, MD; Jay Gopal, MD; Carson Keck, MD; Amit Goyal, MD; Michele Esposito, MD

**Title:** Assessing Invasive Coronary Angiography Interpretation Education and Resources

**Abstract:**

**Background:** The practice of cardiology lies at the intersection of multiple complex imaging modalities, including invasive coronary angiography (ICA), that are not typically taught in medical school curriculum. ICA is the gold standard for the diagnosis of coronary artery disease, the most prevalent heart disease in the US. There is a surprising lack of research surrounding effective teaching and learning methodologies in the field of cardiology, especially in ICA. Therefore, a survey study was designed to assess gaps in education in trainees' interpretation of ICA and available resources.

**Methods:** A twenty-question survey was distributed via an online survey platform. The survey link was disseminated through the CardioNerds email newsletter and CardioNerds X/Twitter. The intended audience included all medical trainees, medical students through subspecialty fellows.

**Results:** Data from 144 respondents predominantly in the United States was acquired. The largest response group was 42% in general cardiology fellowship. Thirty-six percent of participants anticipate future practice in interventional cardiology. Most participants (77%) recorded over 4 weeks of in-person experience in the cardiac catheterization laboratory (CCL) per year. Thirty-five percent of participants spent 4-12 weeks per year and 31% spent 13-24 weeks per year in the CCL. Only 12% noted no exposure to the CCL. Most participants were moderately or less comfortable with interpreting coronary angiography. Only 4% of respondents noted they were highly comfortable and able to interpret angiograms independently. The most utilized resource was on the job training (73%) followed by online resources (60%) and textbooks (39%). Half of participants (50%) only utilized time while at work in learning how to interpret ICA. Over half of participants agreed that this knowledge might have changed or might still have the potential to change their career (strongly agree 29%, agree 31%).

**Conclusions:** The results of this survey study suggest the following: 1) Most students/trainees utilize on the job training to learn ICA, 2) Most respondents were not comfortable interpreting ICA independently, and 3) A better understanding of ICA might have impacted personal choice of specialty. These results imply a need for not only dedicated educational time, but also the creation of modernized learning resources.

Poster #36

**Presenter:** Sarah Godfrey, MD

Medical Education

**Authors:** Sarah Godfrey, MD, MPH; Jill M. Steiner, MD, MS; Abdulla A. Damluji, MD, PhD; Ramya Sampath, MD; Sarah Chuzyi, MD, MS; Sarah Goodlin, MD; Gwen Bernacki, MD, MHSA; Richard Josephson, MD, MS; John Mulrow, MD; Haider Warraich, MD; Ashok Krishnaswami, MD; Caroline Doherty, AGACNP-BC

**Title:** Palliative Care Education in Cardiology Fellowships: A National Survey of Program Directors

**Abstract:**

**Background:** Palliative care (PC) is an essential component of high-quality cardiovascular disease (CVD) care. However, little is known about the current state of PC education in CVD training or attitudes towards integration and implementation among program leadership.

**Methods:** We developed a nationwide, cross-sectional survey querying educational approaches, perspectives, and barriers to PC education in CVD fellowship training. The survey was distributed to 392 members of the American College of Cardiology PD listserv representing 290 CV disease fellowships between 1/2023 and 4/2023. We performed descriptive and chi square analyses of survey data.

**Results:** Fifty-six program representatives completed the survey (response rate = 19.3%). Respondents identified as current PDs (89%), associate PDs (8.9%), and former PDs (1.8%), representing a diverse range of program sizes, types, and regions of the country. Respondents reported use of informal bedside teaching (88%), formal didactics (59%), online or self-paced modules (13%), in-person simulation (11%), and clinical rotations (16%) to teach PC content. Most programs covered PC topics at least annually, although there was variability by topic. We found no associations between program demographics and type or frequency of PC education. Most respondents reported dissatisfaction with the quantity (62%) or quality (59%) of PC education provided. Barriers to PC education included an overabundance of other content to cover (36%) and perceived lack of fellow (20%) or faculty (18%) interest. Comments demonstrated the importance of PC education in fellowship despite lack of a requirement to provide PC education and difficulty covering all topics, and suggestions for how PC skills should be taught.

**Conclusions:** This is the first national survey of CVD educational leadership on approaches to PC education in CVD training. Respondents highlighted both challenges to implementation of formal PC curricula in cardiology training and opportunities for comprehensive PC education.

Poster #37

**Presenter:** Amit Saha, MD

QI/High Value Care

**Authors:** Amit Saha, MD; Jeffrey P. Chidester, MD; Hurst M. Hall, MD; Trushil Shah, MD; Kelly M. Chin, MD; Sonja D. Bartolome, MD; Thomas P. Koshy, MD

**Title:** Same-day Discharge Following Outpatient Balloon Pulmonary Angioplasty: A Single-center Experience

**Abstract:**

**Background:** Balloon pulmonary angioplasty (BPA) now carries a guideline recommendation for the treatment of select patients with chronic thromboembolic pulmonary hypertension (CTEPH). Although operative techniques continue to advance, there remains a paucity of high-quality evidence to guide immediate post-procedure management. Standard of care at many centers remains overnight inpatient observation. We investigated whether a novel, same-day discharge (SDD) strategy following BPA could be safely implemented in our program.

**Methods:** We retrospectively reviewed all BPA sessions performed after the initiation of our institutional SDD protocol from June 4, 2020, through October 31, 2023. Patients were referred for BPA by a multidisciplinary team after comprehensive imaging, including invasive pulmonary angiography, and medical optimization for World Health Organization (WHO) class II or greater symptoms due to CTEPH or chronic thromboembolic disease (CTED). Periprocedural considerations include utilizing low-pressure inflation of intentionally undersized, compliant balloons to reduce risk of segmental vessel injury. Post-procedure management comprised immediate anticoagulation with intravenous unfractionated heparin in a recovery unit for 6 hours before discharge. Pre-and post-intervention hemodynamic data and complications within 30 days were assessed.

**Results:** A total of 28 patients underwent 78 BPA treatments (mean  $2.8 \pm 1.4$  sessions per patient) with SDD intended during the study period. The mean age was  $64.6 \pm 14.6$  years, and 57% ( $n = 16$ ) of subjects were women. The majority (78.6%,  $n = 22$ ) had WHO class III or IV symptoms. Most (71.4%,  $n = 20$ ) were not candidates for pulmonary thromboendarterectomy due to surgical risk or distal lesions. There were significant decreases in mean pulmonary artery pressure (median 32 [IQR 27, 40] vs. 28 [IQR 23, 33] mmHg,  $p = 0.002$ ) and vascular resistance (4.2 [IQR 2.8, 5.7] to 2.7 [IQR 2.1, 4.1] Wood units,  $p = 0.004$ ). Complications occurred in 2 (2.6%) procedures: massive hemoptysis requiring a 3-day admission, and submassive hemoptysis that resolved intraoperatively and did not require admission. There were no episodes of reperfusion lung injury or procedure-related readmissions or deaths within 30 days.

**Conclusions:** With sufficient institutional and operator experience, SDD following BPA can be an effective management strategy without sacrificing hemodynamic benefit or patient safety.

Poster #38

**Presenter:** Marie Christelle Saade, MD

Basic Science

**Authors:** Marie Christelle Saade, MD; Amanda Clark, MD; Kyle Vu; Samir Parikh, MD

**Title:** Quinolinic Acid Excess may Impair Renal Health.

**Abstract:**

**Background:** Acute kidney injury (AKI) and chronic kidney disease (CKD) are settings of reduced NAD<sup>+</sup> biosynthesis. A major metabolite in this biosynthetic pathway, quinolinic acid (Quin), accumulates both locally and systemically. Little is known about Quin other than its effects as a potent neurotoxin. We hypothesized that persistent “local” Quin excess may exacerbate renal tubular health and favor fibrosis.

**Methods:** In this study, 8-week-old wild-type C57BL/6 male mice served as experimental subjects. We compared 72-week-old to 8-week-old mice. Mice were administered 250mg/kg of folic acid (FA) and harvested at 0, 36 hours, day(D)7, and D14. Metabolomics analysis was performed on kidney samples. Next, we administered Quin 0.5g/L through mice’s drinking water on D0 and harvested them on D14. We started mice on Quin 0.5g/L on D0, followed by FA injection 250mg/kg on D14, and harvested on D28. Kidney fibrosis markers were evaluated via qPCR, along with blood urea nitrogen (BUN) and creatinine levels. A cell culture model with several cell lines evaluated the profibrotic effects of Quin 1uM. A Seahorse assay assessed glycolysis changes in HK2 cells when applying Quin. Finally, memantine 250nM, an NMDA-R antagonist, was applied on pericytes +/- Quin.

**Results:** The mouse transcriptomics database, Tabula Muris, indicates a decline in QPRT with aging, a finding we experimentally verified in both aging and CKD settings. Additionally, we demonstrated the accumulation of Quin with CKD advancement. Quin nutritional excess was sufficient to impair normal renal function, as confirmed by increased mRNA expression of fibrosis markers. The introduction of Quin into the FA CKD model via potable water resulted in increased fibrosis and injury markers. Overexpressing QPRT enzyme cleared Quin excess in a tetO-QPRT mice model subjected to cisplatin injury. Quin application to several cell types showed a specific TGFB/ACTA2 response in pericytes. Quin application to HK2 cells revealed an increased extracellular acidification rate. Memantine, NMDA-R antagonist, protected pericytes from the fibrotic effects of Quin.

**Conclusion:** Our findings suggest that Quin triggers fibrosis and contributes to the development of CKD, potentially acting through the NMDA Receptor. These emerging discoveries may unveil novel pathomechanisms and treatment strategies for CKD.



Poster #39

**Presenter:** Ananya Gorrai, MD

Clinical Science

**Authors:** Ananya Gorrai, MD; Faris Araj, MD; Dagny Teiber, RN; Sonia Garg, MD; Robert Morlend, MD; Jennifer Thibodeau, MD, MSCS; Matthias Peltz, MD; Maryjane Farr, MD, MSc; Lauren K. Truby, MD, MS

**Title:** The Role of PCSK9 Inhibition in the Care of Heart Transplant Recipients: A Single-Center Case Series

**Abstract:**

**Purpose:** Hyperlipidemia in heart transplant (HT) recipients is a known contributor to the development of cardiac allograft vasculopathy (CAV) and ischemic events. Lipid management in the HT population remains challenging due to known interactions between standard lipid-lowering therapies and immunosuppressive agents. The efficacy and utility of novel agents, such as PCSK9 inhibitors (PCSK9i), in HT recipients require further investigation.

**Methods:** We identified adult HT recipients at our center on PCSK9i therapy with Evolocumab or Alirocumab. We also identified a control group not receiving PCSK9i, matched by age and date of transplant. The primary outcomes of interest in both groups included the presence and severity of CAV, as measured by epicardial angiography, and changes in LDL cholesterol.

**Results:** Twenty-three adult HT recipients (including two heart-kidney and three heart retransplant) were treated with PCSK9i therapy in the post-transplant setting due to statin intolerance (60.8%) or uncontrolled hyperlipidemia (30.9%). The mean duration of PCSK9i therapy was 568 days. Baseline CAV was found in 48% of these recipients (29% with ISHLT Grade I and 19% with Grade II or III) with only two out of twelve re-catheterized patients demonstrating angiographic CAV progression while on PCSK9i therapy. PCSK9i therapy lowered LDL by an average of 78.1 mg/dL (95% CI 57.0 - 99.2) from baseline to 3 months after initiation, reaching a mean LDL of 60.9 mg/dL. Twenty-six percent of matched controls had CAV at baseline, demonstrating an average increase in LDL of 8.5 mg/dL (95% CI -0.83 - 17.9) from baseline over a matched time frame, reaching a mean LDL of 84.3 mg/dL.

**Conclusion:** HT recipients treated with PCSK9i demonstrated low levels of CAV progression despite a higher disease prevalence at the time of therapy initiation. Patients treated with this novel lipid-lowering therapy achieved a persistently lower LDL than matched control receiving statin therapy, many of whom had known CAV. HT recipients with more stringent LDL goals due to their CAV/CAD risk profile may benefit from PCSK9i therapy.

Poster #40

**Presenter:** Harsh Vardhan Upreti, MD

Clinical Science

**Authors:** Harsh Vardhan Upreti, MD; Jenna Brown; Sophie Lanzkron, MD, MHS; Shruti Chaturvedi, MBBS, MSCI

**Title:** The Greater of Two Evils – Managing Immune TTP in Patients with Coexisting Immune Thrombocytopenia (ITP)

**Abstract:**

**Background:** Thrombotic thrombocytopenic purpura (TTP) is a life-threatening emergency, and recurrent thrombocytopenia usually indicates relapse requiring emergent plasmapheresis. Patients with a coexisting disorder such as ITP pose a challenge to monitoring and treatment. We describe a series of patients with coexisting ITP and TTP, and highlight best clinical practices in managing this challenging situation.

**Methods:** A retrospective analysis was conducted on 164 patients with TTP from the Johns Hopkins Thrombotic Microangiopathy Registry, four of whom had coexisting ITP. ITP episodes were diagnosed based on thrombocytopenia with ADAMTS13 > 20% and exclusion of other causes (with or without response to steroids/IVIG). We compared clinical features of ITP versus TTP episodes.

**Results:** We identified a total of 249 TTP episodes (in 162 patients) and 22 ITP episodes (in 4 patients). Compared to the TTP episodes, ITP episodes were characterized by higher platelet counts [median 99.5 x10<sup>9</sup>/L versus 16.5 x10<sup>9</sup>/L], and lower LDH level [179 U/L versus 983 U/L]. ADAMTS13 activity was higher than in TTP episodes (69% vs. 5%). Same day ADAMTS13 results were used to monitor TTP and make decisions on plasma exchange. As a result, plasma exchange not started for 21/22 thrombocytopenia episodes with ADAMTS13 > 20%. In all cases, pre-emptive immunosuppression (rituximab in 3 cases, prednisone/mycophenolate in 1) was used to try to maintain normal ADAMTS13 activity.

There were no clear predictors of developing ITP in addition to TTP. Median age at diagnosis of TTP was 30.5 years (IQR 24-41) for the subgroup with TTP plus ITP, and 42 years (IQR 28.5-57) for TTP alone. Among patients with TTP alone, 10.2% (n=16) had SLE, and 8.3% (n=13) had other autoimmune disorders, while no patients with both TTP and ITP had lupus or other autoimmune disease.

**Conclusions:** A lower (normal or minimally elevated) LDH level may help identify episodes of ITP versus TTP relapse in patients with known TTP; however, ADAMTS13 activity is the best discriminator. Rapid availability of ADAMTS13 testing enables monitoring of patients with coexisting ITP and TTP, and avoids unnecessary hospitalization and plasma exchange.

Poster #41

**Presenter:** Harsh Vardhan Upreti, MD

Clinical Science

**Authors:** Harsh Vardhan Upreti, MD\*, Ganesh Raman, MD\*, Yu-Min Shen, MD  
(\*joint first authors)

**Title:** Experiences with Emicizumab: A Retrospective Review of Patients on Emicizumab Therapy at the North Texas Hemophilia Treatment Center

**Abstract:**

**Background:** The HAVEN 1-4 trials demonstrated Emicizumab's success in lowering rates of annualized bleeding rates (ABR) among patients with congenital Hemophilia A with and without inhibitors. We sought to evaluate efficacy, side-effects, and barriers to therapy among patients receiving Emicizumab at the North Texas Hemophilia Treatment Center.

**Methods:** We conducted a retrospective review of patients >18 years with congenital Hemophilia A at Parkland and Clements (CUH) Hospitals who were prescribed Emicizumab for prophylaxis.

**Results:** 18 patients at Parkland and 42 patients at CUH were reviewed, 2 patients were excluded due to insufficient documentation. The median age was 36, with majority males (n=57, 98%). Racial demographics include White (55%), followed by Hispanic (23%), African American (13%) and Asian (7%). Mean ABRs across both sites were 0.65 (95% CI 0.57-0.96). Arthralgias were the most common side-effect (n=35, 55%), followed by headaches (n=13, 22%). One patient developed a thrombotic event (TE) on therapy. Four patients died (6.6%) including two due to intracranial bleeds and two due to causes unrelated to Hemophilia. Two patients discontinued treatment, and four had interruptions in therapy. 78% of patients were on a PPO plan and 13% on federal health insurance (FHI). Average time between decision to start medication to administration of first dose was 132 days (95% CI 96-168 days) on a PPO plan and 172 days on an FHI plan (95% CI 0-391 days).

**Discussion:** Our cohort had significant differences compared to HAVEN 1-4 participants including higher median age and larger Hispanic population. We had an increased incidence of arthralgias and lower rate of TMA and TEs. Our ABR was lower than that of HAVEN participants' 1.4 (95% CI 1.1-1.7). Rates of self-discontinuation or interruption of therapy were 10% among our group, comparable to <10% non-adherence among HAVEN participants. Time to administration of Emicizumab was higher for patients on an FHI plan compared to a PPO plan, although statistical significance could not be determined to low sample size of the FHI subgroup. Limitations include smaller sample size (n=60) than HAVEN (n=400) and underestimated ABR given recall bias in clinic contrary to real-time monitoring in other trials.

Poster #42

**Presenter:** Jingwen Zhang, MD

Clinical Science

**Authors:** Jingwen Zhang, MD; Sarah Godfrey, MD, MPH; Melanie S. Sulistio, MD

**Title:** ICD Utilization Among Patients with Heart Failure with Reduced Ejection Fraction at a Major Safety Net Hospital

**Abstract:**

**Background:** Implantable cardioverter-defibrillators (ICDs) are recommended by current guidelines for the prevention of sudden cardiac death in patients with heart failure with reduced ejection fraction (HFrEF)  $\leq 35\%$ . Varying ICD utilization rates have previously been reported, up to 70% in one university-based health system. Little is known about disparities in utilization for underinsured populations. We aim to characterize differences in demographics, healthcare engagement, and optimization of guideline-directed medical therapy (GDMT) between patients with and without ICDs at a major safety net hospital.

**Methods:** We examined ICD utilization in a diverse patient population with left ventricular ejection fraction (LVEF)  $\leq 35\%$  within the past 2 years at Parkland Hospital. Age, sex, race, ethnicity, comorbidities, cardiology clinic visits, GDMT usage, and insurance/payor status were extracted. Patients were stratified by ICD status. Statistical analyses, including t-tests and chi-square tests, were used to detect significant differences. GDMT usage was characterized by a validated scoring system (0 to 9 points, with high usage defined as  $\geq 5$ ). Engagement with cardiology was defined as at least 1 cardiology clinic visit in the past 2 years.

**Results:** Among 1,981 patients with mean age of 56.6 years (SD, 11.4) and mean LVEF of 25.7% (SD, 7.0%), 18.8% had ICDs. Patients were 75.3% male, 47.0% non-Hispanic Black, and 35.0% Hispanic. There were no significant differences in ICD utilization by age, sex, or race. ICD utilization was associated with more comorbidities (hypertension, diabetes, and greater renal dysfunction), increased rates of high GDMT usage (69.6% vs. 56.9%,  $p < 0.001$ ), and increased engagement with cardiology (87.4% vs. 52.2%,  $p < 0.001$ ). Patients with ICDs were more likely to be insured than those without ICDs (commercial insurance, 50.5% vs 34.0%; Medicare/Medicaid, 15.3% vs. 11.4%; charity/self-pay, 29.3% vs. 46.4%).

**Conclusions:** Age, sex, and race were not associated with ICD utilization in this population. Patients with ICDs were more likely to have received optimal GDMT, engaged in cardiology care, and have commercial insurance or Medicare/Medicaid. Overall, patients at this safety-net hospital had lower ICD utilization compared to previously published reports. Among these patients, those without medical insurance also had lower utilization.

Poster #43

**Presenter:** Joy (Le) Huang, MD

Clinical Science

**Authors:** Le Huang, MD; Sarma Satyam, MD

**Title:** Effects of Left Atrial Filling Pressure on Pulmonary Gas Exchange in HFpEF

**Abstract:**

**Background:** Left atrial myopathy is common in patients with HFpEF (heart failure with preserved ejection fraction). This phenotype is characterized by decreased left atrial (LA) compliance and correlates with greater pulmonary vascular disease and decreased survival. The mechanism through which increased LA pressures worsen pulmonary vascular function is unclear. We evaluated the relationship between the v-wave in the pulmonary capillary wedge pressure (PCWP) tracing and pulmonary gas exchange. We hypothesized that patients with HFpEF who had higher v-wave amplitudes and higher PCWP would have worse pulmonary gas exchange as evidenced by lower partial pressure of oxygen in arterial blood (PaO<sub>2</sub>).

**Methods:** Subjects with HFpEF underwent upright invasive hemodynamic exercise testing with right heart catheterization and radial arterial catheterization. PCWP measures and arterial blood gases were obtained during rest and submaximal exercise (20 Watts) on a semi-recumbent cycle. The peak of the v-wave in the PCWP tracing and the mean PCWP was measured manually by a single observer and validated by a second observer. Arterial blood gases were analyzed for PaO<sub>2</sub>.

**Results:** The study cohort included 42 subjects with HFpEF. Mean v-wave peak was 9.98 +/- 4.44 mmHg during rest and 26.64 +/- 14.71 mmHg during exercise. Mean PCWP was 7.93 +/- 4.25 mmHg during rest and 20.47 +/- 8.80 mmHg during exercise. Mean PaO<sub>2</sub> was 86 +/- 12 during rest and 85 +/- 13 mmHg during exercise. Linear regression analyses revealed statistically significant negative correlations between v-wave amplitude and PaO<sub>2</sub> at rest ( $p = 0.03$ ,  $R^2 = 0.12$ ) and during exercise ( $p = 0.0004$ ,  $R^2 = 0.27$ ) and between PCWP and PaO<sub>2</sub> at rest ( $p = 0.003$ ,  $R^2 = 0.20$ ) and during exercise ( $p = 0.00004$ ,  $R^2 = 0.35$ ).

**Conclusions:** Across these patients, higher LA pressures (higher v-wave amplitude and PCWP) appear to correlate with worsening pulmonary gas exchange (lower PaO<sub>2</sub>), suggesting worsening pulmonary gas exchange as a possible mechanism for vascular dysfunction in disease states with increased LA filling pressures like HFpEF with atrial fibrillation.

Poster #44

**Presenter:** Maria Clara Saad Menezes, MD

Clinical Science

**Authors:** Maria Clara Saad Menezes, MD, MPH; Amelia Li Min Tan, PhD; Alexander Hoffman, MBA; Isaac Kohane, MD, PhD; and the 4CE Consortium.

**Title:** Is GPT-4 Ready to Read Medical Notes?

**Abstract:**

**Background:** Physicians invest hours creating patient notes, encapsulating each patient's medical history. Despite the scientific value of such information, its free-text format defies large-scale analysis with traditional methods. GPT-4 reshaped our ability to process unstructured text, yet it is unknown whether this model can handle specialized medical notes. Thus, this project aims to compare GPT-4's ability to interpret medical notes against experienced physicians, being the first project of this kind to involve multiple countries, institutions, and languages.

**Methods:** Seven institutions from three countries (United States, Singapore, and Colombia) participated in this study. Each site provided seven de-identified admission, progress, or discharge notes (either in English or Spanish) from hospitalized patients. Two physicians and GPT-4 independently reviewed and responded to 14 questions per note, which were then compared.

The spectrum of questions varied from simple information (e.g., demographics and medical history) to complex evaluations, including reason for hospitalization, urgency of medical care, application of clinical guidelines, and identification of inconsistencies in the notes. A question-answering system was developed using Python with a temperature of 0.2 (ranging from 0 to 1, with higher values representing higher chances of random responses).

**Results:** There was an agreement between GPT-4 and physicians in 89% of the time (range 85% to 97% across sites). The hardest questions for GPT-4 were applying diabetes guidelines and identifying inconsistencies (agreement of 71% and 65%, respectively). GPT-4 could not recognize that patients already diagnosed with diabetes do not require screening for diabetes. Also, GPT-4 had difficulty distinguishing between intentional blank spaces used for de-identification reasons and actual typographical errors. However, GPT-4 was able to recognize a prescription error on fentanyl dosing, noting it should be 200mcg/hr instead of 200mg/hr. GPT-4's performance was consistent across notes in English and Spanish. Hallucinations (i.e., fabricated data, illogical statements) occurred in 1% of the responses.

**Conclusions:** We concluded that GPT-4's ability to interpret free-text medical notes is leveled with the ability of experienced physicians and this finding is maintained across languages, countries, and institutions. Together, these findings indicate that GPT-4 is ready to automatize the handling of medical notes in a large-scale context.

Poster #45

**Presenter:** Marisa Kometas, MD

Clinical Science

**Authors:** Marisa Kometas, MD; Jonathan Hyak, MD; Fieke Hoff, MD; Vivian Irizarry-Gatell, MD; Alejandro Marinos, MD; Clayton Jackson, MD; Julia Anderson, MD; Julio Alvarenga, MD; Robert H. Collins, MD; Stephen S. Chung, MD; Yazan F. Madanat, MD.

**Title:** Real World Efficacy of Luspatercept in Patients with Lower-risk Myelodysplastic Neoplasms (MDS); a Single Center Study in a Heavily Pretreated Cohort

**Abstract:**

**Background:** Anemia is the most common cytopenia in patients with lower-risk Myelodysplastic Neoplasms(LR-MDS), and leads to transfusion dependence and inferior survival. Luspatercept was recently FDA-approved for anemia treatment in LR-MDS. This retrospective single-center study evaluates the real-world efficacy and safety of luspatercept in LR-MDS, and the impact of baseline characteristics and prior treatments on hematologic response(HI-E).

**Methods:** Patients treated with luspatercept monotherapy for LR-MDS from 01/2020-12/2023 were included. Baseline characteristics including prior therapies, serum erythropoietin (EPO) level, ring sideroblast( RS) status, karyotype, and gene mutations were recorded. Baseline transfusion burden(no=NTD, low=LTB, high =HTB) for all patients and HI-E in patients with  $\geq 16$  weeks of therapy were defined by IWG 2018 criteria. Mann-Whitney U and Fisher Exact Tests were used to compare continuous and categorical variables, respectively. Kaplan-Meier and log-rank testing were used to assess survival outcomes.

**Results:** Median age was 74 y. 51% were female, 16% had therapy-associated MDS, 100% had undergone prior MDS treatments, 78% had RS, 73% were SF3B1-mutated, 32% had high-risk mutations, and 44% had serum EPO $\geq 200$  u/L. Although most prognostic scores connoted lower-risk, 19% of patients had higher-risk disease per IPSS-M. 19% were NTD, 41% were LTB, and 41% were HTB. 31 patients were response evaluable. HI-E was 52%. 48% of transfusion-dependent(TD) patients achieved  $\geq 16$  weeks transfusion independence(TI). Median TI duration(48 weeks) did not differ significantly between HTB and LTB responders. However, serum EPO $<100$  significantly predicted response( $p=0.02$ ). Patients achieved TI at equal rates for doses of 1.00, 1.33, and 1.75mg/kg. TI was lost in 22%, but restored following dose increases in 50% of those initially receiving  $<1.75$ mg/kg. Adverse effects included shortness of breath, falls, fatigue, and hypertension, and precipitated discontinuation in 8% of patients. 11% progressed to HR-MDS or AML. Median leukemia-free OS was not reached, and did not differ between responders and nonresponders( $p=NS$ ).

**Conclusions:** Luspatercept achieved high rates of durable TI in a heavily pretreated cohort of LR-MDS patients. Response was associated with low serum EPO, but not with baseline transfusion burden. Dose escalation often induced or restored TI. Further investigation is indicated to define subsets of patients with greater probability of response.

Poster #46

**Presenter:** Muhammad Shariq Usman, MD Clinical Science

**Authors:** Muhammad Shariq Usman, MD; Matthew Segar, MD; Kershaw Patel, MD; Vinayak Subramanian, MD; Neil Keshwani, MD; Ambarish Pandey, MD, MSCS

**Title:** Frailty Status and Efficacy of an Initial Invasive Strategy in Chronic Coronary Disease

**Abstract:**

**Background:** Frailty is not well characterized in patients with chronic coronary disease (CCD). Moreover, it is not known whether frailty modifies the effect invasive management on clinical outcomes and health-related quality of life (HRQoL) in patients with CCD.

**Methods:** A post-hoc analysis of the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial was conducted. In ISCHEMIA, patients in the invasive strategy arm underwent angiography with revascularization as feasible, while those in the conservative arm received medical therapy only. In the current analysis, frailty was assessed using the frailty index (FI), which was calculated using a 28-variable deficit accumulation model. Participants were categorized into 3 groups: low frailty, intermediate frailty, and high frailty. Outcomes of interest were the primary outcome of ISCHEMIA (composite of cardiovascular death, myocardial infarction, hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest), the Seattle Angina Questionnaire (SAQ) summary score, and the SAQ angina score.

**Results:** This study included 5322 participants with a median FI of 0.20 (IQR: 0.17, 0.21) in the low frailty group, 0.27 (0.25, 0.29) in the intermediate frailty group, and 0.35 (IQR: 0.33, 0.39) in the high frailty group. The high frailty group had significantly lower baseline SAQ summary scores and a significantly higher risk of adverse outcomes on follow-up. In adjusted models, baseline frailty did not modify the effect of the invasive strategy on the primary outcome. Frailty significantly modified the effect of the invasive strategy on HRQoL: at 1-year, the invasive strategy was associated with a the greatest improvement in SAQ summary score in tertile 3 (LSM: 3.11, 95% CI: 1.62, 4.6;  $P < 0.001$ ), followed by tertile 2 (LSM: 1.49, 95% CI: 0.37, 2.62;  $P = 0.009$ ), and then tertile 1 (LSM: 1.12, 95% CI: 0.16, 2.08;  $P = 0.022$ ),  $P$ -interaction  $< 0.001$ . A similar trend was seen with the SAQ angina score.

**Conclusion:** Patients with CCD who have a higher burden of frailty are more likely to experience greater improvements in HRQoL with invasive management, without a higher risk of adverse clinical outcomes.



Poster #47

**Presenter:** Nicolas Sayegh, MD

Clinical Science

**Authors:** Nicolas Sayegh, MD; Yeonjung Jo, PhD; Georges Gebrael, MD; Nishita Tripathi, MD; Beverly Chigarira; Ayana Srivastava; Blake Nordblad, MS; Emre Dal, MD; Chadi Hage Chehade, MD; Benjamin L. Maughan, MD; Sumati Gupta, MD; Neeraj Agarwal, MD; Umang Swami, MD

**Title:** Real-world Efficacy of Single-agent Enfortumab Vedotin in Patients with Metastatic Urothelial Carcinoma

**Abstract:**

**Background:** Enfortumab vedotin (EV) is a Nectin-4-directed antibody and microtubule inhibitor conjugate indicated for patients with metastatic urothelial carcinoma (mUC) who have received prior platinum-based chemotherapy and PD-1/L1 inhibitors or are ineligible for cisplatin-containing regimens and have undergone at least one prior line of therapy. However, real-world effectiveness of EV based on treatment line and impact of prior therapy remains unclear.

**Methods:** This retrospective study utilized the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database. Patients with advanced, recurrent, or mUC of upper or lower urinary tract who received single-agent EV in the second line or beyond after December 18, 2019 (FDA accelerated approval date), were included. Patients without documentation of first-line therapy or without evidence of contact for 90 days from mUC diagnosis were excluded. Time to next therapy (TTNT) and overall survival (OS) were analyzed based on treatment line and prior platinum-based chemotherapy and PD-1/L1 inhibitors using Kaplan-Meier survival estimates and its 95% confidence interval.

**Results:** Between January 17, 2020, and September 30, 2022, 6,566 patients with mUC received systemic treatment, with 431 receiving EV. EV was administered across various lines: second (157), third (132), fourth (62), and fifth (20). Approximately 22% of patients had prior platinum-based therapy, and 48% had prior PD-1/L1 inhibitors. Median TTNT and OS varied across treatment lines, with patients with prior platinum exposure generally showing longer TTNT and OS, notably in those receiving EV in the fourth line setting.

**Conclusions:** EV demonstrates efficacy in mUC patients regardless of prior receipt of platinum-based chemotherapy and PD-1/L1 inhibitors or treatment line. These findings provide valuable insights for patient counseling, prognostication, and therapeutic decision-making in clinical practice.

Poster #48

**Presenter:** Benjamin Lee, MD

Clinical Vignette

**Authors:** Benjamin Lee, MD; Margaret Kypreos, MD

**Title:** Lactic Acidosis Improved by IV Thiamine in a Likely Case of Severe Thiamine Deficiency: A Case Report

**Abstract:**

**Case Presentation:** A 78-year-old female with history of ILD, T2DM, HTN, HLD, OSA, CKD, and recent admission for right-sided heart failure one month prior presented to the ED for 2-3 days of worsening shortness of breath. Of note, the patient had significantly reduced PO intake limited to one Ensure per day since the prior discharge. On presentation, she was afebrile with pulse in 90s, BP 110s/70s, SpO2 90% on 4L NC. Initial workup significant for bicarbonate 12, lactate 16.1, anion gap 31, glucose 12, Cr 2.33 (baseline Cr 1.4-1.6). VBG pH 7.19, pCO2 32.0. The patient was started on broad spectrum antibiotics, high dose thiamine, and D10 infusion. Despite diuresis with 40mg/hr IV furosemide overnight, the patient remained anuric due to suspected right heart failure in the setting of undiagnosed pulmonary hypertension. However, the lactate greatly improved to 1.5 within the first 24 hours. A transthoracic echocardiogram showed a small, pancaked left ventricle from massive right ventricle dilation, LVEF of 64%, RVSP 74mmHg above CVP with a bedside Swan Ganz Catheter confirming elevated right sided pressure: PA 81/40 (mPAP 54) and PCWP 3. Cardiac index was decreased to 1.12 by thermodilution. With the addition of dopamine at 2.5mcg/kg/min, sildenafil, inhaled epoprostenol, and macitentan, urine output significantly increased. The patient clinically improved on this regimen and was able to be weaned off the inhaled epoprostenol prior to downgrade to floor a week later.

**Discussion:** Lactate elevations are characterized by two types. Type-A lactic acidosis occurs when oxygen consumption and delivery mismatch results in anaerobic glycolysis due to hypoperfusion or hypoxia. Type-B lactic acidosis occurs due to issues with metabolizing pyruvate causing shunting to anaerobic metabolism. Thiamine is a vital cofactor for pyruvate dehydrogenase, the enzyme that converts pyruvate to Acetyl-CoA, the starting metabolite for the TCA/Krebs cycle. Of note, it also acts as a cofactor for Alpha-ketoglutarate dehydrogenase within the TCA/Krebs cycle. Thiamine deficiency should be considered as a cause of Type-B lactic acidosis in the setting of poor PO intake, even in ICU level patients when concerns for Type-A lactic acidosis tend to be much higher.

Poster #49

**Presenter:** Cecilia Nguyen, MD

Clinical Vignette

**Authors:** Cecilia H. Nguyen, MD; Dawn C. Zhao, MD

**Title:** A “False” Iparum Presentation of Malaria Re-infection: A Case Study of Post-artesunate Delayed Hemolysis in Severe *P. falciparum* Malaria

**Abstract:**

**Case Presentation:** We present a case of a 38-year-old female with a history of HIV visiting from Nigeria who presented for 4-days of cyclical fevers, nausea, vomiting, and diarrhea. She was found to have severe malaria with peripheral blood smear showing 10.2% parasitemia with plasmodium falciparum. She was treated with intravenous artesunate, which resulted in a decrease in her parasitemia load to less than 1% and was discharged with artemether/lumefantrine to complete at home. Two weeks later, she presented again with progressive malaise and continued cyclical fevers despite completing her malaria treatment. Vitals were significant for fevers every 6 hours. Hemoglobin was 4.9 with additional labs suggesting hemolytic anemia, for which she required daily blood transfusions. Although there was concern for malarial recurrence given her immunosuppression, repeat peripheral smears were negative for parasites. Additional infectious workup for fever and anemia including mycoplasma, rickettsia, typhus, brucella, bartonella, and dengue was negative. Autoimmune workup was additionally negative except for possible cold agglutinin disease, which was eventually ruled out. Given a largely negative workup of febrile hemolytic anemia and the timing of hemolysis two weeks after her initial malaria treatment, she was diagnosed with post-artesunate delayed hemolysis (PADH).

**Discussion:** PADH is an uncommon but significant adverse effect that occurs approximately seven days or more after initiation of intravenous artesunate treatment for malaria infection. High-risk factors include severe *P. falciparum* infection, which is infection of more than 5% of erythrocytes. While the exact pathophysiology of PADH is currently unknown, there are several proposed hypotheses. The “pitting” hypothesis suggests that after malarial parasites in circulating erythrocytes are killed by artemisinin derivatives intracellularly, the erythrocytes undergo pitting inside the spleen to remove dead parasites. The resulting compromised structural integrity leads to a shortened cell life span of approximately 7 to 21 days. Other hypotheses propose that PADH is a drug-induced immune hemolytic anemia or is secondary to bone marrow suppression. Though no fatalities have yet been reported, PADH may lead to life-threatening levels of anemia and warrants close monitoring after intravenous artesunate treatment, especially for patients with high-parasitemia levels.

Poster #50

**Presenter:** Hannah Klatzkow, MD

Clinical Vignette

**Authors:** Hannah Klatzkow, MD; Qi Cai, MD, PhD; Ariel Aday, MD

**Title:** Unveiling Pheochromocytoma: A Puzzling Prelude of Nausea, Vomiting, and Abdominal Pain

**Abstract:**

**Case Presentation:** A 45-year-old woman presented to the hospital with a 1-week history of epigastric abdominal pain and persistent nausea and vomiting. CT imaging showed a mass arising from the left adrenal gland measuring 6.3 x 6.1 x 6.0 cm. It had a heterogenous appearance with low Hounsfield units, suggestive of adrenal myelolipoma. Although the radiological appearance was inconsistent with pheochromocytoma, the decision was made to pursue precautionary biochemical diagnostic testing before proceeding with endoscopy. Plasma metanephrine and normetanephrine levels were then found to be elevated to 0.87 nmol/L (normal 0.00 – 0.49 nmol/L) and 2.22 nmol/L (normal 0.00 – 0.89 nmol/L), respectively. 24-hour urine collection also showed elevated metanephrine to 483 µg/d (normal 36-229 µg/d) and normetanephrine of 495 µg/d (normal). Labs were diagnostic of pheochromocytoma, and the patient subsequently underwent laparoscopic left adrenalectomy. Her abdominal pain, nausea, and vomiting resolved post-operatively.

**Discussion:** Pheochromocytoma remains a challenging diagnosis. The classic triad of symptoms, including headaches, diaphoresis, and tachycardia, accompanied by high blood pressure, is non-specific and overlaps with many other common conditions. There is also variance in the relative concentrations of secreted catecholamines, leading to different phenotypes of symptoms. Additionally, such as in our case, symptoms may be related to the mass effect itself rather than the catecholamine secretion, though there is limited literature on the prevalence of associated gastroenterological symptoms. Our case contributes to the current evidence supporting the potential benefit of a lower threshold for screening those who are found to have adrenal incidentalomas and non-specific symptoms.

Though the incidence of pheochromocytoma is low, it remains a critical differential to consider due to its severe physiological complications, such as end-organ dysfunction and hypertensive crisis. Crises can be triggered by various factors, including anesthesia, diagnostic and therapeutic procedures, use of metoclopramide, and abdominal manipulation, all of which remain particularly relevant when referral for gastroenterological care and evaluation.

Poster #51

**Presenter:** Harsh Vardhan Upreti, MD

Clinical Vignette

**Authors:** Harsh Vardhan Upreti, MD; Roslyn Saplicki; Siayah Rambally, MD; Mingyi Chen, MD, PhD; Mohammad Faizan Zahid, MD

**Title:** Not all Thrombocytopenia in Pregnancy is Immune Thrombocytopenia (ITP)

**Abstract:**

**Case Presentation:** A 27-year-old pregnant woman (28 weeks gestation with twins) was referred for progressive thrombocytopenia over 3 weeks (60,000/uL to 17,000/uL). She was presumptively diagnosed with immune thrombocytopenia (ITP) by a local hematologist, and prescribed steroids without improvement. She reported easy bruising, headache, and recent resolution of cough and nasal congestion. Physical exam showed several ecchymoses and a 5 cm x 3 cm breast mass. CBC revealed mild leukocytosis (14,000/uL), hemoglobin of 10.4 g/dL, and platelet count of 25,000/uL. Peripheral smear illustrated large atypical lymphocytes, nucleated RBCs, decreased number of platelets with unremarkable morphology, and no schistocytes. MRI brain revealed subacute bilateral subdural hematomas. Normal transaminases, normal blood pressure and absence of proteinuria argued against acute fatty liver of pregnancy, pre-eclampsia and HELLP syndrome. While LDH was elevated >800 U/L, normal haptoglobin, reticulocyte count, bilirubin and lack of schistocytes made a thrombotic microangiopathy unlikely. Coagulation profile showed prolonged PT (19.2 seconds), normal PTT (31.5 seconds), D-dimer >34 mg/L and low fibrinogen <70 mg/dL, consistent with disseminated intravascular coagulation (DIC). Clinical evaluation did not indicate sepsis or obstetric complications. A repeat peripheral smear showed abnormal cells concerning for leukemic blasts. CT scan of the breast showed benign findings. Bone marrow biopsy revealed a hypercellular marrow with promonocytes and blasts accounting for ~70-80% of total cellularity consistent with acute myeloid leukemia with monocytic differentiation. Chemotherapy was initiated, and coagulopathy resolved within two days. She underwent induction of labor at 32 weeks of gestation, followed by a stem cell transplant three months later.

**Discussion:** Thrombocytopenia in pregnancy has a broad range of etiologies and management strategies ranging from reassurance for gestational thrombocytopenia to emergent delivery for HELLP syndrome. In this case, there was an anchoring bias on ITP since it is the most common cause of thrombocytopenia in the 2nd trimester. However, the presence of nucleated RBCs and large atypical cells on peripheral smear were clues for marrow infiltration. Additionally, the presence of a consumptive coagulopathy always warrants a workup for an underlying cause. In conclusion, a thorough evaluation to exclude other causes of thrombocytopenia is essential before diagnosing ITP.

Poster #52

**Presenter:** Hunter Pyle, MD

Clinical Vignette

**Authors:** Hunter Pyle, MD; Jet Patterson, MD; Travis Vandergriff, MD; Cristina Thomas, MD; Arturo Dominguez, MD; Haidy Galous, MD

**Title:** Generalized Bullous Fixed Drug Eruption

**Abstract:**

**Case Presentation:** A female in her 40s with history of type II diabetes and hearing loss was admitted for bilateral leg pain and found to have a new pruritic rash on her bilateral lower extremities. The patient noted history of a similar rash several years prior. She denied recent infections or illnesses. Physical examination was significant for round, well-demarcated violaceous patches with rims of erythema and overlying bullae on the bilateral medial thighs, chest, abdomen, groin, and right temple. Notably, there was no acral or mucosal involvement. Rheumatology was consulted to assess for possible systemic rheumatic disease. Dermatology was consulted and performed a punch biopsy of the right thigh, which revealed a superficial and deep perivascular interface dermatitis consisting of lymphocytes, histiocytes, eosinophils, and neutrophils, with individually necrotic keratinocytes scattered through the epidermis. Altogether, morphology, distribution, and pathology supported a diagnosis of generalized bullous fixed drug eruption. The patient was started on cyclosporine 2 mg/kg BID and topical clobetasol. After review of outpatient and inpatient medication timelines, diphenhydramine was determined to be the most likely culprit medication. Over the course of five days, evidence of active inflammation (rims of erythema) resolved and cyclosporine and clobetasol were discontinued. The patient was discharged with petrolatum to prevent superinfection.

**Discussion:** Generalized bullous fixed drug eruption (GBFDE) is characterized by sharply demarcated, circinate, dusky patches with central bullae affecting > 10% body surface area, and lesions characteristically recur in the same location with each exposure to a culprit drug. Importantly, GBFDE mortality is similar to SJS/TEN mortality in cases of similar amount of skin detachment. In determining the responsible drug, review any medication exposures within the two weeks preceding eruption onset. The most common drug associations include antibiotics, NSAIDs, and barbiturates. Management includes stopping the offending medication and counseling patients to avoid future use, in addition to symptomatic treatment with topical or systemic corticosteroids depending on the number of lesions. FDE should be distinguished from erythema multiforme, which are characterized by three-component target lesions, and SJS/TEN, where atypical targets early on, mucosal involvement, and less-defined borders are more common presentations.

Poster #53

**Presenter:** Hunter Pyle, MD

Clinical Vignette

**Authors:** Hunter Pyle, MD; Luise Froessler, MD; Cristina Thomas, MD; Travis Vandergriff, MD; Mahmoud Elsayed, MD

**Title:** A Severe Presentation of Sarcoidosis

**Abstract:**

**Case Presentation:** A 31-year-old male with history of pseudotumor cerebri presented with two days of altered mental status. On presentation, he was hypotensive with systolic blood pressures in the 80s mmHg. Physical examination revealed facial weakness and red-brown papules and plaques involving areas of tattoos, primarily on the face and neck. Labs revealed profound hypercalcemia (15.0 mg/dL) complicated by acute kidney failure. PTH was low, storage and activated vitamin D were within normal limits, and PTHrP was elevated. CT chest/abdomen/pelvis revealed extensive bilateral pulmonary infiltrates, splenomegaly, extensive thoracic, abdominal, and pelvic adenopathy, and hypoattenuation of the posterior right liver concerning for an infiltrative process. Peripheral blood smear was consistent with infiltrative pathology. Further workup for hypotension and hypernatremia was significant for arginine vasopressin deficiency, hypothyroidism, and secondary adrenal insufficiency. MR brain, pituitary, and spine revealed diffuse enhancing lesions throughout the clivus and entire spine. The patient subsequently developed severe bradycardia (30-40 bpm) with first degree and Mobitz 1 AV block. Cardiac MRI revealed multifocal patchy and linear mid-wall late gadolinium enhancement in several areas of the myocardium as would be expected with sarcoidosis. Skin punch biopsy revealed sarcoidal granulomatous dermatitis. Evaluations for mycobacterial, systemic fungal, and other granulomatous diseases were negative. The patient was ultimately diagnosed with sarcoidosis with probable involvement of his CNS, heart, lungs, liver, kidney, spleen, bone marrow, skin, and skeleton. Bradycardia and metabolic abnormalities improved with the initiation of prednisone, thyroid hormone, and DDAVP, with plans for outpatient initiation of methotrexate.

**Discussion:** Sarcoidosis is a multisystem granulomatous disease with varying clinical manifestations depending on organ involvement. Nearly half of sarcoidosis is diagnosed incidentally after abnormal chest imaging. Notably, several organ systems involved in this patient are rarely involved within the first six months of sarcoidosis diagnosis (bone/joint 0.5%, renal 0.7%, cardiac 2.3%, endocrine 3.7%, bone marrow 3.9%). Hypercalcemia in sarcoidosis is mediated by PTH-independent macrophage activation of calcitriol from calcidiol and may also be mediated by PTHrP. Glucocorticoid therapy in granulomatous diseases decreases calcitriol production to reduce intestinal calcium absorption. Recognition of the diversity of sarcoidosis presentations is critical to prompt diagnosis and targeted treatment.

Poster #54

**Presenter:** Khush Kharidia, MD

Clinical Vignette

**Authors:** Khush Kharidia, MD; Vikram Aggarwal, BS; Han Wool Kim, MD ; Mingyi Chen, MD, Ph.D; David Johnson, MD; Eric Steen, MD

**Title:** Synchronous Presentation of Solitary Fibrous Tumor and Chronic Myeloid Leukemia: A Diagnostic Challenge

**Abstract:**

**Case Presentation:** A 58-year-old male presented to the emergency department with progressive dull left upper quadrant abdominal pain that began five days prior while visiting Mexico. His medical history was notable for a WHO grade 2 hemangiopericytoma (or solitary fibrous tumor, SFT) diagnosed 8 years prior. The patient was treated with bi-frontal craniotomy with subtotal resection and adjuvant radiotherapy at the time. The initial complete blood count on presentation was significant for white blood cell count of 83,000 cells/mL. Differential and peripheral blood smear showed no eosinophils or basophils. CT of the abdomen and pelvis revealed liver masses (8 cm and 4 cm in diameter), splenomegaly, and splenic infarcts. MRI abdomen showed multiple heterogeneous, arterial hyper-enhancing lesions throughout the liver, pancreas, and kidneys. MRI brain revealed interval development of an enhancing mass along the margin of the splenium of corpus callosum. Fluorescence in situ hybridization (FISH) from the blood sample was positive for the (9:22) translocation and liver biopsy results stained positively with STAT6, confirming a synchronous diagnosis of chronic myeloid leukemia (CML) and SFT. CML was treated with dasitinib. The SFT was treated with temozolomide and bevacizumab.

**Discussion:** SFTs and CML are both uncommon neoplasms with distinct chromosomal aberrations and distinct clinical presentations. There are no known reported cases of these two rare neoplasms presenting concurrently. Extraneural metastasis of central nervous system SFTs have been reported in up to 23% of patients with a median time to distant metastasis of 97 months. Long-term imaging follow-up for intracranial and extracranial SFT recurrence is thus important. Though leukocytosis and splenic infarcts suggested CML, we found it difficult to reconcile the absence of basophils and the presence of liver masses with this diagnosis. Our suspicion of a neoplastic process increased as the workup for a leukemoid reaction secondary to infection was unrevealing. Clinicians should have a low threshold for hematologic CML workup for leukocytosis over 50,000 cells/ mL despite an atypical blood smear. While clinicians often seek unifying theories to explain a patient's presenting findings, cases like these remind us of the importance of maintaining the possibility of multiple diseases on the differential.



Poster #55

**Presenter:** Mansi Maini, MD

Clinical Vignette

**Authors:** Mansi Maini, MD; Kayla Riggs, MD; Anthony Bavry, MD

**Title:** Discrepancies in Invasive Assessment of Aortic Stenosis

**Abstract:**

**Background:** Hemodynamic evaluation of aortic valve (AV) gradients plays a pivotal role in the severity and management of aortic stenosis (AS). The mother-and-daughter approach and the Langston dual-lumen catheter are commonly used for valvular hemodynamics.

**Case Presentation:** A 69-year-old male with moderate to severe AS presented with dyspnea. An echo reported a mean gradient of 32 millimeters of mercury (mm Hg) and aortic valve area (AVA) of 0.92 square centimeters (cm<sup>2</sup>). Due to discrepant echo findings of valve severity, invasive hemodynamics were obtained. The Langston catheter measured a 50 mm Hg AV gradient with an AVA of 0.81 cm<sup>2</sup> concerning for severe AS. However, upon pullback to the aorta with both pressure ports in the same environment, the catheter had a 15 mm Hg gradient. Therefore, the mother-and-daughter technique was performed via a 6 French x 65 cm Destination sheath to measure aortic pressure and a telescoped 4 French pigtail catheter for left ventricular pressure. This found a mean pressure gradient of 24 mm Hg and AVA of 1.11 cm<sup>2</sup>, meeting criteria for moderate AS. A discrepancy in the aortic pressure from the Langston catheter dual-lumen ports was noted in a series of cases when the mother-and-daughter technique was concurrently performed.

**Decision-making:** The Langston catheter overestimated transvalvular gradient when compared with the mother-and-daughter technique. Obtaining accurate data is critical for decision making, allowing clinicians to determine the severity of valvular obstruction and guide treatment, such as AV replacement. The Langston catheter might best be used for its negative predictive ability. For example, when the Langston catheter documents moderate AS this should be reliable; however, when the calculated AVA is severe, additional testing to establish severity may be required due to concern of overestimated pressure gradient. This case highlights how our tools to evaluate aortic disease should be critically evaluated to ensure accurate data collection. A retrospective case series is underway to provide further insight.

**Conclusion:** Accurate hemodynamic evaluation in AS helps to make appropriate treatment decisions and guide patient outcomes. Quality checks of our commonly used tools are critical for appropriate patient management.

Poster #56

**Presenter:** Vinita Shivakumar, MD

Clinical Vignette

**Authors:** Vinita Shivakumar, MD, MPH; Komal Muradali, MD

**Title:** Atypical Case of aHUS Without Hemolysis

**Abstract:**

**Case Presentation:** A male in his early 50s presented from hematology clinic for further evaluation of severe refractory thrombocytopenia and new dependence on hemodialysis.

His history was notable for a long history of mild thrombocytopenia, otherwise well and active. His thrombocytopenia worsened two years prior to presentation with platelet count of 22 after COVID-19 infection. Due to persistently low platelet counts over the next year, he underwent EGD/colonoscopy which was negative, peripheral smear which showed no abnormal cells, and bone marrow biopsy which showed normocellular bone marrow.

Two months prior to presentation, he was admitted for platelet count of 2 with purpura. He was found to have splenomegaly and lymphadenopathy and treated with high-dose steroids, IVIG, 7 plasma exchange treatments, and Rituxan for presumed catastrophic antiphospholipid antibody syndrome without hemolysis with normal ADAMSTS13. He was discharged on prednisone, Tavalisse and Nplate and weekly Rituxan without significant improvement in platelet count.

One month prior to presentation, he was readmitted for gross hematuria and started on hemodialysis. He underwent splenic embolization and started Promacta.

On admission, he was afebrile, hypertensive to 140s/100 with otherwise unremarkable vital signs. He had healing purpura on arms and 2+ pedal edema. His labs were notable for largely unimpressive hemolysis labs and no significant schistocytes on smear, normal ADAMSTS13, low C4, and normal G6PD. He underwent renal ultrasound, CT chest/abdomen/pelvis, repeat bone marrow biopsy, and repeat EGD which were unrevealing. After extensive multi-disciplinary discussions given risk of bleeding, he underwent renal biopsy with IVIG and platelet transfusion. Renal biopsy showed thrombotic microangiopathy, confirming complement-mediated hemolytic uremic syndrome.

**Discussion:** This is a rare case of hemolytic uremic syndrome in the absence of significant hemolysis – patient had normal LDH, haptoglobin, and no schistocytes on almost all evaluations. Further, patient presented with severe thrombocytopenia, nadir of 2. All immune thrombocytopenia (ITP) related therapies were discontinued and patient was started on eculizumab (with penicillin prophylaxis and plan for meningitis vaccination outpatient). His platelets showed some response to therapy although he remains thrombocytopenic (30-90) on hemodialysis.

Poster #57

**Presenter:** Willis Wong, MD

QI/High Value Care

**Authors:** Willis Wong, MD, MBA; Cindy Cao, MS; Parag H. Joshi, MD, MHS

**Title:** Lipoprotein (a) Screening and Utilization at UTSW from 2017-2021

**Abstract:**

**Background:** Lipoprotein A (Lp(a)) is causally linked to ASCVD events and aortic stenosis. European guidelines currently recommend screening of Lp(a) at least once in adults for risk assessment for ASCVD; American guidelines are more selective. Further, there is variation in measurement modality and unit (mg/dL vs. the preferred nmol/L). It is unclear how Lp(a) measurements are being used at UTSW.

Our study's objectives are to 1) describe Lp(a) measurement practices broadly at UTSW, 2) describe the epidemiology of high Lp(a) levels among patients at UTSW, 3) describe referrals and pharmacological management after detection of high Lp(a) levels for patients at UTSW.

**Methods:** Using ClinDen software, we searched patient encounter data at UTSW between January 1st 2017 to December 31st, 2021 for patients who had ever received any Lp(a) measurement. High Lp(a) was defined as >50mg/dL or >125 nmol/L. Aggregate data on these patients were used to summarize patient demographics, relevant ASCVD co-morbidities, and lipid lowering medication use. Chart-review was conducted on patients with high Lp(a) levels to assess whether post-measurement referrals to specialty clinics were made.

**Results:** From 2017 to 2021, there were 1,065 Lp(a) measurements among 958 patients. On average, testing frequency increased by 32.17% annually. Fewer than 0.1% of all patients at UTSW underwent Lp(a) testing, with most tests ordered by cardiologists (71%). Median Lp(a) levels across all tests were 17mg/dL and 43nmol/L. Lp(a) are high in 30.4% of all initial tests. High Lp(a) is found in Black individuals (50%) more frequently, and less frequently in Hispanic (20%) or Asian (20%). A higher proportion of tests ordered in 2021 by cardiologists (84%) are in nmol/L, the recommended standard, compared with other specialties (55%). Patients with high Lp(a) found by a non-cardiologist follow up with cardiology at low frequency (25%).

**Conclusion:** Lp(a) testing during the study period was rare at UTSW and varies widely between specialties. Lp(a) frequency differed between populations consistent with larger population studies. In addition to improving awareness of Lp(a) among UTSW providers, there is an opportunity to educate non-cardiology specialties at UTSW to measure Lp(a) in nmol/L to standardize practice.

Poster #58

**Presenter:** Willis Wong, MD

QI/High Value Care

**Authors:** Willis Wong, MD; Tin Khine, MBA; Milette Siler, MBA-HC, RDN; Jaclyn Albin, MD

**Title:** One-Year Results of a Novel Culinary Medicine Clinic Innovation at UTSW

**Abstract:**

**Background:** There is a growing demand for evidence-based, practical nutrition and cooking guidance. However, application of nutrition support in healthcare settings remains limited due to lack of time, expertise, and access to registered dietitian nutritionists. To address this challenge at UTSW, the Culinary Medicine consult service was developed and piloted at RedBird beginning in December 2022. This unique, billable service provided patients with outpatient consultation approximately one half-day weekly with both a physician and dietitian certified in culinary medicine.

Our pilot study aimed to evaluate first-year implementation of this novel service and review 1) demographics of patients referred to the clinic and those who ultimately scheduled and attended, 2) the origin of referrals, and 3) how the culinary medicine service is reimbursed by payors.

**Methods:** We analyzed clinical encounter, scheduling, and billing data from December 4th, 2022 to December 4th, 2023 using a Microsoft PowerBI dashboard. Data analyzed included patient demographics (age, sex, race, ethnicity), referral data, referral diagnoses, appointment schedules, reimbursement charges and payments.

**Results:** In the first year, the Culinary Medicine Clinic received 229 total referrals leading to 93 (40.6%) completed new patient consults. 12 unique primary care clinicians from Family Medicine and Internal Medicine generated most of the referrals (87.3%, n=200) with few self-referrals (3.5%, n=8). The mean age at referral was 59 years old. Most referred patients were women (78.6%) and African American (69.4%). Of those referred, women scheduled and attended an initial visit more frequently than men (41% vs. 31% of people referred who ultimately scheduled and attended an appointment, respectively). Patients referred who identified as Hispanic/Latino (27%) were least likely to schedule and attend their initial visit. Due to reimbursement lag, reimbursement data analyzed includes 62 visits, with most completed and reimbursed visits covered by Medicare plans (51 charges).

**Conclusions:** This pilot demonstrated proof-of-concept of a novel, insurance-reimbursable Culinary Medicine consult clinic. Initial data shows opportunities to improve engagement with the Hispanic/Latino community, as well as men. Future directions include increasing patient access, understanding patient-level impacts on health and health behaviors, and understanding impacts of this service on healthcare spending.

Poster #59

**Presenter:** Baijie Xu, PhD

Basic Science

**Authors:** Baijie Xu, PhD; Katherine Lawler, PhD; Steven C Wyler, PhD; Li Li, PhD; FNU Swati, MS; Amanda G. Arnold, BS; Kathleen G. Mountjoy, PhD; I Sadaf Farooqi, PhD; Chen Liu, PhD

**Title:** Orthopedia Regulates Melanocortin 4 Receptor Transcription and Human Obesity Risk

**Abstract:**

**Background:** Children carrying missense mutations in Orthopedia (Otp) develop severe early-onset obesity. A recent inquiry in the UK Biobank (exomes from ~500,000 people) found loss-of-function (LOF) mutations in 5 more people, all of whom are either currently obese or heavy during childhood. Thus, coding variants in Otp are associated not only with monogenic obesity but also obesity in the general population. Nevertheless, since Otp has not been previously implicated in the pathology of human obesity, the cause of weight gain remains unknown. In our lab, we study the transcriptional regulation of the melanocortin 4 receptor. Notably, mutations of Mc4r are the most frequent causes of severe obesity in humans. We find that the expression of Otp, a transcription factor, is enriched in hypothalamic Mc4r neurons that regulate food intake. This finding leads to our hypothesis that Otp regulates Mc4r transcription and energy homeostasis.

**Methods:** To study the physiological role of Otp in vivo, we developed floxed Otp (Otp<sup>fl</sup>) mice. We selectively deleted Otp in specific hypothalamic neurons during development and adulthood and measured its impact on food intake and body weight. We employed multiomic sequencing and transfection analyses to determine how Otp regulates the promoter activity of Mc4r. Finally, to determine whether human OTP variants can cause obesity, we generated transgenic mice expressing a de novo OTP mutation (Q153R) identified previously in a 2-year-old boy with severe obesity (body mass index 4.6 standard deviations above the mean for age).

**Results:** Specific deletion of Otp in neurons of the paraventricular nucleus of the hypothalamus (PVN) during development and adulthood reduces Mc4r expression, causing increased food intake and obesity in mice. Moreover, Otp interacts with cis-regulatory sequences upstream of Mc4r to regulate its expression. Additionally, like the human subject, mice carrying the human Q153R mutation exhibit increased food intake and obesity due to loss of Mc4r expression. Treatment of these mice with setmelanotide, an FDA-approved MC4R agonist, leads to substantial weight loss.

**Conclusions:** Otp is a transcriptional regulator of Mc4r in the PVN, whose disruption causes human obesity, which may be treatable with MC4R agonists.

Poster #60

**Presenter:** Bryan Portillo, BS

Basic Science

**Authors:** Bryan Portillo, BS; Eunsang Hwang, PhD; Jason Ajwani, BS; Kyle Grose, BS; Linh Lieu, BS; Briana Wallace, MS; Anita Kabahizi, BS; Kevin W. Williams, PhD

**Title:** NMDARs in POMC Neurons Connects Exercise with Insulin Sensitivity

**Abstract:**

**Objective:** Increased activity of arcuate proopiomelanocortin (POMC) neurons improves glucose metabolism as well as suppresses appetite, thereby facilitating weight loss. We recently showed that arcuate POMC neurons are activated by exercise. This includes an increase in excitatory glutamatergic input. However, the role of excitatory glutamatergic input in controlling these neurons and the metabolic outcomes of exercise remains undefined.

**Methods:** To investigate this, we developed a mouse model with NMDA receptors (NMDARs) selectively deleted from POMC neurons in adulthood. We then performed a comprehensive metabolic assessment, including weekly monitoring of body weight, detailed body composition analysis, as well as glucose, insulin, and pyruvate tolerance tests. We also examined the metabolic outcomes of these mice in response to exercise, including changes in arcuate POMC neuronal activity and insulin sensitivity.

**Results:** Loss of NMDARs in POMC neurons failed to alter body weight or body composition. Notably, however, we did observe a marked decrease in glucose and insulin sensitivity. Additionally, exercise resulted in activation of arcuate POMC neurons and a sustained improvement in insulin sensitivity, an effect that was abrogated in mice deficient for NMDARs in POMC neurons.

**Conclusions:** These data demonstrate that NMDARs are required for the activation of arcuate POMC neurons following exercise. Moreover, the lack of NMDAR-mediated activation in POMC neurons leads to significantly reduced insulin sensitivity post-exercise. This underscores an important link between exercise, hypothalamic neuron function, and metabolic health. Moreover, this highlights an underappreciated role of hypothalamic POMC neurons in mediating exercise's beneficial effects on glucose metabolism.

Poster #61

**Presenter:** Erik Loyde, BS

Basic Science

**Authors:** Takashi Suzuki, PhD; Erik Loyde, BS; Sara Chen, BS; Valerie Etzrodt, MD; Temitayo O. Idowu, PhD; Amanda J. Clark, MD; Marie Christelle Saade, MD; Brenda Mendoza Flores, BS; Shulin Lu, PhD; Gabriel Birrane, PhD; Vamsidhara Vemireddy, MD; Benjamin Seeliger, MD; Sascha David, MD; Samir M. Parikh, MD

**Title:** Cathepsin K Cleavage of Angiotensin-2 Creates Tie2 Antagonist Fragments in Sepsis

**Abstract:**

**Background:** Elevated Angiotensin-2 is associated with diverse inflammatory conditions including sepsis, a leading global cause of mortality. During inflammation, Angiotensin-2 antagonizes the endothelium-enriched receptor Tie2 to destabilize the vasculature. In other contexts, Angiotensin-2 stimulates Tie2. The basis for context-dependent antagonism remains incompletely understood. Here we show that inflammation-induced proteolytic cleavage of Angiotensin-2 converts this ligand from Tie2 agonist to antagonist.

**Methods:** Vehicle- or ODN- pretreated RAW264.7 cells were stimulated with LPS and incubated with recombinant ANGPT2. ODN (25  $\mu$ M) was added to cells 1 hour prior to LPS and ANGPT2. For mouse survival experiment, hydrodynamic gene transfer of different plasmids (10  $\mu$ g DNA, adjusted to bodyweight); vehicle or ODN (20 mg/kg, I.P.) was administered 1 hour prior to LPS (10 mg/kg) (\*p < 0.05). The empty vector (EV) + ODN group served as a control. For clinical data, we measured cANGPT225 (ng/mL) in sera of healthy controls (healthy, n = 10), patients in the intensive care unit (ICU) with a primary diagnosis of acute respiratory distress syndrome (ARDS, n = 20), ICU patients with a primary diagnosis of ARDS and sepsis (ARDS & Sepsis, n = 10) and ICU patients with a primary diagnosis of sepsis (Sepsis, n = 10) (Kruskal-Wallis, \*\*p < 0.01, \*\*\*p < 0.001).

**Results:** Conditioned media from stimulated macrophages induced Angiotensin-2 secretion. Unexpectedly, this was associated with reduction of the 75 kDa full-length protein and appearance of new 25 and 50 kDa C-terminal fragments. Peptide sequencing proposed Cathepsin K as a candidate protease. Cathepsin K was necessary and sufficient to cleave Angiotensin-2. Recombinant 25 and 50 kDa Angiotensin-2 fragments (cANGPT2-25, cANGPT2-50) bound and antagonized Tie2. Cathepsin K inhibition with the Phase-3 small molecule inhibitor odanacatib improved survival in distinct murine sepsis models. Odanacatib's benefit was reversed by heterologous cANGPT2-25kDa. Full-length Angiotensin-2 enhanced survival in endotoxemic mice administered odanacatib and conversely increased mortality in the drug's absence. Septic humans accumulated circulating Angiotensin-2 fragments, which were associated with adverse outcomes.

**Conclusions:** These results identify a novel proteolytic mechanism for the conversion of Angiotensin-2 from Tie2 agonist to antagonist with therapeutic implications for inflammatory conditions associated with Angiotensin-2 induction.

Poster #62

**Presenter:** Eunsang Hwang, PhD

Basic Science

**Authors:** Eunsang Hwang, PhD; Bryan Portillo, BS; Kyle Grose, BS; Jason Ajwani, BS; Kevin W. Williams, PhD

**Title:** DMH Glucagon-Like Peptide 1 Receptor Neurons are Required for the Full Effect of GLP-1R Agonist Induced Weight Loss

**Abstract:**

**Background:** Arcuate Neuropeptide Y/Agouti-related peptide (NPY/AgRP) neurons play a crucial role in regulating energy balance and glucose metabolism. Despite lacking glucagon-like peptide 1 receptors (GLP-1Rs), GLP-1R agonists (GLP-1Rags) inhibit these neurons by activating presynaptic GABA neurons. Importantly, the location of these presynaptic GABA neurons remains undefined and is a significant gap in knowledge for the field. Previous research has suggested that GABAergic input from the dorsal medial hypothalamus (DMH) regulates feeding behavior via arcuate NPY/AgRP neurons, however, the role of GLP-1Rs or GLP-1R agonists in this circuit is unknown.

**Methods:** Here we test the hypothesis that GLP-1Rags such as liraglutide indirectly inhibit NPY/AgRP neurons by activating presynaptic GABA neurons in the DMH. We performed chemo- and opto-genetics, as well as patch-clamp recordings, to observe and manipulate DMH GLP-1R+ and arcuate NPY/AgRP activity. We also assessed the impact of GLP-1R agonists on the activity of these neurons as well as resulting changes in food intake and body weight.

**Results:** Our findings reveal that liraglutide activates DMH GLP-1R+ neurons while simultaneously inhibiting NPY/AgRP neurons both ex-vivo and in-vivo ( $p < 0.05$ ). Furthermore, DMH GLP-1R+ neurons are synaptically (8/8 neurons) and functionally linked to NPY/AgRP neurons, as activation of DMH GLP-1R+ neurons inhibits NPY/AgRP neurons and suppresses feeding (37% compared to the control group). We also found that inhibiting DMH GLP-1R neurons or activating NPY/AgRP neurons abrogated the liraglutide-induced hypophagia and weight loss.

**Conclusions:** These data suggest that GLP-1R expressing neurons in the DMH act as an interneuron relay to inhibit arcuate NPY/AgRP neurons, and blocking this neural activity diminishes the effects of GLP-1Rags on energy balance. These findings provide insight into how GLP-1Rags affect metabolism via the CNS, and have potential clinical implications; as GLP-1Rags are commonly used therapeutics in diabetes treatment and chronic weight management.



Poster #63

**Presenter:** Jason Ajwani, BS

Basic Science

**Authors:** Jason Ajwani, BS; Eunsang Hwang, PhD; Bryan Portillo, BS; Kyle Grose, BS; Mohamad Mokadem, MD; Kevin W. Williams, PhD

**Title:** Neuroplasticity of Arcuate POMC and NPY/AgRP Neurons Following Bariatric Surgery

**Abstract:**

**Background:** Bariatric surgery (i.e. Vertical Sleeve Gastrectomy - VSG and Roux-en-Y Gastric Bypass - RYGB) promotes significant weight loss and glycemic control across species. Current evidence suggests that these benefits are partly mediated through neural-hormonal mechanisms, which remain undefined. Within the hypothalamic arcuate (ARC) nucleus, the orexigenic neuropeptide Y/Agouti-related peptide (NPY/AgRP) neurons and the anorexigenic POMC-expressing cells play key roles regulating downstream Melanocortin 4 receptor (MC4R) signaling and resulting changes in metabolism. Given the reliance of RYGB (but not VSG) on MC4R signaling for its metabolic benefits, we hypothesize that RYGB and VSG differentially modulate these critical neuronal pathways to improve metabolism. This study aims to further our understanding of how bariatric surgery influences neuroplasticity and offers a novel perspective on post-surgical improvements in metabolism.

**Methods:** Utilizing transgenic mouse models, we assessed the metabolic and neuronal impact of RYGB, VSG, and sham surgeries on diet-induced obese mice. This includes monitoring body weight, food intake, energy expenditure, and oral glucose tolerance tests (OGTT), followed by assessing electrophysiological properties of ARC NPY/AgRP and POMC neurons.

**Results:** RYGB and VSG led to significantly improved OGTT and sustained weight loss that coincided with surgery specific effects on energy balance and neuronal excitability. In particular, VSG significantly reduced food intake while RYGB enhanced energy expenditure. Notably, VSG - not RYGB - inhibited ARC NPY neurons, whereas RYGB resulted in anatomically distinct responses of rostral vs. caudal ARC POMC neurons.

**Conclusions:** Our findings suggest a differential response of ARC POMC and NPY/AgRP neurons in the metabolic improvements following RYGB and VSG. By exploring the distinct neuroplastic alterations by RYGB and VSG, this study lays the groundwork for future non-invasive therapies that may replicate these metabolic benefits.

Poster #64

**Presenter:** Kyle Grose, BS

Basic Science

**Authors:** Kyle Grose, BS; Eun-sang Hwang, Bryan Portillo, BS; Jason Ajwani, BS; Yanbin Dong; Kevin W. Williams, PhD

**Title:** The Impact of Exercise and GLP-1 Producing Neuron Activity on the Melanocortin System.

**Abstract:**

**Background:** Glucagon-like peptide 1 (GLP-1) receptor agonists are revolutionizing metabolic pharmacology due to their ability to facilitate weight loss and improve blood-glucose control, an effect that is enhanced with exercise. Exercise naturally increases insulin sensitivity, which leads to improved glucose uptake in muscle and reduced hepatic glucose production. Endogenous GLP-1 is primarily produced within intestinal L-cells, pancreatic islets, and hindbrain neurons located in the Nucleus Tractus Solitarius (NTS). Activation of NTS GLP-1 neurons decreases food intake and suppresses hepatic glucose production. Similarly, activation of hypothalamic proopiomelanocortin (POMC) neurons improves glucose metabolism and decreases feeding, leading to weight loss. We recently demonstrated that hypothalamic POMC neurons are activated in response to exercise, and preliminary data suggests that NTS GLP-1 neurons are also activated over a similar temporal window as hypothalamic POMC neurons. This led us to further investigate the role of NTS GLP-1 neuron activation and its relationship with GLP-1's effects on hypothalamic POMC neurons.

**Methods:** We utilized transgenic mouse models and whole-cell patch-clamp electrophysiology to determine the requirement of NTS GLP-1 neuron activity on the exercise-induced changes in arcuate POMC neuron activity.

**Results:** Similar to our previous observations in arcuate POMC neurons, exercise activated NTS GLP-1 neurons for up to 3 days after a single exercise bout. Exercise-induced activation of NTS GLP-1 neurons was sustained in response to exercise training. Interestingly, genetically abrogating vesicular glutamate release from NTS GLP-1 neurons effectively abolishes the exercise-induced POMC neuron activity. This effect mirrors the impact of deleting GLP-1 receptors from POMC neurons, negating the exercise-induced activation.

**Conclusions:** These data suggest that activation of NTS GLP-1 neurons and the resulting release of glutamate and GLP-1 are crucial for the activation of hypothalamic POMC neurons following exercise. This dual requirement may underscore a complex interplay between neurotransmitter and peptide signaling in mediating exercise's beneficial effects on metabolism.

**Presenter:** Kyle Vu

Basic Science

**Authors:** Kyle Vu, Amanda Clark, MD; Samir Parikh, MD

**Title:** Downregulation of NNMT: A Therapeutic Approach to Ameliorating AKI

**Abstract:**

**Background:** Nicotinamide adenine dinucleotide (NAD<sup>+</sup>) is the quintessential redox cofactor in cellular metabolism and is required for kidney cell function. Reduced NAD<sup>+</sup> abundance is a pathologic feature of both acute (AKI) and chronic kidney diseases (CKD). While NAD<sup>+</sup> biosynthesis is suppressed in periods of kidney injury, multiple studies demonstrate an upregulation of nicotinamide N-methyltransferase (NNMT) during injury. NNMT catalyzes the methylation of nicotinamide (NAM), the most significant precursor of NAD<sup>+</sup> biosynthesis. Methylated NAM is permanently removed from NAD<sup>+</sup> circulation. Further, via production of methyl-NAM, NNMT permanently removes methyl groups from circulation. Thus, NNMT induction during AKI may represent an actionable target to reduce AKI severity as well as elucidating a mechanism where acute injury induces long-term changes in gene expression that could underly the AKI to CKD transition.

**Methods:** NNMT expression was measured using qPCR in mouse kidneys after AKI induced by cisplatin, folic acid, and ischemic reperfusion injury (IRI). A novel inducible renal tubule specific NNMT overexpression mouse (iNephNNMT) was created by crossing a Pax8rtTA transgene to a tetO NNMT mouse. iNephNNMT had kidney function (GFR) estimated via measurement of serum creatinine after 3 months of overexpression or after 4 weeks of overexpression followed by IRI. Wild type mice were given IRI along with vehicle or NNMT inhibitors me-NAM and JBSNF, and injury severity was assessed using serum creatinine. RNASeq and ATACSeq were performed on kidneys from iNephNNMT mice.

**Results:** NNMT induction is a conserved feature across 3 distinct AKI mouse models. iNephNNMT mice had reduced GFR at baseline and more severe injury after IRI. Structurally disparate pharmacologic NNMT inhibitors ameliorated AKI by inducing the same renal-protective effects of increasing NAD<sup>+</sup>. RNASeq and ATACSeq data from iNephNNMT kidneys demonstrate that NNMT overexpression increases chromatin accessibility at the NNMT locus and leads to sustained overexpression of NNMT.

**Conclusions:** NNMT induction during AKI is a conserved, maladaptive feature of AKI that may be a therapeutic target. Further, NNMT induction during periods of stress may lead to long-term increased NNMT expression that may slow recovery and exacerbate the development of fibrosis.

Poster #66

**Presenter:** Lara Bideyan, PhD

Basic Science

**Authors:** Lara Bideyan, PhD; Steven Wyler, PhD; Joel Elmquist, DMV, PhD

**Title:** Dissecting the Transcriptional Diversity of VMH in Response to Exercise

**Abstract:**

**Background:** Exercise prevents many metabolic disorders such as type-2 diabetes and cardiovascular diseases through improvements in glucose and lipid metabolism, insulin and leptin sensitivity, and muscle function. Steroidogenic Factor (SF-1) expressing neurons in the ventromedial nucleus of hypothalamus (VMH) are shown to facilitate some of these metabolic adaptations to exercise. Our preliminary data shows that SF-1 neurons are activated in response to exercise training and the deletion of SF-1 in the VMH blunts transcriptional adaptation in skeletal muscle to exercise, endurance capacity, and improvements in body composition from exercise training. However, we have a limited understanding of the complexity of different cell populations within the VMH and which populations of SF-1 neurons mediate these metabolic benefits is unknown.

**Methods:** To address this, we trained mice for 4-weeks using a medium-intensity exercise protocol. We used single-nucleus RNA-Seq to profile the transcriptional landscape of the VMH of these exercise-trained mice and their sedentary controls.

**Results:** We identified 18 different neuronal populations within VMH that represented by the expression of SF-1, LepR, Foxp2, Nfib, and Esr1 genes among others. We found sex differences in nuclear receptor signaling, potassium channel and glutamate receptors within the ventrolateral VMH (vlVMH) populations. Within vlVMH populations, we found a cell cluster exclusively found in females strongly expressing estrogen, androgen and progesterone receptor. In response to exercise training, electron transport genes and early activation genes such as Junb and Jund were activated in certain clusters. Several subunits of potassium channels and glutamate receptors are change in expression in a cluster-specific fashion. Foxp2 cluster showed the most differentially expressed genes, upregulation of Junb, downregulation of voltage-gated and calcium-activated potassium channel subunits and upregulation of metabotropic and ionotropic glutamate receptors aligned with an increased activation.

**Conclusions:** Sex impacts the neuronal populations and their transcriptional profile. Exercise training regulates the expression of some common and some cluster specific genes. Potassium channels and glutamate receptors are modulated to adapt to exercise training. Foxp2+ neurons showed promising changes in response to exercise. We are following up on them through electrophysiology and plan on testing their contribution to metabolic adaptations to exercise training.

Poster #67

**Presenter:** Li Li, PhD

Basic Science

**Authors:** Li Li, PhD; Ciria C. Hernandez, PhD; Baijie Xu, PhD; FNU Swati, MS; Roger Cone, PhD; Chen Liu, PhD

**Title:** The Atypical Antipsychotic Clozapine Targets Kir7.1 to Cause Weight Gain

**Abstract:**

**Background:** Antipsychotic drugs (APDs)-induced metabolic syndrome presents a significant clinical challenge. However, the underlying mechanism remains poorly understood. It is due, in part, to a lack of animal models that recapitulate APD's metabolic effects.

**Methods:** To this end, we have developed a mouse model that reproduces excessive weight gain, increased adiposity, and glucose intolerance by clozapine, one of the commonly used APD.

**Results:** We find that clozapine treatment promptly disrupts the energy balance in C57BL/6 mice, with hyperphagia being the driving force of the weight gain. Notably, we reveal for the first time that clozapine activates the inward rectifying potassium channel Kir7.1 via the functional coupling between Kir7.1 and the melanocortin 4 receptor (MC4R). Furthermore, mice with selective deletion of Kir7.1 in Mc4r-Cre neurons are resistant to clozapine-induced weight gain. Lastly, we demonstrate that treatment with ML418, a Kir7.1-specific antagonist, effectively mitigates hyperphagia and obesity in clozapine-treated mice.

**Conclusion:** In summary, our findings suggest that targeting MC4R/KIR7.1 signaling could be a potential therapeutic approach for alleviating clozapine's metabolic side effects.

Poster #68

**Presenter:** Mahesh Kathania, PhD

Basic Science

**Authors:** Mahesh Kathania, PhD; Thirupugal Govindarajan, PhD; Ramakrishna Nimma, PhD; K. Venuprasad, PhD

**Title:** ZNF22-TOX Axis Regulates CD8+ T Cell Exhaustion

**Abstract:**

**Background:** CD8+ cytotoxic T cells play a critical role in anti-tumor responses but become dysfunctional and exhausted in the tumor microenvironment (TME). Exhausted T cells lose their effector functions and express inhibitory receptors such as PD-1, CTLA4, and Tim3. Recent studies have shown that TOX, a crucial transcription factor, is involved in tumor progression and T cell exhaustion. However, a clear understanding of the regulation of TOX in T cell dysfunction in cancer remains unclear, which is essential to overcome the current limitations of immunotherapies for cancer.

**Methods:** TILs were isolated from MC38 tumors grown in C57BL/6 mice, and the exhausted (PD1+Tim3+) CD8+ TILs were sorted. The cell lysate was incubated with anti-TOX antibody, and immunoprecipitation assay was performed, followed by mass spectrometric (MS) analysis. CO-IP experiments were performed to confirm ZNF22 and TOX interaction. SUMOylation assay was performed to check SUMOylation of ZNF22. Insilco analysis was performed to check TOX and SUMO3 interaction. Chromatin immunoprecipitation (ChIP) assay was performed to check the binding of ZNF22 to the PD1 promoter.

**Results:** We have found that ZNF22, a novel transcription factor, binds to the TOX in exhausted CD8+ TILs. MS analysis and CO-IP experiments confirmed ZNF22 binding to TOX. Amino acid sequence analysis confirmed conserved SUMOylation sites on ZNF22 and SUMO interacting motif (SIM) on TOX. In vitro experiments confirmed the SUMOylation of ZNF22 was essential for interaction with TOX. Insilco analysis confirmed the TOX-SIM domain and SUMO3 interaction. Deletion of ZNF22 in TILs restored their effector function (expression of IFN- $\gamma$ , TNF- $\alpha$ , GzmB). Chromatin immunoprecipitation (ChIP) assay showed that the ZNF22-TOX complex binds to the PD1 promoter.

**Conclusions:** Our results show that ZNF22 interacts with TOX in exhausted CD8+TILs, and SUMOylation of ZNF22 was essential for interaction with TOX. We will further elucidate the molecular mechanism by which ZNF22 regulates TOX and antitumor immunity using *Znf22*<sup>-/-</sup> mice. We will explore the therapeutic potential of targeting ZNF22 in CAR-T cells using patient-derived xenograft models of colon cancer. A clear understanding of the ZNF22 and TOX protein could overcome the current limitations of immunotherapy in cancer.

Poster #69

**Presenter:** Marco Galvan, BSc

Basic Science

**Authors:** Marco Galvan, BSc; Mina Fujitani, PhD; Jasmine Dushime, BSc; Safia Baset, BSc; Bandy Chen, BSc; Carlos M. Castorena, PhD; Joel K. Elmquist, DVM, PhD; Teppei Fujikawa, PhD

**Title:** Skeletal Muscle *Adrb2* is Required for Metabolic Benefits of Exercise

**Abstract:**

**Background:** Exercise is the most economical and effective treatment for metabolic abnormalities. However, the mechanisms underlying metabolic benefits of exercise remain unclear. Our previous studies have shown that the hypothalamus-the sympathetic nervous system (SNS) axis plays substantial roles in metabolic adaptations to exercise, hence metabolic benefit exercise. It is still unclear that the hypothalamus-the SNS axis directly acts on skeletal muscle, the primary organ for metabolic benefits of exercise, to regulate metabolic adaptations to exercise. Here, using genetically-engineered mice, we investigated the role of adrenergic receptor  $\beta 2$  ( $\beta 2$ -AdR, gene name; *Adrb2*), which is a predominant form of adrenergic receptors in skeletal muscle cells, in the regulation of metabolic adaptations to exercise.

**Methods:** We generated mice lacking  $\beta 2$ -AdR only in skeletal muscle cells (*SKM $\Delta$ Adrb2*) by crossing HAS-MCM and *Adrb2* floxed mice. HAS-MCH mice express tamoxifen-inducible Cre recombinase only in skeletal muscle cells and *Adrb2* floxed mice bear two loxP sites flanking a *Adrb2* exon. First, we tested whether *SKM $\Delta$ Adrb2* mice exhibit refractory responses to  $\beta 2$ -AdR agonist administration. Subsequently, we assessed the endurance capacity of *SKM $\Delta$ Adrb2* mice. Further, we examined whether  $\beta 2$ -AdR only in skeletal muscle cells is required for exercise-induced transcriptional changes in skeletal muscle after exercise. Finally, we investigated whether  $\beta 2$ -AdR only in skeletal muscle cells is required for metabolic benefits of exercise using the treadmill apparatus while mice were fed with a high-calorie diet.

**Results:** *SKM $\Delta$ Adrb2* mice demonstrated refractory responses to both injection of  $\beta 2$ -AdR agonist and exercise. Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1 $\alpha$ ) was used as the readout of  $\beta 2$ -AdR actions. Previous studies have shown that both  $\beta 2$ -AdR agonist and exercise substantially increase mRNA levels of PGC-1 $\alpha$  in skeletal muscle. Intriguingly, *SKM $\Delta$ Adrb2* mice demonstrated higher capacity of endurance. *SKM $\Delta$ Adrb2* mice gained greater adipose tissues after 4 weeks exercise trainings, suggesting that  $\beta 2$ -AdR in skeletal muscle cells is required for metabolic benefits of exercise.

**Conclusion:** Combined with previous studies, our investigation in this study unravels that the hypothalamus-the SNS axis coupled with  $\beta 2$ -AdR in skeletal muscle cells is a key for metabolic benefits of exercise.

**Presenter:** Mina Fujitani

Basic Science

**Authors:** Safia Baset, BSc; Mina Fujitani, PhD; Lara Bideyan, PhD; Eunsang Hwang, PhD; Kevin W. Williams, PhD; Joel K. Elmquist, DVM, PhD; Teppei Fujikawa, PhD

**Title:** Evaluation of the Role of Nr5a1 in VMHdm/c Neurons in Adults in the Regulation of Whole-body Metabolism

**Abstract:**

**Background:** The mechanisms underlying the metabolic benefits of exercise remain to be elucidated. We have shown that an exercise intervention in mice increased expression of Nr5a1 (also known as steroidogenic factor-1; SF-1) in the dorsomedial and central parts of the ventromedial hypothalamic nucleus (VMHdm/c) and knockdown of Nr5a1 in VMHdm/c neurons hampers exercise-induced improvements in body compositions and glycemia. These data led us to hypothesize that augmented Nr5a1 in VMHdm/c neurons is critical for metabolic benefits of exercise. The timing of gene manipulation is important to investigate the role of VMH; therefore, we tested our hypothesis with the adult gain- and loss-of-the-function studies with adeno-associated virus (AAV) approaches.

**Methods:** We knockdowned Nr5a1 in adults by injections of AAV containing Cre recombinase into Sf-1 floxed mice and measured metabolic parameters. We also performed RNA-sequencing analysis (RNA-seq) and electrophysiology experiments before differences in body weight emerged between wild-type mice and knockdown mice. To complement this loss-of-function study, we developed AAV bearing Cre-dependent Nr5a1 cDNA (AAV-DIO-Nr5a1-OE), allowing us to overexpress Nr5a1 specifically in VMHdm/c neurons (VMHdm/cOE-Nr5a1). We injected AAV-DIO-Nr5a1-OE into Sf-1-BAC-Cre mice and measured metabolic parameters.

**Results:** Adult knockdown of Nr5a1 in VMHdm/c neurons (VMHdm/cKD-Nr5a1) exaggerated high-fat diet (HFD)-induced insulin resistance. VMHdm/cKD-Nr5a1 caused increased body weight on a normal diet, although previous studies have shown that postnatal (~P21) knockdown of Nr5a1 does not affect body weight on a normal diet. VMHdm/cKD-Nr5a1 increased food intake but did not change energy expenditure. Electrophysiology showed that VMHdm/cKD-Nr5a1 decreased basal membrane potential and firing frequency. RNA-seq data showed that VMHdm/cKD-Nr5a1 altered many genes including *Cacna2d1*, which is one of the subunits for voltage-dependent calcium channels and highly expressed in the VMHdm/c. Intriguingly, disruption of *Cacna2d1* using its inhibitor pregabalin reduced basal membrane potential in VMHdm/c Nr5a1 neurons. VMHdm/cOE-Nr5a1 improved body weight in HFD-induced obesity and insulin resistance.

**Conclusions:** Our study revealed a crucial role of Nr5a1-modulated VMHdm/c neuron activity in the regulation of body weight, food intake, and glucose homeostasis. Further, our results suggest the importance of the timing of genetic manipulation in VMHdm/c neurons.



Poster #71

**Presenter:** Newton Cao, BS

Basic Science

**Authors:** Laurent Gautron, PhD; Newton Cao, BS; Warda Merchant, BS

**Title:** Mouse Intestinal GLP-1 Cells Do Not Contact Vagal Neurons

**Abstract:**

**Background:** The communication between intestinal Glucagon like peptide 1 (GLP-1)-producing cells and the peripheral nervous system has garnered renewed interest considering the availability of anti-obesity and anti-diabetic approaches targeting GLP-1 signaling. While it is well-established that intestinal GLP-1 cells can exert influence through paracrine mechanisms, recent evidence suggests the possible existence of synaptic-like connections between GLP-1 cells and peripheral neurons, including those of the vagus nerve.

**Methods and Results:** In this study, using a reporter Phox2b-Cre-Tomato mouse model and super-resolution confocal microscopy, we demonstrated that vagal axons made apparent “contacts” with less than 0.5% of GLP-1 cells. Moreover, immunohistochemistry combined with super-resolution confocal microscopy revealed abundant post-synaptic density 95 (PSD-95) immunoreactivity within the enteric plexus of the lower intestines of C57/BL6 mice, with virtually none in its mucosa. Lastly, utilizing RNAScope in situ hybridization in the lower intestines of mice, we observed that GLP-1 cells expressed generic markers of secretory cells such as Snap25 and Nefm, but neither synaptic markers such as Syn1 and Nrnx2, nor glutamatergic markers such as Slc17a7.

**Conclusion:** Through theoretical considerations and a critical review of the literature, we concluded that intestinal GLP-1 cells communicate with vagal neurons through paracrine mechanisms, rather than synaptic-like contacts.

Poster #72

**Presenter:** Omprakash Singh, PhD

Basic Science

**Authors:** Omprakash Singh, PhD

**Title:** Defining the Role of the Suprachiasmatic Nucleus in Ghrelin Action

**Abstract:**

**Background:** The hormone ghrelin increases food intake, body weight, GH secretion, and blood glucose. A direct role for the suprachiasmatic nucleus (SCN), a key brain region regulating circadian rhythms, in mediating these effects of ghrelin is possible due to high expression of the ghrelin receptor (GHSR). Yet, only sparse data regarding ghrelin action in the SCN is available. Here, we aimed to determine contributions of GHSR-expressing SCN neurons to ghrelin's metabolic effects.

**Methods:** We analyzed publicly available single-cell RNA sequencing data of SCN neurons and performed in situ hybridization histochemistry on the C57Bl/6N mice perfused at two Zeitgeber time (ZT) to further characterize SCN *Ghr* expression. We delivered inhibitory AAV2-hSyn-DIO-hM4(Gi)-mCherry (n=14) and stimulatory AAV5-hSyn-DIO-hM3(Gq)-mCherry viruses (n=9) to the SCN of *Ghr*-IRES-Cre mice, followed by CNO administration, to chemogenetically modulate activity of GHSR-expressing SCN neurons. Then, we assessed spontaneous food intake at ZT 0-4, ZT 4-8, ZT 12-16, and ZT 16-20 and administered ghrelin-induced food intake. We used histochemistry to characterize these mice as being correctly targeted ("hits") or incorrectly targeted ("misses") with the chemogenetic viruses.

**Results:** Fourteen percent of SCN neurons, including neurons in all 6 distinct SCN clusters, expressed *Ghr*, with arginine-vasopressin (AVP) and gastrin-releasing peptide (GRP) neurons showing the highest expression. *Ghr* expression in the SCN was higher at night than daytime. Chemogenetic inhibition of GHSR-expressing SCN neurons reduced spontaneous food intake (by 45.5%) at ZT 4-8 (during the light phase), but did not affect spontaneous food intake at the other tested ZT ranges. Chemogenetic stimulation of GHSR-expressing SCN neurons increased food intake at all tested ZT ranges, with the greatest increase observed at ZT 4-8. Administered ghrelin-induced food intake was unaffected by chemogenetic modulation of SCN neurons.

**Conclusions:** These findings highlight the dynamic regulation of GHSR expression in the SCN and its potential role in modulating feeding behavior across the circadian cycle. Specifically, the usual amounts of spontaneous food intake occurring between ZT 4-8 are dependent on normal activity of GHSR-expressing SCN neurons.

Poster #73

**Presenter:** Ramakrishna Nimma, PhD

Basic Science

**Authors:** Ramakrishna Nimma, PhD; Mahesh Kathania, PhD; Venuprasad Poojary, PhD

**Title:** ZC3H15 Regulates PD1 Expression in CD8+ T Cells and Anti-tumor Immunity

**Abstract:**

**Background:** CD8+ cytotoxic T cells play a pivotal role in anti-tumor responses but become dysfunctional and exhausted in the tumor microenvironment (TME). Exhausted T cells lose their effector functions and express inhibitory receptors such as PD1, CTLA4, and Tim3. The binding of PD1 to PDL1 (expressed on tumor cells) sends negative signals in tumor-infiltrated T cells (TILs), resulting in reduced expression of cytotoxic mediators (IFN- $\gamma$ , TNF- $\alpha$ , Granzyme B, perforins) and tumor-killing ability. However, the transcriptional regulation of PD1 in TILs remains unclear, which is necessary to target the PD1-PDL1 axis and restore anti-tumor immunity successfully.

**Methods:** TILs were isolated from MC38 tumors, and the exhausted (PD1+Tim3+) CD8+ TILs were FACS sorted. The cell lysate was incubated with a biotinylated PD1 promoter, and a pull-down assay was performed, which was followed by mass spectrometric (MS) analysis. Chromatin immunoprecipitation (ChIP) assay was performed to confirm the binding of ZC3H15 to the PD1 promoter. PD1 promoter-driven luciferase assay and gRNA-mediated knockdown were performed to analyze the function of ZC3H15 in regulating PD1 promoter activity. Effector (PD1-Tim3-) and exhausted (PD1+Tim3+) CD8+ TILs from MC38 tumors were analyzed for the expression of Zc3h15. We also compared the expression of Zc3h15 in exhausted and effector CD8+ T cells in publicly available RNA sequencing (RNA-seq) data. Zc3h15-/- mice were generated by CRISPR-Cas9 to study the in vivo function of ZC3H15 in the regulation of anti-tumor immunity.

**Results:** We have found that ZC3H15, a novel transcription factor, binds to the PD1 promoter in exhausted CD8+TILs. ZC3H15 markedly upregulated PD1 promoter-driven luciferase activity in Jurkat T cells. Deletion of ZC3H15 in TILs abrogated PD1 expression and restored their effector function (expression of IFN- $\gamma$ , TNF- $\alpha$ , GzmB). Elevated expressions of Zc3h15 were found in exhausted CD8+ TILs compared to effector CD8+ TILs from MC38 tumors. TCGA data confirmed the increased expression of ZC3H15 in colon adenocarcinoma. Higher ZC3H15 expression correlated with reduced overall survival rates in these cancers.

**Conclusions:** Our results show that ZC3H15 is upregulated in exhausted CD8+TILs, and ZC3H15 binds to the PD1 promoter and induces PD1 expression. We will further elucidate the molecular mechanism by which ZC3H15 regulates PD1 and antitumor immunity using Zc3h15-/- mice. We will explore the therapeutic potential of targeting ZC3H15 in CAR-T cells using patient-derived xenograft models of colon cancer. A clear understanding of the ZC3H15-PD1 pathway could overcome the current limitations of immunotherapy for cancer.

Poster #74

**Presenter:** Salil Varshney, PhD

Basic Science

**Authors:** Salil Varshney, PhD; Kripa Shankar, PhD; Deepali Gupta, PhD; Sean B. Ogden, PhD; Omprakash Singh, PhD; Subhojit Paul, PhD; Avi W. Burstein, BA; Andrea Pineda Sanchez, MS; Sherri Osborne-Lawrence, MS; Nathan P. Metzger, MS; Corine P. Richard, MS; Connor Lawrence, BA; Jeffrey M. Zigman, MD, PhD

**Title:** Combining Mirabegron and Atenolol Limits Weight Gain and Elevated Blood Pressure in Diet-induced Obese Mice

**Abstract:**

**Background:** Activation of brown adipose tissue (BAT), as can be achieved by  $\beta$ 3-adrenergic receptor (AR) agonists represents an intriguing new target for treatment of overweight/obesity and co-morbid pre-diabetes/diabetes. Previous small human studies have shown that treatment with the  $\beta$ 3-AR agonist mirabegron, which is currently approved to treat overactive bladder, can increase BAT metabolic activity, increase energy expenditure, and/or improve blood glucose, although often at the expense of raising blood pressure when high doses are used. Here, we investigated whether adding the  $\beta$ 1-AR antagonist atenolol to mirabegron would sensitize the body to mirabegron's actions to increase BAT metabolic activity – so as to achieve both weight loss and improved glycemia – while avoiding the potential untoward cardiovascular side effects associated with high-dose  $\beta$ 3-AR agonist regimens.

**Methods:** To test this hypothesis, we conducted a proof-of-concept, preclinical trial in mice. Five week-old C57BL/6N male mice were fed 42% HFD for 4 weeks, after which they were randomized to one of the following 4 treatment groups while being maintained on HFD for another 4 weeks: Placebo, high-dose mirabegron (8mg/kg BW by gavage daily), atenolol (provided ad lib in drinking water at a concentration of 0.5mg/mL), or high-dose mirabegron + atenolol. Body weight, food intake, water intake, and body composition were measured over the course of the study. Glucose tolerance, blood pressure, heart rate, and cholesterol levels were determined at the end of the study.

**Results:** Both mirabegron alone and combined mirabegron + atenolol treatment limited increases in body weight (by ~ 33 and 30 %) and fat mass (by ~ 62 and 55 %), lowered total and LDL cholesterol (by ~15 and 12 % - 19 and 18%), and improved glucose tolerance (28 % lower glucose AUC). Combined mirabegron + atenolol treatment prevented the rises in mean, systolic, and diastolic blood pressure readings (12%, 11%, and 12%) otherwise induced by mirabegron alone. Mirabegron alone and combined mirabegron + atenolol raised heart rate.

**Conclusions:** Adding the  $\beta$ 1-AR antagonist atenolol to the  $\beta$ 3-AR agonist mirabegron limits gains in body weight and adiposity and improves glucose tolerance and cholesterol while preventing undesired increases in blood pressure.

Poster #75

**Presenter:** Sepideh Sheybani Deloui, PhD

Basic Science

**Authors:** Sepideh Sheybani-Deloui, PhD; Omprakash Singh, PhD; Jeffrey M. Zigman, MD, PhD

**Title:** Defining the Spatiotemporal Expression Pattern of GHSR (ghrelin receptor) in the Murine Suprachiasmatic Nucleus

**Abstract:**

**Background:** Ghrelin is a stomach-derived hormone that increases food intake, growth hormone secretion, adiposity, body weight, and blood glucose. Ghrelin exerts its effect through binding and activating growth hormone secretagogue receptors (GHSRs) encoded by the *Ghsr* gene. *Ghsr* is densely expressed in the suprachiasmatic nucleus (SCN), the master light-entrainable regulator of cellular rhythms. Exogenous ghrelin has a circadian time (CT)-specific effect on the pattern of neuronal activity in SCN slices in the dish, and GHSR deficiency results in lower locomotor activity specifically in the early dark phase of the light/dark cycle in mice. GHSR actions in the SCN and the chemical identities of the SCN cells that express *Ghsr* are unknown. Here, we characterized the spatiotemporal pattern of *Ghsr* expression relative to both the time of the day and external light stimulation.

**Methods:** Raw single-cell RNA-seq data from two published studies (GSE167927 and GSE148252) were used for integration and downstream analyses using the RStudio package Seurat v4.3.0.

**Results:** Among 15,446 high-quality SCN cells, *Ghsr* expression was readily observed in 10% of all 6 SCN neuronal clusters, including the previously well-characterized *Avphigh*, *Viphigh*, and *Grp/Alcam+* clusters, and those marked by *Syt1/Penk*, *Trh/Bdnf*, and *Sncb/Gad2*. The majority of *Ghsr+* neurons were *Avphigh* (28.9%), followed by *Grp/Alcam+* (22.5%). *Ghsr* expression was at least 25% higher in all major neuronal subtypes at the subjective night (CT15.5) than at the subjective day (CT7.5). Further, *Ghsr* was the only upregulated gene at CT15.5 (p-value: 6.88E-13) in the *Ghsr+* AVP neurons, while 35 genes -- including some previously characterized as "day-distinguishing" genes (*Prok*, *Rgs16*, and *Dbp*) -- were downregulated. Re-analysis of data from SCN during the dark-phase with and without 1-hour light stimulation revealed that a light impulse is sufficient to decrease *Ghsr* expression in AVP neurons by 23% (p-value: 0.003). Dark-phase *Ghsr+* AVP neurons exhibited a 1.5-2 fold higher expression of *Pcsk1n* (encoding for a prohormone peptidase enzyme) and *Magi2* (a synaptic scaffolding molecule involved in both excitatory and GABAergic synaptic transmission).

**Conclusions:** We found higher expression of *Ghsr* and genes involved in synaptic transmission particularly in the AVP neurons of the SCN during the dark phase, independent of food availability.

Poster #76

**Presenter:** Warda Merchant, BS

Basic Science

**Authors:** Warda Merchant, BS; Steven Wyler, PhD; Joel Elmquist, DVM, PhD

**Title:** Deletion of Ligand Dependent Corepressor-Like Protects Against Diet-induced Obesity

**Abstract:**

**Background:** Genome Wide Association Studies (GWAS) in humans, dogs, and livestock have uncovered genes which may play a role in metabolism. However, functional analysis is required to link the metabolic phenotype with the associated gene. Here we identified the Ligand Dependent Corepressor-Like (LCoRL) as a potential metabolic regulator.

**Method:** We used CRISPR/Cas9 approaches in mice to generate a *Lcorl* null allele (*Lcorl*<sup>-/-</sup>). We characterized *Lcorl*<sup>-/-</sup> mice by assessing body weight, body composition, food intake, and glucose homeostasis. We also performed RNA sequencing (RNA-Seq) in the livers of three-week-old mice. Additionally, we challenged mice with a 60% high fat diet (HFD). We generated floxed mice to examine the tissue specific functions of LCoRL. By using *Vglut2-Cre*, we profiled the effects of loss of LCoRL specifically in glutamatergic neurons (*Lcorl*<sup>Vglut2KO</sup>).

**Results:** Mice homozygous for loss of *Lcorl* are viable and fertile. However, *Lcorl*<sup>-/-</sup> pups show stunted postnatal growth for the first few weeks of life. They catch up to their wildtype littermates by 7-9 weeks of age. Three-week-old mice show reduced circulating insulin-like growth factor-1 (IGF-1) levels without a change in pituitary growth hormone (Gh) mRNA levels. Gene expression analysis of livers of three-week-old mice showed changes that indicated an energy deficient state. Interestingly, *Lcorl*<sup>-/-</sup> mice remain lean compared to wildtype littermates as they age. This is associated with a decrease in daily food intake. Additionally, *Lcorl*<sup>-/-</sup> mice show a greater amplitude of their respiratory exchange ratio (RER) compared to controls, suggesting differential usage of fat and carbohydrates across the light/dark cycle. Consistent with enhanced metabolic health, *Lcorl*<sup>-/-</sup> mice also show improved glucose tolerance and insulin sensitivity. Finally, *Lcorl*<sup>-/-</sup> mice are protected against high-fat diet-induced obesity. Some of these phenotypes such as protection from high-fat diet-induced obesity were present in *Lcorl*<sup>Vglut2KO</sup> mice.

**Conclusion:** This phenotypic characterization of the *Lcorl*<sup>-/-</sup> mouse reveals that LCoRL is a causal gene resulting in the changes in metabolism seen in GWAS in humans and livestock. LCoRL in glutamatergic neurons might be contributing to these phenotypes. Altogether, this study provides novel mechanistic insights of a gene important in diseases and traits in humans and animals.

Poster #77

**Presenter:** Darine Daher, MD

Clinical Science

**Authors:** Darine Daher, MD; Karim Seif El Dahan, MD; Nicole E. Rich, MD, MSCS; Nabihah Tayob, PhD; Vincent Merrill, PhD; Daniel Q. Huang, MD; Ju Dong Yang, MD; Anand V. Kulkarni, MD; Fasiha Kanwal, MD, MS; Jorge Marrero, MD, MS; Neehar Parikh, MD, MS; Amit G. Singal, MD, MS

**Title:** Hepatocellular Carcinoma Screening in a Contemporary Cohort of At-Risk Patients

**Abstract:**

**Background:** Cohort studies demonstrating an association between hepatocellular carcinoma (HCC) screening and reduced mortality are prone to lead-time and length-time biases. We characterized the clinical benefits of HCC screening, adjusting for leadtime and length time biases, in a diverse, contemporary cohort of at-risk patients.

**Methods:** We conducted a retrospective cohort study of patients diagnosed with HCC between January 2008 and December 2022 at two large health systems. Screen-detected HCC was defined by abnormal screening-intent abdominal imaging or AFP level within 6 months before diagnosis. Cox regression analysis was used to characterize differences in overall survival between patients with screen- and non-screen detected HCC; lead and length time adjustments were calculated using the Duffy parametric formula.

**Results:** Among 1313 patients with HCC (mean age 61.7 years; 75.6% male; 56.3% BCLC 0/A), HCC was screen-detected in 556 (42.3%) and non-screen detected in 757 (57.7%). Patients with screen-detected HCC had higher proportions of early-stage HCC (70.7% versus 45.7%, RR 1.54, 95%CI 1.41 – 1.70) and curative treatment receipt (51.1% versus 33.5%, RR 1.40, 95%CI 1.07 – 1.83). The screen-detected group had significantly lower mortality, which persisted after correcting for lead-time bias (HR: 0.75, 95%CI 0.65 – 0.87) in fully adjusted models. Both groups had similar tumor doubling times (3.8 versus 5.6 months,  $p=0.4$ ) and proportions of indolent tumors (35.4% versus 38.1%, RR 0.93, 95%CI 0.60 – 1.43). Adjustment for length-time bias decreased survival estimates, although 3- and 5-year survival for screen-detected HCC remained longer than non-screen detected HCC.

**Conclusions:** In this cohort study, HCC screening is associated with reduced mortality even after accounting for lead and length time biases. However, these biases should be considered in future studies.

Poster #78

**Presenter:** Darine Daher, MD

Clinical Science

**Authors:** Darine Daher, MD; Karim Seif El Dahan, MD; Sruthi Yekkaluri, PharmD; Purva Gopal, MD; Nicole E. Rich, MD, MSCS; Neehar D. Parikh, MD, MS; Caitlin C. Murphy, MD, MS; Amit G. Singal, MD, MS

**Title:** Adherence to Hepatocellular Carcinoma Surveillance in Patients with Cirrhosis Measured as Proportion Time Covered

**Abstract:**

**Background:** Hepatocellular carcinoma (HCC) surveillance is associated with improved early tumor detection, but effectiveness is limited by underuse. We characterized adherence to HCC surveillance using proportion of time covered (PTC) and estimated its association with clinical outcomes among patients with cirrhosis.

**Methods:** We conducted a retrospective cohort study of patients diagnosed with HCC between January 2008 and December 2022 at two large U.S health systems. We characterized PTC by imaging in the 12- and 24-months prior HCC diagnosis. We used multivariable logistic and Cox regression analysis to assess the association between PTC and early HCC detection, receipt of curative treatment, and overall survival.

**Results:** Among 2027 patients with HCC, 331 (51.4% BCLC 0/A) had been followed for at least 12 months prior to diagnosis. Median PTC was 24.9% (IQR 1.1 – 50.7%), with only 16.0% having semi-annual imaging and 42.0% having annual surveillance. Semi-annual and annual surveillance decreased to 6.3% and 29.6% when assessed over 24 months, although median PTC remained unchanged at 24.9%. Receipt of gastroenterology/hepatology care had the strongest association with PTC, with median PTC of 36.7% and 3.8% for those with and without gastroenterology/hepatology care. PTC was independently associated with improved early HCC detection, curative treatment receipt, and overall survival. Median survival was 15.7, 26.8, and 32.7 months among those with PTC of <25% (n=168 patients), PTC 25-50% (n=69 patients), and PTC >50% (n=94 patients), respectively.

**Conclusion:** The proportion time covered by HCC surveillance in patients with cirrhosis remains low, highlighting a need for multi-level interventions.



Poster #79

**Presenter:** Denis Wakeham, PhD

Clinical Science

**Authors:** Denis J. Wakeham, PhD; James P. MacNamara, MD; Sarah L. Hissen, PhD; Benjamin D. Levine MD, Christopher M. Hearon Jr., PhD

**Title:** Functional Sympatholysis of Neuropeptide Y-mediated Vasoconstriction in Humans

**Abstract:**

**Background:** Metabolic inhibition of sympathetic vasoconstriction (functional sympatholysis) is essential for adequate perfusion of skeletal muscle during exercise. Functional sympatholysis occurs primarily through post-junctional attenuation of norepinephrine and  $\alpha$ -adrenergic-mediated vasoconstriction, though other non-adrenergic neurotransmitters are co-released with norepinephrine. Neuropeptide Y (NPY) is a neurotransmitter that elicits robust vasoconstriction and is co-released with norepinephrine during exercise in an intensity dependent manner. Evidence from animal models indicate that NPY is sensitive to metabolic inhibition, however metabolic inhibition of NPY-mediated vasoconstriction has not been tested in humans. We tested the hypothesis that NPY-mediated vasoconstriction would be attenuated during handgrip exercise in humans.

**Methods:** In 10 healthy adults (7M:3F, age:  $30\pm 7$  years, BMI:  $24\pm 5$ ) we measured forearm blood flow (Doppler ultrasound), blood pressure (brachial artery catheter), and calculated changes in forearm vascular conductance (FVC) to local intra-arterial infusions of phenylephrine (PE;  $\alpha 1$ -agonist) or NPY (Y1R-agonist) during 1) intra-arterial infusion of sodium nitroprusside (SNP; nitric oxide donor) to serve as a non-metabolic vasodilatory control or 2) dynamic rhythmic handgrip exercise (EX; 15% maximal voluntary contraction).

**Results:** The vasoconstrictor responses to PE and NPY were quantified as a percent  $\Delta$ FVC during each condition (SNP vs. EX) and were compared by two-way RM-ANOVA. The magnitude of sympatholysis ( $\Delta$ FVC during exercise expressed as a percent of control) for PE and NPY was compared by a paired t-test. As expected, the vasoconstrictor response to PE was attenuated during handgrip exercise compared to SNP ( $\Delta$ FVC: SNP:  $-50\pm 24$  vs. EX:  $-17\pm 9$  %;  $p=0.002$ ). Similarly, NPY-mediated vasoconstriction was blunted during handgrip exercise compared to SNP ( $\Delta$ FVC: SNP:  $-32\pm 22$  vs. EX:  $-11\pm 7$  %;  $p=0.029$ ). There was no difference in the magnitude of sympatholysis between PE and NPY (PE:  $68\pm 18$ , NPY:  $52\pm 34$  %;  $p=0.28$ ).

**Conclusions:** These data indicate that NPY-mediated vasoconstriction is sensitive to metabolic inhibition in humans, and the magnitude of sympatholysis is not different from  $\alpha 1$ -adrenergic vasoconstriction.

Poster #80

**Presenter:** Fatemeh Khashami, PhD

Clinical Science

**Authors:** Fatemeh Khashami, PhD; Ivan E. Dimitrov, PhD; Maximilian Fuetterer, PhD; Sebastian Kozerke, PhD; Crystal E. Harrison, PhD; Jae Mo Park, PhD; Zoltan Kovacs, PhD; Craig R. Malloy, MD, PhD; Anke Henning, PhD; Nisha Unni, MD; Vlad G. Zaha, MD, PhD

**Title:** Evaluation of Cardiac Metabolic and Mechanical Functional Effects of Therapy with Doxorubicin, Without or With Immunotherapy, in Patients with Breast Cancer

**Abstract:**

**Background:** Current breast cancer diagnosis and treatment protocols achieve survival rates of >80% at 10 years. However, long-term cancer survivors have > 4-fold higher incidence of cardiovascular complications, including heart failure. This increase is due to underlying traditional cardiovascular risk factors and cardiotoxic therapies, including conventional chemotherapy with anthracyclines and immunotherapies. Therefore, we aimed to determine the effects of therapy for breast cancer with doxorubicin, without or with the immune checkpoint inhibitor pembrolizumab, on cardiac metabolic and mechanical function.

**Methods:** Conventional cardiac magnetic resonance imaging (CMRI) and magnetic resonance spectroscopic imaging (MRSI) with a nonradioactive metabolic substrate, hyperpolarized (HP) [1-13C] pyruvate, were performed at baseline and after completion of standard of care oncology therapy protocol. HP [1-13C] pyruvate MRSI allows the detection of downstream metabolites of pyruvate within the myocardium: [1-13C] bicarbonate from mitochondrial oxidation, and [1-13C] lactate from anaerobic cytosolic metabolism. Hyperpolarized pyruvate samples were prepared using SPINlab™ (GE Healthcare). Imaging of hyperpolarized pyruvate was conducted using a 13C transmit/receive Helmholtz loop-pair coil (PulseTeq, UK) on a 3T scanner (Philips Healthcare). 13C data were acquired from a short-axis slice, ECG-triggered in end-systole. 1H-MRI were analyzed using CVi42 (Circle Cardiovascular Imaging Inc., Canada), and 13C-MRI images were analyzed using MATLAB R2021a. Left ventricular mid-myocardium, and blood pool were segmented for metabolites quantitation.

**Results:** Cardiac studies were performed in a consecutive series of 25 women treated for breast cancer. Of these 17 (68%) were Caucasian, 5 (20%) Black, and 3 (12%) Asian, with ages ranging 46±11 years. Treatment plans were based on tumor type: 11 patients were received dose-dense anthracycline-cyclophosphamide therapy, and 14 also received pembrolizumab.

**Conclusions:** Acquisition of proton CMRI for assessment of mechanical function, and of HP [1-13C] pyruvate MRSI for measurement of cardiac metabolic parameters is feasible and well tolerated in a diverse group of patients with breast cancer undergoing standard of care therapy. These studies allow to correlate the effects of oncological therapy on cardiac metabolism and mechanical function.

Poster #81

**Presenter:** Karim Seif El Dahan, MD

Clinical Science

**Authors:** Karim Seif El Dahan, MD; Darine Daher, MD; Nicole E. Rich, MD, MSCS; Anish J. Nayak; Megha B. Bhongade; Prasun K. Jalal, MD; Fasiha Kanwal, MD, MSHS; Amit G. Singal, MD, MS

**Title:** Causes of Mortality Among Patients with Early-Stage Hepatocellular Carcinoma

**Abstract:**

**Background:** Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer-related death worldwide. Although most patients succumb to HCC-related causes, patients can have competing risks of mortality from liver dysfunction or other comorbidities (e.g., cardiopulmonary diseases, infections). We aimed to characterize primary causes of death and outcomes in a cohort of patients with early-stage HCC.

**Methods:** We conducted a retrospective cohort study at two US health systems of patients diagnosed with early-stage HCC (BCLC stages 0/A) between January 2008 and December 2022. HCC-related death was defined by large tumor burden and/or serum AFP>1,000 within 6 months of death or death within 1 month of HCC treatment. Liver-related (non-HCC) death was defined by MELD>20 or Child-Pugh class C within 3 months of death or if the patient died from variceal bleed, liver-related infection, or hepatorenal syndrome. We used multivariable Cox regression analysis to characterize associations with overall survival.

**Results:** Of 707 patients with early-stage HCC, 72.8% were male with median age at diagnosis of 60.4 years. The cohort was diverse regarding race/ethnicity (42.4% White, 25.6% Black, 25.2% Hispanic) and liver disease etiology (63.4% hepatitis C, 35.8% alcohol, 13.6% MASLD). A total of 378 (53.5%) deaths occurred during the follow-up period, of which 149 were HCC-related, 62 non-HCC liver-related, 96 were related to other non-liver non-HCC comorbidities, and 71 were of unknown cause. Median survivals were 24 (95%CI 21-32) months for HCC-related death, 19 (95%CI 15-24) months for liver-related death, and 24 (95%CI 19-30) months for non-liver, non-HCC related death. Patients with HCC-related death had better survival than patients with non-HCC liver-related death (HR 0.72, 95%CI 0.53-0.98) but not patients with other causes of death (HR 1.08, 95%CI 0.84-1.41). There was no significant difference in curative therapy receipt as last treatment between patients with HCC-related death vs. other causes of death (OR 0.84, 95%CI 0.55-1.28).

**Conclusions:** The causes of death varied among patients with early-stage HCC, with a significant number dying from causes other than HCC. Understanding of mortality patterns is critical to improve prognosis of patients with HCC as well as better understand the optimal target population for HCC screening efforts.

Poster #82

**Presenter:** Traci Tiemann Betts, DPT

Clinical Science

**Authors:** Traci Betts, DPT; Lajjaben Patel, MD; Ritika Dhruve, MD; Vinayak Subramanian, MD; Matthew W. Segar, MD, MS; Alvin Chandra, MD; Neil Keshvani, MD; Ambarish Pandey, MD, MSCS

**Title:** Association of the Objective Measures of Physical Function with Exercise Capacity, Quality of Life, and Left Heart Filling Pressures Among Patients with Heart Failure with Preserved Ejection Fraction

**Abstract:**

**Background:** Older patients with heart failure and preserved ejection fraction have a high burden of physical dysfunction and exercise intolerance. The association of objective physical function measures with exercise capacity and quality of life has not been well characterized among contemporary HFpEF patients. Furthermore, the relative contribution of peripheral skeletal muscle dysfunction and central cardiac impairments to exercise intolerance is not well established.

**Methods:** Participants in the UT Southwestern HFpEF Registry were included in this study. Participants had a clinical diagnosis of HFpEF and underwent cardiovascular and exercise phenotyping, consisting of resting and exercise right heart catheterization, cardiopulmonary exercise testing, assessment of quality of life by the Kansas City Cardiomyopathy Questionnaire (KCCQ) – 12, and the SPPB. The SPPB assesses multiple domains of physical function, including balance, gait speed, and lower extremity strength. The association of SPPB with KCCQ summary scores, VO<sub>2</sub>peak, and elevated left heart filling pressures (Pulmonary Capillary Wedge Pressure [PCWP] > 15 mmHg at rest or > 25 mmHg with exercise) was assessed with generalized linear models. Finally, the relative contribution of SPPB, a measure of peripheral skeletal muscle impairment, and elevated PCWP, a measure of central cardiac impairment, towards VO<sub>2</sub>peak was assessed using age, sex, and race-adjusted linear regression models.

**Results:** The study included 133 participants (mean age 72 years, 62% female, mean SPPB =9). 13.5% of participants had an SPPB < 6, and 52% had an SPPB of 6-10. Participants with the worst physical function (SPPB < 6, vs. best: SPPB > 10) were older (79 vs. 67 years, p = 0.001) with a greater prevalence of medical comorbidities and higher resting PCWP (17 vs. 12 mmHg, p = 0.01), lower resting cardiac index (2.6 vs 3.2, p = 0.03), and lower peak VO<sub>2</sub> (10.2 vs 13.1 mL/kg/min, p<0.001) without differences in exercise PCWP, KCCQ summary score, and sex. In adjusted analysis, higher SPPB was associated with higher KCCQ and peak VO<sub>2</sub> but not elevated PCWP (see Table 1). In adjusted models evaluating predictors of peak VO<sub>2</sub>, total SPPB (Parameter estimate: 0.5, 95% CI 0.2 – 0.9, p = 0.002), but not elevated PCWP (estimate -1.1, 95% CI -2.7 – 0.5, p = 0.2), was significantly associated with VO<sub>2</sub>peak.

**Conclusion:** Physical function impairment in participants with HFpEF is associated with lower aerobic capacity and worse quality of life but not elevated left heart filling pressures.

Poster #83

**Presenter:** Yassin EL-Najjar, MD

Clinical Science

**Authors:** Yassin El-Najjar, MD; Jianyi Yin, MD, PhD; Noelle Cordova, PharmD; Mary-Joe Touma, MD; Noelle Nguyen; Moheb Boktor, MD; Ezra Burstein, MD, PhD; David I. Fudman, MD

**Title:** Short-term Use of Upadacitinib in Combination with Biologic Therapy for Inducing Clinical Remission in Patients with Active Inflammatory Bowel Disease

**Abstract:**

**Background:** Upadacitinib is a Janus kinase inhibitor with rapid onset of action. It may therefore have a role for short-term use, either to avoid corticosteroids or as a bridge to a slower-onset therapy.

**Methods:** We retrospectively reviewed patients who were prescribed upadacitinib alongside a biologic therapy to induce clinical remission of inflammatory bowel disease. Patients with a plan for upadacitinib therapy for  $\leq 16$  weeks were included. Patients who received upadacitinib as next-line monotherapy were excluded.

**Results:** We identified 12 patients, 8 with ulcerative colitis (UC) and 4 with Crohn's disease (CD), who initiated upadacitinib either as add-on therapy to a partially effective biologic ( $n=10$ ), or as bridge therapy during initiation of another advanced therapy ( $n=2$ ). Three (25%) patients were taking oral corticosteroids before initiation of upadacitinib. Median follow-up was 26 weeks (interquartile range [IQR], 21-34.5). Paired values were compared by Wilcoxon signed-rank test.

We observed a reduction in median partial Mayo (pMayo) score from 5.5 to 0 in UC patients ( $p=0.008$ ) and Harvey-Bradshaw index (HBI) from 5 to 3 in CD patients ( $p=0.5$ ). Nine of 11 (81.8%) patients who were not in steroid-free clinical remission (SFCR, defined as pMayo $<2$  or HBI $<5$  without receiving corticosteroids) achieved SFCR after initiation of upadacitinib. Paired fecal calprotectin and C-reactive protein decreased after upadacitinib therapy from medians of 1109 to 311  $\mu\text{g/g}$  ( $p=0.02$ ) and 13 to 2.8 mg/L ( $p=0.06$ ), respectively. Five (41.7%) patients discontinued upadacitinib within 16 weeks (median: 8, IQR: 6.5-14) and were maintained on a single biologic. Seven patients (58.3%) required extended use of upadacitinib for over 16 weeks, all of which had ongoing use at the last follow-up. Minor adverse events observed were acne (2 patients) and influenza infection (1 patient).

**Conclusion:** Upadacitinib prescribed with intent for short-term use in combination with biologic therapy appears to be well tolerated and effective in inducing steroid-free clinical remission in patients with active IBD. The addition of upadacitinib to a biologic may allow patients to avoid steroid use and offer a window for optimization of biologic therapy, but a substantial proportion of patients may not be able to de-escalate their therapy in the short term.

Poster #84

**Presenter:** Benjamin Moon, PhD

QI/High Value Care

**Authors:** Benjamin Moon, PhD; James Roberts, MD; Bonnie Bermas, MD; Kathryn Dao, MD; Puneet Bajaj, MD; Brooke Mills, MD

**Title:** Improving Documentation Rates of Contraception and Reproductive Healthcare in Rheumatic Disease Patients Through an Automated Pre-visit Questionnaire

**Abstract:**

**Background:** Systemic rheumatic diseases primarily affect women during their reproductive years, putting them at a higher risk for pregnancy complications. Additionally, some medications used to manage these conditions are teratogenic. With recent legislative changes, options for reproductive care may be limited, so discussions regarding pregnancy goals and effective contraception are paramount. This project aimed to increase the documentation of contraception and pregnancy planning within Rheumatology providers' notes from a baseline of less than 20% to above 50% in 6 months.

**Methods:** We included female patients aged 18-45 years old with rheumatic diseases seen in 4 different UT Southwestern Rheumatology clinics. Data was collected from 30 randomly selected charts per month via the Electronic Health Record (EHR). The primary outcome variable was documentation of contraception and pregnancy planning within providers' notes. We also recorded numerous secondary variables such as race, age, and type of contraception. After baseline data collection for 5 months, we implemented our intervention in June 2023. A Reproductive Health Assessment questionnaire was integrated into the EHR and sent to all the patients for completion through the patient portal one week prior to or during the clinical encounter. We then collected 6 months of post-intervention data from July 2023 to December 2023.

**Results:** We obtained data from a total of 148 pre-intervention and 176 post-intervention charts. There was a statistically significant ( $p < 0.0001$ ) increase in provider documentation of both contraception (44.6% to 70.5%) and pregnancy planning (15.5% to 60.2%) after implementation of the questionnaire. High-risk patients currently on teratogenic medications also had significantly ( $p < 0.0001$ ) better documentation of pregnancy planning after the intervention. Secondary analyses found that age, race/ethnicity, telehealth vs face to face, or provider gender had no significant impact on documentation rates.

**Conclusion:** By integrating an electronic, pre-visit questionnaire into the patient portal, we significantly improved documentation of contraception and pregnancy planning. This intervention was immediate, durable up to 6 months, and effective across patient subsets including those on teratogenic medications. Overall, our study shows that web-based surveys can improve provider documentation of reproductive healthcare. Further studies are needed to see if improved documentation will facilitate more discussions between patients and healthcare providers and improve reproductive health outcomes.

Poster #85

**Presenter:** Zach Blair, MD

Clinical Science

**Authors:** Zach W. Blair, MD; Greg Barton, PhD; Nataly Sanchez Solano, MD; J. Berry, MD; Alvin Chandra, MD; Kara N. Goss, MD

**Title:** The Long-term Impact of Birth Weight on Right Ventricular Structure and Function After Preterm Birth

**Abstract:**

**Rationale:** Adolescents and adults born premature have smaller cardiac chamber sizes, and while cardiac function is preserved in most, right ventricular (RV) dysfunction develops in some. Risk factors for RV dysfunction into adulthood remain unclear.

**Methods:** Preterm born participants (born moderately to extremely premature or very low birth weight, defined as <33 weeks or <1500 grams, respectively) aged 12-40 years were recruited from the Parkland Hospital Neonatal ICU registry (Dallas County, Texas). Healthy term-born similarly aged participants were recruited from the surrounding area. Study visits included anthropometric measurements, a cardiopulmonary exam, and echocardiography. Least squares logistic regression was used to determine the main effect of birth weight for right ventricular structure and function after adjusting for age, sex, and BMI using GraphPad Prism 10 software. If the main effect of birth weight was significant, preterm participants were stratified by birth weight (<1000g, 1001-1500g, >1500g, and term) and differences were determined using a one-way ANOVA.

**Results:** Preterm participants (n=106; 33% male) had an average gestational age of 29.3 weeks and birth weight of 1321 grams (2 lbs 15 oz). Average age of assessment was of 26 years old. Compared to preterm participants, term participants (n=46; 41% male) were slightly older, taller, and with lower body mass index (BMI; see table). Echocardiography demonstrated smaller right atrial (RA) volume and right ventricular (RV) diameters indexed to body surface area (BSA). Tricuspid annular plane excursion (TAPSE) and pulmonary artery acceleration time (PAAT) were similar between term and preterm participants. However, RV  $s'$  was lower in preterm participants with a clear dose response based on birth weight (Term:  $12.33 \pm 1.4$  cm/s; Preterm, weight >1500g:  $12.18 \pm 1.5$ ; Preterm, weight 1,001-1500 g:  $11.31 \pm 1.7$ ; Preterm, weight <1000 g:  $10.68 \pm 1.2$ ;  $p=0.0001$ ). The association between lower birth weight and RV function was stronger than the association between gestational age and RV function. RV systolic pressure estimates were not completed in the majority of participants due to poor tricuspid regurgitant jet velocity envelope.

**Conclusions:** RV  $s'$  was reduced in adolescents and adults born preterm, with a clear association between RV  $s'$  and birth weight. Although TAPSE was normal, RV  $s'$  is thought to be a more sensitive echocardiography-based measure of early RV dysfunction. Given that PAAT was similar between groups, this finding gives further support to the hypothesis that preterm birth and particularly low birth weight results in an independent insult to the developing RV with lifetime implications.

Poster #86

**Presenter:** Peter Carlsgaard, MD

Basic Science

**Authors:** Peter B. Carlsgaard, MD; Benjamin R. Kroger, BS; Toby Thomas, BS; Stephen S. Chung, MD

**Title:** Assessing the Role of Venetoclax in Promoting Clonal Hematopoiesis

**Abstract:**

**Background:** The BCL-2 inhibitor venetoclax has been increasingly used to induce cancer remission in myeloid malignancies such as acute myeloid leukemia (AML) and the myelodysplastic syndromes (MDS), as well as in lymphoid malignancies such as chronic lymphocytic leukemia (CLL). Recently, clonal expansion of mutations related to age-related clonal hemopoiesis (CH) was observed in the myeloid cell compartment of CLL and AML patients, despite no known association of venetoclax therapy to clonal hematopoiesis. We aim to explain the cause of this unexpected result.

**Methods:** We screened a tissue bank of bone marrow samples obtained at our institution from patients with AML before and after treatment with venetoclax. We performed targeted DNA sequencing to complement available clinical sequencing. Single cell DNA sequencing was performed in two patients over multiple time points.

To simulate clonal hematopoiesis, chimeric mice were created via competitive transplant of 20 FACS-sorted hematopoietic stem cells (HSC) from DNMT3A or TET2 conditional knock-out mutant donor bone marrow along with 200k cells from wild-type rescue whole bone marrow into mice conditioned with lethal-dose radiation. After 28 days, baseline donor chimerism was tested, and the mice were treated with either venetoclax, venetoclax and intraperitoneal azacitidine, or vehicle by oral gavage for 21 days. Donor chimerism in the peripheral blood and bone marrow was monitored at two-week intervals to assess the effect of treatment on the expansion of mutant donor clones.

**Results:** Twenty patients had post-remission bone marrow available for analysis after induction with at least one round of treatment with venetoclax. Ten (50%) had evidence of clonal hematopoiesis mutations which increased in variant allele frequency (VAF) or became detectable only after venetoclax treatment. Single cell analysis confirmed the emergence and persistence of these distinct non-malignant clones throughout treatment.

**Conclusions:** Together, our studies of primary patient samples reveal a pattern of venetoclax-related clonal hematopoiesis. Analysis is ongoing of the mouse model described. Further experiments will aim to establish a mechanism by which these mutant clones gain an advantage in the setting of this molecule, to reveal the means to exploit this mechanism for antineoplastic therapy, and to understand the aging hematopoietic system.



Poster #87

**Presenter:** Ali Noorbaksh, MD

Clinical Science

**Authors:** Ali Noorbaksh, MD; Aditi Shankar, MD; James MacNamara, MD; Christopher Hearon Jr, PhD; Benjamin D. Levine, MD; Satyam Sarma, MD

**Title:** Effects of Yearlong High Intensity Aerobic Exercise on Reducing Left Atrial Epicardial Adipose Tissue

**Abstract:**

**Background:** Left atrial epicardial adipose tissue (LA EAT) is often elevated in patients with heart failure and has been linked to abnormal atrial function and increased risk for atrial fibrillation. Whether LA EAT is potentially modifiable is unknown. We tested the hypothesis that one year of high intensity interval training (HIIT) would reduce LA EAT area and in turn be associated with improved atrial function in an obese cohort at risk for developing heart failure with preserved ejection fraction (HFpEF).

**Methods:** Middle-aged obese adults (n = 80, age 40-55 yrs) enriched for increased HFpEF risk (N-terminal pro-B-type natriuretic peptide >40 pg/mL or high-sensitivity cardiac troponin T >0.6 pg/mL; visceral fat >2kg) were randomized to one year of HIIT or attention control. Outcome variables included LA EAT area and LA strain. LA EAT area was quantified through tracings of anterior, posterior, and lateral EAT depots in long axis views on cardiac MRI. LA strain was measured with MRI feature tracking as reservoir strain during left ventricular (LV) systole, conduit strain during early LV diastole, and contractile strain during late LV diastole.

**Results:** Fifty-three participants completed the study. There was no difference in LA EAT area after one year in either the HIIT group (n = 26) or controls (n = 27); difference in mean = -0.17 cm<sup>2</sup>, 95% CI = -0.93 to 0.59, p = 0.66. However, amongst all participants, reduction in LA EAT was associated with improvement in LA reservoir strain (r = -0.50, 95% CI = -0.68 to -0.26, p < 0.001) and LA conduit strain (r = 0.51, 95% CI = 0.27 to 0.68, p < 0.001) but not LA contractile strain (r = 0.15, 95% CI = -0.13 to 0.40, p = 0.298).

**Conclusions:** One year of HIIT did not reduce LA EAT in at-risk obese patients. However, regardless of assignment, decreased LA EAT was associated with improved LA reservoir and conduit strain, suggesting efforts to reduce LA EAT may improve LA function in at-risk obese patients.

Poster #88

**Presenter:** Ali Noorbaksh, MD

Clinical Science

**Authors:** Ali Noorbaksh, MD; Shiva Reddy, MD; Aditi Shankar, MD; James MacNamara, MD; Christopher Hearon Jr, PhD; Benjamin D. Levine, MD; Satyam Sarma, MD

**Title:** Characterizing Regional and Global Effects of Epicardial Adipose Tissue on Left Atrial Function

**Abstract:**

**Background:** Obesity is associated with left atrial (LA) dysfunction. Excess epicardial adipose tissue (EAT) deposition is one potential mechanism for this dysfunction. However, it is unknown if the effects of EAT on LA function are mediated via adjacency to LA tissue or rather, represent effects of generalized cardiometabolic dysfunction, also common in obesity. We hypothesized EAT located around the LA would be associated with LA function compared to EAT located distally on the left ventricle (LV).

**Methods:** Cardiac MRI was performed in 54 middle-aged obese adults (n = 54, age 40-55 yrs) enriched for increased heart failure risk (N-terminal pro-B-type natriuretic peptide >40 pg/mL or high-sensitivity cardiac troponin T >0.6 pg/mL; visceral fat >2kg). EAT was quantified by tracing the area of LV EAT depots on short axis and LA EAT depots on long axis. LA strain was assessed by MRI feature tracking as reservoir strain during LV systole, conduit strain during early LV diastole, and contractile strain during late LV diastole. Linear regression was performed between EAT area and LA strain components. LA function was quantified by LA reservoir, conduit, and contractile strain.

**Results:** LA EAT was associated with decreased LA reservoir strain ( $r = -0.28$ , 95% CI = -0.51 to -0.01,  $p = 0.041$ ) and LA conduit strain ( $r = 0.39$ , 95% CI = 0.14 to 0.60,  $p = 0.004$ ). There was no association with contractile strain. There were no relationships between LV EAT and LA function.

**Conclusion:** Increased LA EAT was associated with worse LA strain. In contrast, LV EAT had no demonstrable effect on LA strain. Our results suggest LA EAT may have direct mechanical or paracrine effects on atrial tissue function and may be a therapeutic target for improving LA function in obese patients.

Poster #89

**Presenter:** Courtney Bess, MD

Clinical Science

**Authors:** Courtney Bess, MD; Puja Mehta, MD; Gina Lundberg, MD

**Title:** Lipid Profile Differences Among Premenopausal And Postmenopausal African American Women And Implications For Treatment Per Guideline

**Abstract:**

**Background:** Postmenopausal women have an increased cardiovascular disease (CVD) risk compared to premenopausal women. Though literature demonstrates a relationship between abnormal CVD risk factor patterns, namely lipids, and menopause, less is known about this association in minority racial and ethnic groups. Examining this association in African Americans (AA) is important because they experience disproportionate CVD outcomes. Moreover, recent studies have shown that AA eligible for statin therapy were less likely to receive treatment.

**Methods:** A cohort of 962 women (mean age  $50 \pm 14$  years) from the 10,000 Women Project were categorized into self-declared premenopausal ( $n = 475$ , mean age  $40 \pm 9.8$  years) and postmenopausal ( $n = 487$ , mean age  $61 \pm 9.1$  years) groups. Data was obtained at community health screening events through self-declared health history surveys. Lipid profiles were obtained through a non-fasting point-of-care cholesterol test. Several CVD risk factors were compared among these groups that include serum total cholesterol (TC), low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), triglycerides (TG), pooled cohort Atherosclerotic Cardiovascular Disease (ASCVD) 10-year risk of heart disease or stroke score, BMI, waist circumference, and blood pressure. Student's T test was utilized for statistical analysis.

**Results:** Cholesterol testing revealed a significant increase in serum TC ( $p < 0.0001$ ), LDL ( $p = 0.0001$ ), and TG ( $p = 0.001$ ) in the postmenopausal group compared to the premenopausal group. Interestingly, there was also a significant increase in serum HDL in the postmenopausal group ( $p = 0.0081$ ). Additionally, the ASCVD risk score, which is heavily weighted on age, was significantly higher in the postmenopausal group compared to the premenopausal group ( $p < 0.0001$ ).

**Conclusion:** Menopause is associated with a more abnormal lipid profile and an elevated ASCVD risk score in AA women which places this group at a higher risk of CVD. Prioritizing lipid management, by adhering to cholesterol treatment guidelines, may assist with CVD risk reduction in this high-risk group.

Poster #90

**Presenter:** Diana De Oliveira Gomes, MD

Clinical Science

**Authors:** Diana De Oliveira Gomes, MD; Tiffany L. Brazile, MD; James P. MacNamara, MD; Sauyeh K. Zamani; Christopher M. Hearon Jr, PhD; Denis J. Wakeham, PhD; Michael D. Nelson, MD; Benjamin D. Levine, MD; Satyam Sarma, MD

**Title:** Effects of Epicardial Adipose Tissue on Cardiac Function and Exercise Hemodynamics in Patients with Heart Failure with Preserved Ejection Fraction.

**Abstract:**

**Background:** Obesity is a significant risk factor for developing Heart Failure with Preserved Ejection Fraction (HFpEF). Epicardial adipose tissue (EAT), an ectopic fat depot located between the epicardium and the pericardium, has emerged as a potential risk factor for various cardiovascular diseases, including HFpEF. Previous studies have linked increased EAT thickness, measured by echocardiography, to adverse cardiac filling pressures at rest and during exercise, and systolic and diastolic dysfunction. Compared to echo, MRI has improved our ability to assess EAT. This study aimed to investigate the potential association between EAT quantified with MRI and cardiac function and exercise hemodynamics in patients with HFpEF during upright exercise.

**Methods:** We studied 32 patients with HFpEF (19 women; BMI,  $37\pm 6$ kg/m<sup>2</sup>; age,  $69\pm 6$ years). Total and visceral fat were assessed with dual-energy x-ray absorptiometry. MRI was used to quantify EAT volume across short axis slices and global longitudinal strain (GLS). Exercise was performed on a cycle ergometer (seated upright) and filling pressures (right heart catheterization), oxygen uptake ( $\dot{V}O_2$ ), cardiac output ( $\dot{Q}_c$ , direct Fick), and diastolic function (echocardiography) were assessed at rest, 20 Watts, and peak exercise ( $87\pm 35$  Watts).

**Results:** EAT was moderately correlated with visceral adiposity ( $r=0.57$ ,  $P<0.001$ ) but not with total body fat. EAT was not associated with markers of diastolic function (early tissue Doppler relaxation velocity [ $e'$ ], mitral inflow velocity ratio [ $E/A$ ], early mitral inflow/ $e'$  ratio [ $E/e'$ ]) or cardiac filling pressures (right atrial pressure, and pulmonary capillary wedge pressure) or mean pulmonary artery pressure, at rest or during exercise. In addition, there was no association between GLS and total EAT ( $r=-0.06$ ,  $P=0.735$ ) or EAT located over the left ventricle ( $r=-0.05$ ,  $P=0.749$ ). Similarly, there was no association between right ventricle (RV) EAT and RV strain ( $r=-0.06$ ,  $P=0.764$ ).

**Conclusions:** In patients with HFpEF, total EAT volume quantified with MRI did not correlate with measures of cardiac function at rest or during exercise. Specifically, there were no global or regional effects of EAT on GLS, diastolic function or exercise pressures. While EAT is a risk factor for developing HFpEF, our results suggest ventricular EAT does not further impact cardiac function in patients with obesity and HFpEF.

Poster #91

**Presenter:** Emily Decicco, MD

Clinical Science

**Authors:** Emily Decicco, MD; Caroline Abe, MD, MPH; Stephen Eason, MBA\*; Frances Compton, MD\*; Merlyn Sayers MBBCH, PhD\*; Amit Khera, MD; Zahid Ahmad, MD\*; Carter BloodCare North Texas

**Title:** Blood Donation as a Novel Means for Screening and Identification of Hypertriglyceridemia

**Abstract:**

**Background:** Hypertriglyceridemia is a risk for cardiovascular disease and hypertriglyceridemic pancreatitis, however is underrecognized in those without healthcare access. Community-based screening at blood donation centers offers a novel opportunity to screen large populations.

**Methods:** We prospectively measured non-fasting triglyceride levels among volunteer blood donors at Carter BloodCare North Texas over 3 weeks (December 2023-January 2024). Adults aged 18-75 had a triglyceride test added to routine blood testing. Donors with severe hypertriglyceridemia (triglycerides  $\geq$ 500 mg/dL) were notified and sent a follow-up RedCap survey.

**Results:** Triglyceride levels were measured in 10,175 unique blood donors [35.2% female, age 53 years (42-62), BMI 29.4 (26-33), 71.6% White]. Overall, 58.4% had normal triglycerides [triglyceride 111 mg/dL (84-140)], 39.2% had moderate hypertriglyceridemia [triglyceride 243 mg/dL (204-309)], and 2.4% severe hypertriglyceridemia [triglyceride 582 (539-705)]. Of note, 7 donors had triglycerides > 1000 mg/dL (min 1051- max 2342).

Of the 246 individuals notified, 17 (7%) completed a RedCap survey. Respondents age was 62 years (33-67), male (n=14, 82.5%), Caucasian (n=13, 76.5%), and BMI 32.9 kg/m<sup>2</sup> (22.5-48.7 kg/m<sup>2</sup>). Compared to those with severe hypertriglyceridemia in the general population, respondents on average were older (average age 63 years vs. 52 years), reported similar gender, ethnicity, and BMI (male 83%; Caucasian 67.5%, 30.9 kg/m<sup>2</sup>). 18.8% of respondents reported no known prior diagnosis of high triglycerides. 88.2% indicated intent to seek follow-up. 76.5% had not seen a medical professional since their blood donation. 11.8% reported no source of medical care. 64.7% had never taken a medicine to lower triglycerides. Reported risk factors included diabetes (11.8%), thyroid disease (17.6%), autoimmune disorder (5.9%), testosterone use (17.6%), high fat diet (52.9%), and alcohol consumption (64.7%).

**Conclusions:** Our pilot study demonstrates the feasibility of non-fasting community-based screening for hypertriglyceridemia among volunteer blood donors. The majority of respondents indicated intent to seek medical care given new knowledge of their high triglycerides, demonstrating the opportunity for blood donation to identify risk outside of traditional health care settings. Nearly 12% had no source of medical care and thus indicates the need for interventions to link donors to routine care.

Poster #92

**Presenter:** Fieke Hoff, MD, PhD

Clinical Science

**Authors:** Fieke W. Hoff, MD, PhD; Ying Huang, MD; Robert H. Collins, MD; Prapti A. Patel, MD; BEAT AML Consortium; Amy Burd, MD; Ashley O. Yocum, MD; Uma M. Borate, MD; Alice S. Mims, MD; John C. Byrd, MD; Yazan F. Madanat, MD

**Title:** Proposed Refinement of the 2022 ELN Risk Stratification in Older Adults with Newly Diagnosed Acute Myeloid Leukemia Treated with Lower-Intensity Treatment

**Abstract:**

**Background:** Acute myeloid leukemia (AML) is a heterogeneous disease that predominantly occurs in older adults. The 2022 European LeukemiaNet (ELN) recommendations incorporate the most updated AML risk-classification. While it has been proven to be predictive in patients treated with intensive-chemotherapy (IC) and/or patients <60yrs, it is unclear whether it applies to adults ≥60yrs treated with lower-intensity (LI) regimens. We aimed to test the 2022 ELN risk stratification in patients ≥60yrs with newly diagnosed (ND) AML.

**Methods:** Patients ≥60yrs with ND AML that were enrolled in the Beat AML clinical trial (NCT03013998) before May 2023 were included. Cytogenetic analysis, FLT3-ITD-ratio assessment and next-generation sequencing were obtained. Overall survival (OS) was estimated using the Kaplan-Meier method. Cox proportional hazard models were used to describe the relative-risk on death over time.

**Results:** A total of 1028 patients were included in the final analysis. ELN-risk was available for 940 patients: favorable-risk (14.9%), intermediate-risk (11.6%) and adverse-risk (73.5%). Patients were treated with LI-therapy (N=584), IC (N=132), supportive care (N=58) or unknown (N=166). 2022 ELN classification was prognostic for OS in patients who received LI-treatment or IC (N=716) (P<0.001) but did not stratify favorable-risk from intermediate-risk (P=0.22).

Next, we evaluated the impact of molecular abnormalities in adverse-risk AML patients treated with LI-treatment (N=460). Multivariable analysis was performed on a training set (N=303) and identified IDH2 mutation as an independent favorable prognostic factor, and KRAS, MLL2 and TP53 mutations as independent unfavorable factors (P<0.05). A “mutation-score” was calculated for each combination of mutations assigning patients into two risk-groups: -1 to 0 points (“intermediate”) vs 1+ points (“adverse”). A validation cohort analysis was performed (N=157) resulting in a prognostic separation (P=0.004). Finally, ELN 2022 “favorable-risk” and “intermediate-risk” were combined as a “favorable-risk”, resulting in a refined risk-model (18-month-OS: 57% vs 40% vs 19%, respectively; P<0.001).

**Conclusions:** The 2022 ELN risk-classification is prognostic in older patients with ND AML but does not distinguish favorable from intermediate-risk and classifies most patients as adverse-risk. We proposed a refined 2022 ELN-classification for older patients with adverse 2022 ELN-risk treated with LI-therapy using a “mutation-score” incorporating IDH2, MLL2, KRAS and TP53 mutations.

Poster #93

**Presenter:** Haitao Xu, MD

Clinical Science

**Authors:** Haitao Xu, MD; Courtney Roberts, BS; Alana Christie, MS; Jeffrey Miyata, BS; Payal Kapur, MD; James Brugarolas, MD, PhD

**Title:** Common Genetic Biomarkers and Their Clinical Implications for Metastatic Renal Cell Carcinoma to the Pancreas and Other Sites: A Multicenter Retrospective Study

**Abstract:**

**Background:** Metastatic renal cell carcinoma (mRCC) patients with pancreatic metastases (PM) have improved survival. However, the biological determinants of improved clinical outcomes have not been completely elucidated. In a two-institution study, we previously reported for the first time that tumor genomics may influence tissue tropism of metastases. Here, we expand our analyses to what is possibly the largest cohort of mRCC with PM. We performed tissue analyses to dissect putative biomarkers.

**Methods:** We analyzed 193 tumor samples histologically and by immunohistochemistry along with associated clinical data from 113 patients with PM evaluated at 7 academic centers across Europe and the US. Samples were stained for PBRM1, BAP1, and histone H3 lysine 36 trimethylation (H3K36me3), as surrogates for the functions of the tumor suppressor genes PBRM1, BAP1, and SEDT2, respectively, which represent the 3 most commonly differentiating genetic events in mRCC observed in 50%, 15% and 15% of tumors. Tumor were also categorized as “aggressive,” “intermediate/mixed,” or “indolent” based on their architecture. Samples from PM cohort were compared to an external cohort of patients without PM (non-PM). Kaplan-Meier estimate were used for survival analysis and Fisher exact test for categorical variables.

**Results:** Compared to non-PM, the PM cohort had a higher rate of PBRM1 loss (77% vs 62%,  $p=0.02$ ), lower rate of BAP1 loss (2% vs 25%,  $p<0.0001$ ), and higher frequency of “indolent” architectures (60% vs 33%,  $p=0.002$ ). Interestingly, the PM cohort could be subdivided according to PBRM1 status (PBRM1- vs PBRM1+). Among pts with PM, PBRM1- patients had a longer overall survival (OS) than patients with PBRM1+ status (median 116 mo vs 53 mo;  $p=0.004$ ). Furthermore, PBRM1 loss was associated with improved response to VEGF inhibitors (median NR vs 25mo;  $p=0.0003$ ) but not immune checkpoint inhibitors (median 63mo vs. 53mo;  $P=0.9$ ), which are the two mainstays of mRCC therapy.

**Conclusions:** These results show that tissue tropism of metastasis may be genetically determined and may have not only prognostic, but also therapeutic implications. To our knowledge, this is one of the first such examples in RCC.

Poster #94

**Presenter:** Jimin Hwang, MD, MPH

Clinical Science

**Authors:** Jimin Hwang, MD, MPH; Anand Gupta, MBBS, MPH; Eric D. Peterson, MD, MPH; Evelyn Sarnes, PharmD, MPH; Kristin Gillard, PharmD, PhD; Ann Marie Navar, MD, PhD

**Title:** Impact of Utilization Management on Initial Adoption of Bempedoic Acid Therapy

**Abstract:**

**Background:** During the first years after approval, patient uptake of PCSK9 inhibitors was limited by prior authorization (PA) practices and patient abandonment of prescriptions due to high out-of-pocket costs. Bempedoic acid (BPA) is a novel non-statin lipid lowering agent approved February 2020, however initial uptake has been low to date.

**Methods:** We performed a retrospective claims database analysis on pharmacy transaction data that covers >80% of US prescriptions and includes a full life cycle of pharmacy claims, from submission to final dispense. For all patients prescribed BPA for the first time through 12/31/2022 excluding refills, we evaluated approvals (i.e., whether prescriptions were approved or rejected). Multivariable logistic regression was performed to assess factors associated with approval. Among patients with approved prescriptions, fill rates were evaluated by patient out-of-pocket cost. For patients rejected BPA, follow-up changes in lipid-lowering therapy were described.

**Results:** Overall, 116,176 patients were prescribed BPA with median age 67, and 56.6% women. Ultimately, n=80,056 (68.9%) received approval, while n=36,120 (31.1%) faced rejection. Among those with approved prescriptions, 17.6% (n=14,087) abandoned their medications at the pharmacy despite approval, representing 12.1% of all prescriptions. Factors associated with increased likelihood of approval included: commercial insurance (OR 1.58, 95% CI 1.52–1.64), cardiologist as prescriber (OR 1.39, 95% CI 1.34–1.44 vs. primary care physicians), and higher prescriber volume (OR 1.44, 95% CI 1.38–1.51 for 4th [highest] quartile vs. 1st [lowest] quartile prescribers). Fill rates declined with increasing OOP costs, which were substantially higher in those with government insurance. For those failed to initiate BPA, only one-thirds underwent an escalation of lipid-lowering therapy after one year.

**Conclusions:** Similar to PCSK9i, high rates of payer rejections and patient abandonment have limited patient access to BPA. Prescription abandonment was a substantial barrier to obtain BPA for a subset of patients, driven by OOP cost more so in those with government insurance. Cardiology providers and prescriber prescription volume were associated with improved approval rates, suggesting interventions to improve provider familiarity navigating the PA process may help with prescription success.



Poster #95

**Presenter:** John Deng, MD

Clinical Science

**Authors:** John Deng, MD; Beverly Kyalwazi, MD; Jonathan Melendez-Torres, MD; Donglu Xie, MS; Amit G. Singal, MD, MS; Jeremy Louissaint, MD

**Title:** Patient Portal Use in Cirrhosis is Associated with Patient Age and Hepatic Decompensation

**Abstract:**

**Background:** Patient engagement in the patient portal has increased since the COVID-19 pandemic. While studies have highlighted key baseline characteristics associated with patient portal use, much of the literature is from the pre-pandemic period and lacks the inclusion of a diverse study cohort. In this study, we examined characteristics associated with patient portal use in a demographically and socioeconomically diverse cohort of patients with cirrhosis.

**Methods:** We identified patients with cirrhosis with at least one hepatology appointment between 1/1/2021 and 8/1/2023 who were enrolled in the patient portal excluding those with history of liver transplantation. We collected demographic (age, sex, race, ethnicity), clinical (hepatic decompensation), and census tract-level characteristics (poverty, internet access, and smartphone or computer access). We performed a multivariable logistic regression model to determine covariates associated with portal use. Patient portal use was defined as having at least one portal login during the 90 days preceding or 14 days after the patient's most recent hepatology appointment date.

**Results:** The cohort (N=529) had a median age of 63 years (IQR 53-70), and 45.6% were female. Patients were racially diverse (64.8% Non-Hispanic White (NHW), 21.7% Hispanic, 4.5% Black). Decompensated cirrhosis was present in 61% of patients. Median census tract lack of internet access was 8.5% (IQR 3.1-17.2), lack of smartphone or computer access 4.2% (IQR 1.5-10.2), and poverty level was 8.6% (IQR 4.0-15.8). Portal login during the 90 days prior or 14 days after most recent hepatology appointment was observed in 399 (75.4%) patients. In multivariable analysis, patients in the highest age quartile (age >70 years) had a 53% decreased odds (OR 0.47, p=0.014) of portal use versus those in the lowest quartile (age < 53 years), and a history of hepatic decompensation was associated with higher odds of portal use (OR 1.54, p=0.046).

**Conclusion:** We found that more than one-fourth of patient portal enrollees did not have a portal login around the time of their hepatology appointment. Portal use was directly associated with hepatic decompensation and inversely associated with older age. Studies are needed to evaluate how best to leverage and optimize portal use to improve patient outcomes.

Poster #96

**Presenter:** Luis Chinaea, MD

Clinical Science

**Authors:** Luis Chinaea, MD; Hannah Chang, MD; Isaac Chan MD, PhD,

**Title:** Identifying Mutations in ctDNA to Predict of Antibody-Drug Conjugates Response in Breast Cancer

**Abstract:**

**Background:** Metastatic breast cancer (mBC) is a complex disease, and outcomes remain poor because new therapies are needed. Antibody-drug conjugate (ADC) has shown effectiveness across all breast cancer subtypes. The advent of circulating tumor DNA (ctDNA) offers a unique noninvasive method to capture breast cancer (BC) heterogeneity. The clinical implications to predict response to ADC therapy in BC remains unclear. Here we test the hypothesis that ctDNA can detect mutations that predict response to ADCs.

**Methods:** We analyzed patients with mBC who underwent ctDNA testing using the Tempus xF liquid biopsy sequencing panel. The data was analyzed from a single academic medical center between 2019 to 2023. We identified detectable mutations from patients and addressed a relationship by using Metascape. Relevant signaling pathways were identified: APOBEC, ErbB signaling, p53 and Ras-MAPK pathway. Patients with triple negative, HER2, and HR+ BC were examined for ADC response and associated mutations. Survival analyses were estimated using Kaplan-Meier and Gehan Breslow Wilcoxon test for statistical analysis.

**Results:** We identified 43 patients with HR+ mBC with >1 mutation within the Ras-MAPK pathway and 10 of 43 received ADC therapy. Median overall survival (mOS) of patients who received ADC therapy 58 months (n = 10) vs not receiving ADC therapy 33 months (n = 33) (p < 0.05). Of the ten patients who received ADC treatment, 60% had 1+ HER2 staining on tissue biopsy. Patients with >1 mutation within APOBEC, ErbB signaling, and p53 pathways did not have statistically significant differences in mOS.

**Conclusions:** In HR+ mBC, detection of mutated genes associated with the Ras-MAPK pathway by ctDNA was associated with a more favorable response when treated with ADCs. These findings are exciting because HR+ BCs are being targeted with ADCs regardless of HER2 or TROP2 expression, highlighting the need for new biomarkers to distinguish which HR+ patients to treat. Our retrospective analysis findings are limited by the number of patients with ctDNA testing and timing of testing. Further studies are needed to solidify the observed correlation between Ras-MAPK pathway mutations and favorable response to ADC treatment.

Poster #97

**Presenter:** Mausam Patel, MD

Clinical Science

**Authors:** Mausam J. Patel, MD; Bill Y. Zhang, BS; Thomas G. Cotter, MD; Ahmad Anouti, MD

**Title:** The Effects of Underlying Inflammatory Bowel Disease on the Outcomes of Primary Sclerosing Cholangitis Liver Transplant Recipients

**Abstract:**

**Background:** PSC commonly occurs in patients with IBD, and LT is often required as definitive treatment. The presence of concomitant IBD influences PSC severity, however, the impact of IBD on PSC LT outcomes is poorly understood. We aimed to elucidate the impact of IBD in modulating PSC LT outcomes.

**Methods:** Using UNOS data from 2010 through 2021, we identified PSC LT candidates with and without ( $\pm$ ) IBD and explored LT outcomes among waitlist additions, outcomes, and graft survival rates. We used adjusted competing-risk regression analysis to evaluate waitlist outcomes, Kaplan-Meier analysis to assess graft survival, and Cox proportional hazards modeling to identify factors associated with graft survival.

**Results:** 5,586 PSC candidates were added to the waitlist, 3,652 of whom had IBD. Older age (SHR 1.01; 95%CI 1.01-1.02) and initial MELD/PELD (SHR 1.03; 95%CI 1.02-1.04) were associated with increased risk of waitlist mortality, while private insurance (SHR 0.002; 95%CI 0.0005-0.008) was associated with reduced risk of waitlist mortality. Of the PSC-IBD waitlist candidates, 2,456 underwent LT. Notably, PSC-IBD LT recipients had a significantly increased prevalence of cholangiocarcinoma (4.8% vs 3.4%,  $p=0.005$ ). Longer donor cold ischemia times (HR 1.06; 95%CI 1.03-1.09), presence of recipient diabetes (HR 1.52; 95%CI 1.13-2.05), and employment (HR 0.75, 95%CI 0.60-0.94) were associated with increased risk of graft failure among PSC patients with IBD, while there were no significant associations with graft failure among PSC patients without IBD.

**Conclusion:** Regardless of IBD, LT for PSC results in excellent outcomes in waitlist mortality and graft survival. The presence of certain donor and recipient clinicodemographic and biologic factors impacted waitlist and recipient mortality, highlighting potential targets to enhance outcomes.

Poster #98

**Presenter:** Mausam Patel, MD

Clinical Science

**Authors:** Mausam Patel, MD; Yue Jiang, PhD; Amit Singal, MD, MS; Sarah Lieber, MD, MSCR

**Title:** Psychiatric Disorders in Patients with Hepatocellular Carcinoma: A Large US Cohort of Commercially Insured Individuals

**Abstract:**

**Background:** Patients with hepatocellular cancer (HCC) are vulnerable to psychological distress given a new cancer diagnosis superimposed on pre-existing chronic liver disease. We aimed to characterize the burden of psychiatric disease in HCC, identify associated factors, and describe related treatment patterns.

**Methods:** We used the IQVIA PharMetrics® Plus for Academics database, a large claims database nationally representative of the commercially insured U.S. population, to identify psychiatric diagnoses and treatment patterns among patients with newly diagnosed HCC. Multivariable logistic regression modeling identified factors associated with psychiatric diagnoses and pharmacotherapy use.

**Results:** Of 11,609 patients with HCC, 2,166 (18.6%) had a psychiatric diagnosis recorded after HCC diagnosis, with the most common being depression (58.3%) and anxiety (53.0%). Women (aOR 1.33, 95% CI [1.19-1.49]), presence of encephalopathy (aOR 1.05, 95% CI [0.80-1.37]), pre-existing psychiatric diagnoses (aOR 9.12, 95% CI [8.08-10.3]), and type of HCC treatment (transplant: aOR 2.15, 95% CI [1.66-2.77]; resection: aOR 1.45, 95% CI [1.20, 1.75]; ablation: aOR 1.40, 95% CI [1.08-1.79]; radiation: aOR 1.74, 95% CI [1.52-1.99]; hospice: aOR 2.43, 95% CI [1.79-3.29]) were associated with psychiatric diagnoses. Among the 2,166 patients with psychiatric diagnosis after HCC, 1,573 (72.6%) had a psychiatric diagnosis pre-HCC diagnosis. Psychiatric medications were used by 2,130 patients with a psychiatric diagnosis prior to HCC diagnosis, of whom 1,222 (70.6%) continued the same pharmacologic therapy, 510 (29.4%) changed classes of medication, and 398 (18.7%) discontinued therapy. Of the 2,166 patients with a new psychiatric diagnosis after HCC diagnosis, pharmacotherapy was used in 1,392 (64.3%) patients, with antidepressants (46.2%) and anxiolytics (32.8%) most commonly used. Psychiatric diagnoses increased from 14.8% in 2006-2009 to 21.1% in 2018-2021 ( $p < 0.001$ ); concordantly, the use of pharmacologic therapy increased from 39.2% in 2006-2009 to 50.0% in 2018-2021.

**Conclusions:** Nearly 2 out of 10 HCC patients were diagnosed with a psychiatric illness after HCC diagnosis with 64% receiving pharmacologic therapy. These data highlight certain populations at risk for increased psychological burden and the need for early evaluation and treatment among patients with newly diagnosed HCC.

Poster #99

**Presenter:** Niharika Neela, MD

Clinical Science

**Authors:** Niharika Neela MD; Nicholas S. Hendren MD; Spencer Carter MD; Sandeep R. Das MD, MPH

**Title:** Prescription of Teratogenic Medications for Reproductive-age Women with Heart Failure with Reduced Ejection Fraction in a Safety-Net Health System

**Abstract:**

**Background:** Angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), angiotensin receptor blocker-nephrilysin inhibitors (ARNi), and mineralocorticoid receptor antagonists (MRA) have been proven to improve morbidity and mortality in patients with heart failure with reduced ejection fraction (HFrEF); however, they have known teratogenic effects. It is uncertain how often reproductive-age women are prescribed these medications and whether they are prescribed contraception.

**Methods:** We included all patients in our health system with documented left ventricular ejection fraction  $\leq 45\%$  within the past 2 years. Patients were excluded from the present study if they had a creatinine  $\geq 2.0$  mg/dl (women) or  $\geq 2.5$  mg/dl (men), as these are contraindications to MRA. Individuals were stratified into reproductive-age women (age  $\leq 45$ ), women age  $>45$ , and men (any age). Contraception prescription was queried via chart review for all reproductive-age women. Rates of ACEi/ARB/ARNi, and MRA, were then compared across 4 subgroups.

**Results:** Of 3,003 patients who met the inclusion criteria, 130 were women  $\leq 45$ y, 709 were women  $> 45$ y, and 2164 were men. Among the 81/130 (62%) reproductive-aged women not prescribed contraception, 78% had an active prescription for either an ACEi, ARB, or ARNi and 56% had an active MRA prescription (Figure). Comparing reproductive-age women not on contraception with all other groups, the ACEi/ARB/ARNi prescription rates were 78% vs 78% ( $p = 0.36$ ) and the MRA prescription rates were 56% vs 49% ( $p = 0.16$ ).

**Conclusion:** In a large safety net health system, most reproductive-aged women with HFrEF were not prescribed contraception, yet they were commonly prescribed teratogenic heart failure medications. This is an important safety concern that should be addressed at the health system level.

Poster #100

**Presenter:** Olgert Bardhi, MD

Clinical Science

**Authors:** Olgert Bardhi, MD; Yue Jiang, PhD; Alex R. Jones, MD; Prajwal Gowda, BS; William Tirone, MS; Madhukar Patel, MD; Parsia Vagefi, MD; Steven Hanish, MD, Van Ngo, PharmD; Mary Olumesi, PharmD; Raelene E. Trudeau, PharmD; Arjmand Mufti, MD; Amit G. Singal, MD, MS; Lisa B. VanWagner, MD, MSc; Sarah R. Lieber, MD, MSCR

**Title:** Opioid Use after Adult Liver Transplantation: Predictors of High-Risk Use and Opioid-Related Complications

**Abstract:**

**Background:** Opioid use contributes to high morbidity and mortality. Liver transplant recipients (LTRs) are high-risk given pre-existing substance use, psychiatric comorbidities, and post-operative pain. Limited data exist on opioid use surrounding LT at the national level, especially as compared to other solid organ transplant (SOT) recipients. We described opioid prescribing practices, factors associated with high-risk use, incident use, and opioid-related complications among LTRs.

**Methods:** Adult LTRs were identified from 2006-2021 using IQVIA PharMetrics® Plus for Academics, a claims database representative of the commercially insured US population. Opioid use was evaluated 30-120 days after LT; high risk use was defined as >50 morphine milligram equivalents per day or concurrent benzodiazepine use. Factors associated with high-risk and incident use were identified using multivariable logistic regression analysis. Landmark survival analysis was used to assess opioid-related complications post-LT: depression, anxiety, substance use disorder, chronic pain syndromes, altered mental status, or fractures/falls. To contextualize opioid use relative to other SOTs, we compared prescriptions between LTRs and kidney transplant recipients (KTRs).

**Results:** Among 1,001 LTRs, 321 (32.1%) received opioids 30-120 days post-LT; 43 (13.3%) had high-risk use, with 178 (18%) incident use. Factors associated with incident use: female sex, simultaneous liver kidney transplant, pre-LT substance use, and pre-LT psychiatric disorder. Factors associated with opioid use: female sex, pre-LT substance use, and pre-LT opioid use. High-risk opioid use was associated with female sex, U.S. southern region, pre-LT opioid use, and psychiatric diagnosis. Overall, 61.3% of opioid users had complications compared to 46.2% of non-users 1-year post-LT ( $p < 0.001$ ). Opioid use had increased complications, especially among high-risk users, with 1.85 higher risk of opioid-related complications at 90 days post-LT compared to no opioid use. LTRs exhibited higher opioid use 30-120 days post-transplant (32%) compared to KTRs (8%) ( $p < 0.001$ ), with a higher incidence of high-risk opioid use (4% vs. 1%) 30-120 days post-LT.

**Conclusion:** ~1 in 4 LTRs were prescribed opioids 30-120 days post-LT, despite being beyond the acute 1-month post-operative period. High-risk opioid use was associated with more complications. Prescription opioids, particularly high doses with benzodiazepines, should be cautioned in LTRs especially with pre-existing psychiatric or pain conditions.

Poster #101

**Presenter:** Olgert Bardhi, MD

Clinical Science

**Authors:** Olgert Bardhi, MD; Darine Daher, MD; Mausam Patel, MD; Karim Seif El-Dahan, MD; Nicole E. Rich, MD, MSCS; Neehar D. Parikh, MD; Anjana Pillai MD; Laura M. Kulik, MD; Ju Dong Yang, MD; Anand Kulkarni MD; Purva Gopal, MD; Amit G. Singal, MD, MS

**Title:** Age Disparities in Clinical Outcomes of patients with Hepatocellular Carcinoma: A Meta-Analysis and Systematic Review

**Abstract:**

**Background:** Older age is associated with decreased treatment eligibility and worse survival in several cancers, although there is no consensus on how age impacts outcomes in patients with hepatocellular carcinoma (HCC).

**Methods:** We performed a search of MEDLINE and EMBASE databases from January 2000 to July 2022 to identify studies reporting tumor stage, curative treatment receipt, and overall survival among patients with HCC, stratified by age (younger vs. older). We calculated pooled risk ratios (RR) and hazard ratios (HR) for curative treatment receipt and overall survival among younger and older patients using the DerSimonian and Laird method for random effects models.

**Results:** We identified 122 studies (n=240,209 patients) that reported treatment receipt in young vs. old patients with HCC, although age thresholds varied across studies. Overall, younger patients were more likely to receive curative treatment than older patients (RR 1.05, 95%CI 1.02 – 1.07). In subgroup analyses, patients younger than age 65 were more likely to undergo any curative treatment (RR 1.18, 95%CI 1.12 – 1.25) including surgical resection (RR 1.26, 95%CI 1.11 – 1.42). Patients younger than age 70 were more likely to undergo liver transplantation (RR 2.28; 95%CI 1.07 – 4.84). Younger patients had reduced mortality (HR 0.85; 95%CI 0.78 – 0.93) compared to older patients.

**Conclusion:** Older patients are less likely to undergo curative treatment and experience higher mortality. Studies need to identify reasons for this disparity, including differences in tumor burden, liver dysfunction, comorbidities, or patient preferences.

Poster #102

**Presenter:** Paige Della-Penna, MD

Clinical Science

**Authors:** Paige L. Della-Penna, MD; Aseel Dweik, MD; Chaitanya Malladi, MD; Kyle Geurink, MD; Sandeep Das, MD, MPH

**Title:** GLP1-RA Prescription Rates Following an MI Among Patients with T2DM Stratified by Concomitant Use of Injected Insulin

**Abstract:**

**Background:** GLP1 Receptor Agonists (GLP1-RA) reduce major adverse cardiovascular events in patients with T2D and known atherosclerotic cardiovascular disease, yet their utilization remains poor as demonstrated by national data. To test whether willingness to take injectable therapies is related to prescription of GLP-1RA, we examined prescription rates GLP1-RA stratified by insulin co-prescription at two large teaching hospitals in Dallas, TX, with prescription rates of the non-injectable evidence-based SGLT2 inhibitors (SGLT2i) as a control.

**Methods:** Using data from the hospital EHRs for all patients with T2D and GFR>30 ml/mi/1.73m<sup>2</sup> hospitalized with a type 1 MI between 2018-2021, we determined prescription rates for SGLT2i and GLP1-RA at one year.

**Results:** Of the 106 patients prescribed insulin, 19 (18%) were prescribed GLP1-RA and 45 (42%) were prescribed SGLT2i at one year. In contrast, among the 161 not prescribed insulin at time of MI, 13 (8%) were prescribed GLP1 and 90 (56%) were prescribed SGLT2i.

**Conclusion:** While patients on injectable therapies were statistically more likely to be prescribed GLP1-RA, overall prescriptions rates are poor and lower than SGLT2i prescription rates. This suggests that lack of prescription of GLP-1RA is unlikely to be explained by patient unwillingness to take injectable therapies.



Poster #103

**Presenter:** Rohit Nathani, MD

Clinical Science

**Authors:** Rohit Nathani, MD; Qiang Li, BS, MSc; Saket Girotra, MD

**Title:** Association Between In-hospital Cardiac Arrest Incidence and Survival

**Abstract:**

**Background:** Survival after an in-hospital cardiac arrest (IHCA) varies markedly across hospitals in the U.S. However, it remains unclear whether hospitals that achieve high IHCA survival also excel in “preventing” IHCA events in hospitalized patients.

**Methods:** Using 2013-2019 data from the Get-With-The-Guidelines – Resuscitation (GWTG-R) registry linked with Medicare files, we identified all patients aged 65 years or older who experienced IHCA at participating hospitals. Using hierarchical (two-level) multivariable regression models, we calculated hospital-level rates of IHCA incidence (adjusted for case-mix index) and survival to discharge (Risk Standardized Survival Rates (RSSR) adjusted for patient and cardiac arrest characteristics). We examined the correlation between hospital rates of IHCA incidence and survival. We then divided hospitals into quartiles based on incidence rates of the IHCA and compared hospital and patient characteristics among these quartiles. We used T-tests (for continuous variables) and Chi-Square test (for categorical variables) to compare these hospital and patient characteristics.

**Results:** Among a total of approximately 10 million admissions among Medicare beneficiaries at 335 hospitals during 2013-2019, 77676 patients experienced an IHCA. The overall incidence of IHCA was 7.8 per 1000 admissions. Among those who experienced an IHCA, the overall survival was 22.1%. Incidence and survival rates per 1000 patient discharges were 7.8 and 1.7 respectively. At the hospital level, the median incidence rate, adjusted for case-mix, was 7.54 per 1000 admissions (IQR 5.74-9.88), and the median risk-standardized survival was 22.1% (IQR 20.5%-23.7%), respectively. There was a weak negative correlation between hospital rates of case-mix adjusted incidence and risk-standardized survival ( $\rho = -0.11$ ;  $p$ -value 0.037).

**Conclusion:** Hospital rates of incidence of IHCA were weakly correlated with risk-standardized survival. Given that IHCA survival has plateaued in recent years, our findings highlight that future efforts need to focus on reducing incidence (prevention of IHCA) for additional gains in improving in-hospital resuscitation care.

Poster #104

**Presenter:** Stephanie Moreno, MD

Clinical Science

**Authors:** Stephanie Moreno, MD; Colby Ayers, MS; Nga Nguyen, MD; Emily S. Lau, MD; Anand Rohatgi MD, MSc

**Title:** Lipid Changes Across Menopause Status Point to Increased Cardiovascular Risk

**Abstract:**

**Background:** While women develop cardiovascular disease (CVD) approximately ten years later than men, risk of CVD in women rises precipitously following menopause. The mechanisms underlying this acceleration in CVD risk are not well elucidated, but adverse changes in lipid measures are known to occur during the perimenopause period. Previous investigations have been largely restricted to traditional lipid measures and have not examined changes in lipoprotein particles including lipid subfractions and particle number.

**Purpose:** We sought to examine longitudinal changes in lipoprotein particles that occur during the menopause transition.

**Methods:** A total of 1305 participants in the Dallas Heart Study with known menopause status underwent measurement of LDL-P, HDL-P, sd-LDL, and Id-HDL by NMR LipoProfile LP4 algorithm (LabCorp, Raleigh Durham, NC, U.S.A.) at 2 examinations (between 7-8 years between DHS studies). We compared longitudinal changes in lipoprotein measures between pre-, peri-, post-menopausal women and men using multivariable adjusted linear regression models. For our analysis peri- is the group that was pre-menopause at DHS 1 and post-menopause at DHS 2, not to mean the period before menopause.

**Results:** There 1346 men (referent group) included in the study with a mean age of  $43 \pm 9.4$  years. There was a total of 1246 women with a mean age of  $42 \pm 5.6$  for peri-group,  $54 \pm 6.2$  for post-group, and  $34 \pm 3.08$  for the pre-group. Of the women 440 (35.3%) were pre-menopausal, 298 (23.9%) were peri-menopausal, and 508 (40.8%) were post-menopausal. Over a median follow-up time of 7 years. All three groups had an increase in LDL-P but the greatest percent change is between peri and post, 18.30 (SE 3.05,  $P < 0.001$ ). When compared to men the post-group has the greatest percent change of HDL-P with a negative change of 4.77 (SE 0.948  $P < 0.0001$ ). Small-dense LDL had the highest percent change in the peri- group when compared to men with a change of 578.62 (SE 288.45,  $P < 0.045$ ). Large-dense HDL had greatest percent change in the post- group when compared to men with negative change of 37.84 (SE 12.83,  $P < 0.0032$ ).

**Conclusions:** We found that menopause is associated with adverse changes in lipoprotein profiles, with the most pronounced changes in LDL-particles and subfractions observed for peri-menopausal women. By contrast, post-menopausal women demonstrated the greatest reductions in HDL-particles and subfractions. Taken together, these changes suggest that menopause is associated with a transition to a more atherogenic lipoprotein profile. Further research is needed to investigate whether these adverse changes in lipoproteins translate to greater CV risk.

Poster #105

**Presenter:** Susan Zhang, MD

Clinical Science

**Authors:** Susan Zhang, MD; Fnu Sidra, MD; Carlos Alvarez, PharmD; Mustafa Kinaan, MD; Ildiko Lingvay, MD, MPH, MSCS; Ishak Mansi, MD

**Title:** Acute Healthcare Utilization, Mortality, and Cardiovascular Events Following GLP1-RA Initiation by Patients with Advanced Chronic Kidney Disease: A Real-World Comparative Study

**Abstract:**

**Introduction & Objective:** Treatment with glucagon-like peptide-1 receptor agonists (GLP1-RA) in patients with type 2 diabetes and chronic kidney disease (CKD) may attenuate the progression of renal disease and cardiovascular events but their real-world impact on healthcare utilization and mortality in this population are not well-defined. This study aims to compare outcomes following initiation of GLP1-RA vs Dipeptidyl peptidase-4 inhibitors (DPP4i), as active comparators, in patients with diabetes and advanced CKD.

**Methods:** Retrospective cohort study using data from Veterans Health Administration during fiscal years 2006 to 2021. Inclusion criteria included U.S. veterans aged 35 years or older with advanced CKD who filled either GLP1-RA or DPP4i prescriptions. The primary outcome was acute healthcare utilization. Secondary outcomes were all-cause mortality and acute cardiovascular events (not including death).

**Results:** The eligible cohort included 26,997 GLP1-RA users and 37,708 DPP4 users. After propensity score matching (16,076 pairs) and 2.2 years mean follow-up duration, use of GLP1-RA was associated with lower annual rate of acute healthcare utilization (coefficient of regression  $\beta = -0.15$ , 95% CI -0.25 to -0.05,  $p=0.004$ ) and lower all-cause mortality as compared to the DPP4i group (OR 0.84, 95% CI 0.79 to 0.89,  $p<0.01$ ) with time-to-death analysis showing a HR of 0.86 (95%CI: 0.82-0.90,  $p <0.001$ ). There was no significant difference in cardiovascular events between groups (OR 0.98, 95% CI 0.92 to 1.06,  $p=0.66$ ).

**Conclusions:** Use of GLP1-RA in patients with advanced CKD was associated with lower annual rate of acute healthcare utilization and decreased all-cause mortality. There was no significant difference in cardiovascular events between the matched groups.

Poster #106

**Presenter:** Syed Rizvi, MD

Clinical Science

**Authors:** Syed Rizvi, MD; Nidhish Lokesh, BS; J. Wyatt Miller, BS; Ambarish Pandey, MD, MSCS; Neil Keshvani, MD

**Title:** Adverse Social Determinants of Health in a Low-Income Population Hospitalized with Heart Failure

**Abstract:**

**Background:** Heart failure (HF) is a leading cause of hospitalization and readmission in the United States. The burden of adverse social determinants of health (SDOH) among hospitalized patients with heart failure at a safety-net hospital is poorly understood.

**Methods:** We conducted a prospective, cross-sectional study to identify the prevalence of adverse SDOH among patients hospitalized with HF at Parkland Memorial Hospital (PMH), a county safety-net hospital. English or Spanish-speaking patients hospitalized for HF were enrolled between 11/2022-6/2023. We collected data across 5 SDOH domains based on the Healthy People 2030 SDOH Model from the U.S. Department of Health and Human Services: Economic Stability, Education Access and Quality, Healthcare Access and Quality, Neighborhood and Built Environment, Social and Community Context. The overall burden of adverse SDOH parameters was assessed. Multivariable logistic regression models adjusted for age, sex, race/ethnicity, left ventricular ejection fraction, and comorbidity burden were used to assess the association with individual SDOH parameters with 90-day readmission and/or emergency room (ER) visits.

**Results:** 174 individuals were included (median age 55, 73.6% male, 17.2% Non-Hispanic White, 61.5% Black, 20.7% Hispanic). The burden of adverse SDOH parameters was high, with 60.3% of patients unemployed, 65% of patients earning under 130% of the federal poverty line, 53% having food insecurity, 48.8% having low social support, and 40.3% having housing instability. In multivariable analysis, increasing comorbidity burden (OR 4.84, 95% CI 2.04-12.5,  $p < 0.001$ ), being uninsured (OR 3.57, 95% CI 1.59-8.50,  $p = 0.002$ ), having low social support (OR 3.06, 95% CI 1.48-6.53,  $p = 0.003$ ), having dependents (OR 2.98, 95% CI 1.13-8.38,  $p = 0.03$ ), and having difficulty paying bills (OR 0.43, 95% CI 0.20-0.88,  $p = 0.02$ ) were associated with increased odds of 90-day readmission or ER visit.

**Conclusions:** Among hospitalized patients with HF at a safety-net hospital, we report a substantial burden of adverse SDOH, and after adjusting for demographic and clinical covariates, individual adverse SDOH parameters were independently associated with increased odds of 90-day readmission or ER visit.

Poster #107

**Presenter:** Tejus Satish

Clinical Science

**Authors:** Tejus Satish, MD; Nicholas S. Hendren; MD, Matthias Peltz, MD; Christopher Heid, MD; Maryjane Farr, MD, MSc; Anthony Bavry, MD; Saket Girotra, MD, SM; Dharam J. Kumbhani, MD, SM; Mark H. Drazner, MD, MSc; W.H. Wilson Tang, MD; Justin L. Grodin, MD, MPH

**Title:** Surgical Revascularization Provides Consistent Benefits Across Mixture-Model Derived Systolic Heart Failure Phenogroups with Different Long-Term Risk Profiles

**Abstract:**

**Background:** Coronary artery bypass grafting (CABG) provides mortality benefits in coronary artery disease (CAD) and heart failure with reduced ejection fraction (HFREF), but whether phenotypic heterogeneity in this population influences the long-term benefits of CABG is unknown. We posited that cluster analysis of the STICHES trial would identify novel phenogroups differing in CABG response and long-term risk.

**Methods:** Model-based clustering with a penalty function was applied to STICHES to derive phenogroups of demographic/clinical characteristics. Multivariable Cox models were used to test the association of group assignment with death, cardiovascular (CV) death, and a composite of death/CV hospitalization and whether group assignment modified the effect of CABG versus medical therapy on these outcomes.

**Results:** Four phenogroups were optimal in the derivation (n=753) and validation (n=459) cohorts. Phenogroups differed in demographic/clinical characteristics and long-term risks. Measures of diastolic function (E/A ratio, mitral valve E velocity) and kidney function (creatinine, blood urea nitrogen (BUN), history of chronic kidney disease) were highly discriminatory between phenogroups. Compared with the lowest-risk group, the highest-risk group was at a 2-fold greater risk of death (adjusted HR 2.0, 95% CI 1.4-2.9, P<0.001) and CV death (adjusted HR 2.0, 95% CI 1.3-3.1, P=0.002), and a 1.5-fold greater risk for death/CV hospitalization (adjusted HR 1.5, 95% CI 1.1-2.1, P=0.016). There was no significant interaction between phenogroup assignment and the effect of CABG (P-interaction>0.05 for all).

**Conclusions:** We identified HF phenogroups at different long-term risk of death, CV death, and death/CV hospitalization. Phenogrouping did not modify the effects of CABG, implying that surgical revascularization is associated with lower risks of all studied outcomes despite phenotypic heterogeneity in HFREF and CAD. Despite phenotypic heterogeneity in patient with HFREF and CAD, our evidence confirms CABG provides significant benefit to this group.

Poster #108

**Presenter:** Tyler Wall, MD

Clinical Science

**Authors:** Tyler Wall, MD; Nataly Solano, MD; Gregory Barton, PhD; Merrill Dane, MS; Connie Hsia, MD; Kara Goss, MD

**Title:** The Role of Race and the Childhood Opportunity Index in Predicting Lung Function Outcomes Among Adolescents and Adults Born Premature

**Abstract:**

**Background:** Extreme preterm birth is a recognized risk factor for reduced pulmonary function over an individual's lifetime. We aimed to evaluate pulmonary function in a multiethnic population of adolescents and adults born premature. Our secondary aim was to evaluate risk factors including race and socioeconomic factors contributing to lower pulmonary function.

**Methods:** Preterm participants aged 12-40 years of age were recruited from the Parkland Hospital Neonatal ICU Registry (Dallas County, Texas). Healthy term-born participants were recruited from the surrounding area. All participants completed pulmonary function testing and predicted values were calculated with Global lung initiative (GLI) race-neutral reference equations. To characterize early life socioeconomic factors potentially impacting lung function, birth addresses for preterm participants were used to quantify socioeconomic ratings for the quality of birth area resources and conditions using the Child Opportunity Index (COI, 2015). Statistical tests included Fisher's exact, Unpaired T-tests and multiple linear regression using GraphPad software.

**Results:** Participants included 105 preterm and 49 term individuals. Overall, spirometry and lung volumes were similar between preterm and term participants, while diffusion capacity was significantly lower ( $91 \pm 14.6$  vs  $100 \pm 14.1\%$ ,  $p < 0.001$ ). When preterm data were compared between the largest 2 racial groups, Hispanic White versus African American, all pulmonary functions were lower among those of African American race. COI scores were also lower across all domains in the African American preterm population. Next, multivariate models were constructed to explore neonatal, social and subsequent risk factors for lower function. The strongest multivariate models to predict FEV1 z-score included race, COI, smoking history and BMI ( $R^2=0.34$ ,  $p < 0.0001$ ). While race remained the primary predictor of FEV1 z-score ( $p < 0.0001$ ) in the preterm population, COI was significant with an additive impact ( $p=0.02$ ). When subcategories of the COI were considered independently, Health/Environment score and Social/Economic score were each significant predictors in the models, whereas education was not. Similar results were found for FVC and DLCO.

**Conclusions:** African American adolescents and young adults born preterm demonstrated significantly lower lung function. While COI plays a role in determining adult lung function, race remained the primary predictor within this cohort suggesting the potential for additional unmeasured factors contributing to overall lung function.

Poster #109

**Presenter:** Vinayak Subramanian

Clinical Science

**Authors:** Vinayak Subramanian, MD; Traci Betts, DPT; Lajjaben Patel, MBBS; Matthew Segar, MD; Ambarish Pandey, MD, MSCS

**Title:** Efficacy of an m-Health Cardiac Rehabilitation Program in Heart Failure with Preserved Ejection Fraction

**Abstract:**

**Background:** Supervised exercise training has been shown to improve physical function and quality of life (QOL) among older patients with HFpEF. However, the access, availability, and utilization of supervised cardiac rehabilitation among HFpEF patients is limited. Home-based cardiac rehabilitation (home-CR) using m-health platforms is emerging as an alternative approach to CR. However, whether home-CR is feasible and effective in improving functional and patient-reported outcomes among older patients with HFpEF is not known.

**Methods:** Older patients (Age>60 y) with chronic stable HFpEF with significant exercise intolerance (exercise capacity <80 percent of predicted for age- and sex) or physical dysfunction (Short Physical Performance Battery [SPPB] score <10) were randomized to receive home-CR using an m-health platform (Movn Health, CA, USA) vs. attention control (AC) for 6 months (clinicaltrials.gov: NCT05002075). The home-CR program was tailored to each participant's baseline physical function deficits. The primary outcomes of interest were changes in the QOL, measured using the KCCQ questionnaire, and physical function (SPPB score) from baseline to 6-month follow-up. Secondary outcomes of interest were changes in peak exercise capacity (VO<sub>2</sub>peak) assessed using the maximal bicycle ergometer stress test and six-minute walk distance (6MWD). Subgroup analyses were also performed among participants with impaired physical function at baseline (SPPB<10).

**Results:** We randomized 69 participants (home-CR: 35, AC: 34). Adherence to the home-CR program was 87%. In the overall study cohort, the improvement in KCCQ from baseline to 6-month follow-up was significantly greater in the home-CR vs. AC arm (median [IQR] change in KCCQ: 13.2[3.6, 31.1] vs. 6.2 [-7.7, 11.6], p-value: 0.01). In contrast, the change was comparable among home-CR and AC arm (median [IQR] change in SPPB: 1.0 [0, 3.0] vs. 1.0 [0, 1.0], p-value: 0.46). In the subset of participants with physical dysfunction at baseline (SPPB <10, N=44), a significantly greater improvement was noted in both SPPB as well as KCCQ among participants in the home-CR vs. AC arm. There were no significant between-group differences in the changes in VO<sub>2</sub>peak and 6MWD across the two study arms.

**Conclusion:** Among older patients with HFpEF who have impaired exercise capacity or physical dysfunction at baseline, a 6-month home-CR program (vs. AC) was associated with significantly greater improvement in QOL but not physical function on follow-up. Furthermore, significant improvements in physical function were observed in the subset of participants with physical dysfunction at baseline. Larger RCTs among older HFpEF patients with significant baseline physical function impairment are needed to confirm the clinical efficacy of home CR in this vulnerable population.

Poster #110

**Presenter:** Vinayak Subramanian, MD

Clinical Science

**Authors:** Vinayak Subramanian, MD; Alvin Chandra, MD; Matthew Segar, MD, Katarina Yaros, MD; Ross Upton, PhD; Ashley P. Akerman, PhD; Amil Shah, MD; Ambarish Pandey, MD, MSCS

**Title:** Performance of an Automated Echocardiographic Artificial Intelligence Model to Detect Subclinical Heart Failure with Preserved Ejection Fraction (HFpEF) in Community-dwelling Older Adults

**Abstract:**

**Background:** Heart failure (HF) with preserved Ejection Fraction (HFpEF) is common among older adults and associated with a high burden of morbidity and mortality. Early identification of subclinical HFpEF, defined by abnormalities in cardiac structure and function without symptoms of HF, can prompt early initiation of evidence-based therapies to prevent HFpEF. However, scalable strategies for the identification of subclinical HFpEF are lacking.

**Methods:** The study included participants of the Dallas Hearts and Minds Study without HF who underwent cardiovascular and exercise phenotyping with resting and exercise echocardiography and maximal cardiopulmonary exercise testing. The resting apical 4C echocardiographic images were analyzed by the AI echo algorithm to identify the HFpEF phenotype (AI-HFpEF). The gold standard determination of subclinical HFpEF was based on the presence of resting or exercise  $E/e' > 14$  and Peak exercise oxygen uptake ( $VO_{2peak}$ )  $< 25$ th percentile for the cohort. The performance of the AI algorithm to detect subclinical HFpEF was determined using the area under the receiver operating curve and decision curve analysis and was compared with the previously validated H2FpEF score. The association between the AI-HFpEF phenotype and the presence of subclinical HFpEF,  $VO_{2peak}$ , exercise  $E/e'$ , left ventricular strain, and left atrial strain was assessed using multivariable-adjusted logistic and linear regression models.

**Results:** The study included 511 participants (mean age: 61 y, 57% women, mean  $VO_{2peak} = 16.9$  ml/kg/min). Using the AI echo algorithm, subclinical HFpEF was detected in 10% of participants ( $n=76$ ), and 10% were non-diagnostic. The participants with (vs. without) AI-HFpEF phenotype were older and had a higher burden of CVD risk factors, left ventricular hypertrophy, and left atrial dilation. Subclinical HFpEF, as defined by the gold standard criteria, was present in 5.3% of participants. The AUROC for diagnosis of subclinical HFpEF using the AI-HFpEF algorithm was 0.85 vs. 0.78 by the H2FpEF score. In the adjusted analysis, the AI-HFpEF phenotype was significantly associated with greater odds of subclinical HFpEF by exercise and echocardiographic phenotyping criteria, higher  $E/e'$  with exercise, lower  $VO_{2peak}$ , and worse LV and LA strain. In decision curve analysis, the AI-HFpEF algorithm identified 23 additional cases of subclinical HFpEF per 1000 screened participants compared with the H2FpEF score.

**Conclusion:** The AI-HFpEF algorithm can reliably identify community-dwelling individuals with subclinical HFpEF characterized by diastolic dysfunction at rest or exercise and impaired exercise capacity. Future studies are needed to assess the utility of the AI-HFpEF algorithm in screening for subclinical HFpEF in health systems.



Poster #111

**Presenter:** Zainali Chunawala, MD

Clinical Science

**Authors:** Zainali S. Chunawala, MD; Sadiya S. Khan, MD; Arman Qamar, MD, MPH; Sameer Arora, MD, MPH; Marat Fudim, MD; Muthiah Vaduganathan, MD; Robert J. Mentz, MD; Deepak L. Bhatt, MD, MPH; Justin L. Grodin, MD, MPH; Melissa C. Caughey, PhD; Ambarish Pandey MD, MScS

**Title:** Biomarker Enhanced Risk Prediction of Incident Heart Failure in Low-Risk Patients: The Atherosclerosis Risk in Communities (ARIC) Study

**Abstract:**

**Background:** Primary prevention strategies to reduce heart failure (HF) burden are urgently warranted. The Pooled Cohort equation to Prevent HF (PCP-HF) risk score is a previously validated risk score that utilizes easily available parameters obtained in a primary care setting, to estimate the 10-year risk for incident HF. Although PCP-HF performs well for high-risk individuals, the model's predictive utility for low-risk individuals may potentially be enhanced by the integration of biomarkers.

**Methods:** In this study, the PCP-HF risk score was derived from data collected at visit 5 (2011-2013) of the ARIC cohort study and its 5-year predictive accuracy was investigated using cohort surveillance data captured up to 2019. Patients with <10% PCP-HF risk probability of incident HF were classified as low-risk. Incremental improvement in predictions of incident HF by including biomarker and echocardiographic parameters in the low-risk population was analyzed by logistic regression, by calculating the area under the curve (AUC) from receiver operating characteristics.

**Results:** Of 4980 study participants with 5 years of follow up, 47% had a low PCP-HF risk score (mean age 73 years, 32% Black). Of these, 3% developed HF within 5 years. Study participants with low PCP-HF risk score were younger, more often female and Black; had lower left ventricular (LV) mass index and left atrial volume index, higher magnitude of LV global longitudinal strain, and lower levels of NT-proBNP and hs-TnT. On further analysis in this low-risk population, the model incorporating laboratory and imaging-based biomarkers exhibited greater predictive accuracy for incident HF (AUC: 0.85 vs 0.62) compared to the original PCP-HF risk score. Furthermore, integrating laboratory biomarkers alone with PCP-HF also enhanced the performance of the model in the low-risk individuals (AUC: 0.83 vs 0.62).

**Conclusion:** The integration of laboratory and imaging-based biomarkers with the PCP-HF risk score enhances the predictive accuracy of risk modeling for incident HF, especially in individuals identified as low-risk by the 10-year risk prediction tool.

Poster #112

**Presenter:** Zainali Chunawala, MD

Clinical Science

**Authors:** Zainali S Chunawala, MD; Deepak L Bhatt, MD, MPH, MBA; Arman Qamar, MD, MPH; Muthiah Vaduganathan, MD, MPH; Robert J. Mentz, MD; Kunihiro Matsushita, MD, PhD; Justin L. Grodin, MD, MPH; Ambarish Pandey, MD, MSCS; Melissa C. Caughey, PhD

**Title:** Recurrent Admission of Acute Decompensated Heart Failure Among Patients With and Without PAD and Its Significance in the CKD Population: The ARIC Cohort Study

**Abstract:**

**Background:** Peripheral artery disease (PAD) and chronic kidney disease (CKD) are common comorbidities in patients with heart failure (HF). Importantly, CKD is associated with a greater risk of incident PAD and is a known risk factor for worse outcomes in HF patients. However, it is unclear whether the concomitant existence of PAD and CKD increases the risk of recurrent hospitalization for acute decompensated heart failure (ADHF).

**Methods:** Since 2005, the Atherosclerosis Risk in Communities (ARIC) study has conducted hospital surveillance of ADHF with events verified by physician review. Demographics, comorbidities, laboratory data, and medications were abstracted from medical record by trained personnel. Hazard ratios of ADHF readmissions were analyzed using repeat-events Cox regression. Models were adjusted for age, race, sex, year and hospital of admission, coronary artery disease (CAD), COPD, and diabetes mellitus. CKD was defined by glomerular filtration rate [GFR]  $\leq 60$  mL/min/1.73m<sup>2</sup>.

**Results:** From 2005-2018, there were 1049 index hospitalizations for ADHF (mean age 77 years, 66% white) with measured creatinine, who were discharged alive. Of these, 155 (15%) had a diagnosis of PAD and 66% had CKD stage 3a or worse (GFR  $\leq 60$  mL/min/1.73m<sup>2</sup>). Patients with PAD had a greater prevalence of smoking, CAD, myocardial infarction, and stroke. The 1-year ADHF readmission rate tended to be higher in patients with PAD, irrespective of CKD stage, compared to those without PAD (Figure 1). After adjustments, PAD was associated with greater hazards of 1-year ADHF readmissions, both in patients with CKD stage 3a or worse (HR, 1.71; 95% CI: 1.25 - 2.32) and without CKD (HR, 1.84; 95% CI: 1.07-3.15).

**Conclusion:** Patients with ADHF and concomitant PAD have a higher prevalence of cardiovascular comorbidities and higher likelihood of 1-year ADHF readmission, irrespective of the CKD status. Focused strategies to prevent ADHF readmission in this high-risk group are warranted.

Poster #113

**Presenter:** Karim Seif El Dahan, MD

Clinical Science

**Authors:** Karim Seif El Dahan, MD; Takeshi Yokoo, MD, PhD; Mishal Mendiratta-Lala, MD; David T. Fetzer, MD; Matthew S. Davenport, MD; Darine Daher, MD; Nicole E. Rich, MD, MSCS; Edward Yang, MD; Neehar D. Parikh, MD, MS; Amit G. Singal, MD, MS

**Title:** Multicenter Comparison of Abbreviated MRI versus Ultrasound for Detecting Early-Stage Hepatocellular Carcinoma in Patients with Cirrhosis

**Abstract:**

**Background:** Abbreviated magnetic resonance imaging (AMRI), consisting of a short (~15 min) and focused liver exam, is increasingly recognized as a potential alternative to ultrasound for hepatocellular carcinoma (HCC) surveillance given promising detection performance. However, existing data is limited by single-center samples, spectrum bias, and lack of comparative data for AMRI versus ultrasound as HCC surveillance tools. We compared the sensitivity and specificity of AMRI to ultrasound for the detection of early-stage HCC in a large multicenter patient cohort.

**Methods:** We conducted a retrospective case-control study at three US health centers among patients with cirrhosis (cases with early-stage HCC per Milan Criteria; controls without HCC) who underwent an ultrasound and a dynamic contrast-enhanced MRI within 6 months between 2012-2019. Dynamic AMRI examinations were simulated from the full MRI by selecting relevant sequences. Independent, blinded interpretations of ultrasounds and AMRIs were performed using LI-RADS algorithms. Ultrasounds were considered positive if US-3 observations were detected. AMRI was considered positive if LR-4, LR-5, or LR-M were detected. Per-patient sensitivity and specificity for early-stage HCC detection were estimated, and cross-modality differences were tested.

**Results:** We included 216 cases and 432 controls. Patient-level sensitivity and specificity of AMRI were significantly higher than ultrasound: 80.1% (95%CI: 76.1-83.6) vs. 71.1% (95%CI: 66.6-75.2),  $p < 0.001$ , and 91.9% (95%CI: 89.9-93.5) vs. 72.3% (95%CI: 69.3-75.2),  $p < 0.001$ , respectively. AMRI sensitivity was significantly higher than ultrasound among patients with Child Pugh B (80.8% vs. 57.4%,  $p < 0.001$ ) but not among those with Child Pugh A (84.7% vs. 78.6%,  $p = 0.07$ ) or Child Pugh C (52.6% vs. 68.4%,  $p = 0.18$ ). While liver disease etiology did not adversely affect AMRI sensitivity (79.3% for MASLD vs. 84.8% for viral liver disease;  $p = 0.65$ ), MASLD was associated with lower ultrasound sensitivity (58.6% vs. 76.7% for viral liver disease;  $p = 0.08$ ).

**Conclusions:** Dynamic AMRI may be more sensitive and specific than ultrasound for early-stage HCC detection, although both tests have suboptimal performance in those with Child-Pugh class C cirrhosis. Future large prospective trials and cost-effectiveness analyses are needed to further clarify the performance of AMRI and determine at-risk patients who may benefit the most, including those at greatest risk of poor ultrasound quality.

Poster #114

**Presenter:** Alex Jones, MD

Clinical Vignette

**Authors:** Alex Jones, MD; Ankitha Lingamaneni, MD; Roopa Vemulapalli, MD; Haidy Galous, MD

**Title:** Metastatic Esophageal Squamous Cell Carcinoma with Paraneoplastic Raynaud's Phenomenon

**Abstract:**

**Case Presentation:** A 61-year-old male with hypertension, hyperlipidemia, and alcohol use disorder presented with digital ulceration and dysphagia. Dysphagia to solids began 3 months prior to presentation and he experienced 20 pounds of unintended weight loss. Subsequently, he developed Raynaud's phenomenon (RP) with progression to digital ulceration. He was prescribed nifedipine 60 mg daily by his primary care provider, however, his symptoms persisted and he presented to the hospital for further evaluation. Physical examination was notable for dry gangrene of the left 2nd and 3rd and the right 2nd and 5th digits. There was no evidence of skin thickening and the oral aperture was normal in size.

Computed tomography was notable for circumferential thickening of the distal esophagus and bulky retroperitoneal lymphadenopathy. Endoscopy revealed a large, fungating, and ulcerating mass in the distal esophagus. Biopsy was consistent with moderately to poorly differentiated, invasive squamous cell carcinoma (SCC). Antinuclear antigen was positive with 1:2560 titer in a speckled pattern and SSA antibodies were elevated. Scl-70 antibody, rheumatoid factor, cryoglobulins, cytoplasmic neutrophil antibodies and anti-centromere antibodies were negative. These findings in concert with concomitant development of RP and esophageal SCC resulted in a diagnosis of paraneoplastic RP.

**Discussion:** RP is intermittent and transient ischemia, most often affecting the digits, resulting from vasospasm induced by cold or emotional stressors. It is thought to affect 5 percent of the population. Primary RP is more common in younger individuals, while secondary RP can present later in life. There are many etiologies of secondary RP including connective tissue disorders, and less frequently malignancy. In particular, paraneoplastic acral vascular syndrome may manifest with RP, and is usually observed with adenocarcinoma.

Herein, we describe a case of paraneoplastic RP occurring in the setting of metastatic esophageal SCC. Although adenocarcinoma is more commonly associated with paraneoplastic RP, there are previous descriptions of cases related to SCC in other organs. A number of paraneoplastic syndromes have been described for esophageal malignancy including acral vascular syndrome with RP. However, this is the first report of esophageal malignancy with SCC histology to be associated with paraneoplastic RP to our knowledge.

Poster #115

**Presenter:** Blake Lackey, MD

Clinical Vignette

**Authors:** Blake Lackey, MD; Langdon Stone, MD; Ramesh Saxena, MD, PhD

**Title:** A Case of Gitelman's Syndrome Mistaken for Chronic Alcohol-related Renal Magnesium Wasting

**Abstract:**

**Background:** Gitelman's syndrome is a well-documented, autosomal recessive tubulopathy most well characterized by a constellation of hypokalemia, metabolic alkalosis, hypercalcemia, and hypomagnesemia with significant impairment in renal calcium excretion and magnesium retention. It has been isolated to mutations in genes encoding the sodium chloride cotransporter (NCC) on the apical membrane of the distal convoluted tubule. Persistent hypomagnesemia is one of the hallmarks of the disease, and often leads to confusion when cementing the diagnosis.

Alcohol use is also known to cause direct renal magnesium wasting. In this renal magnesium wasting, there is usually concomitant hypocalcemia due to impaired intact parathyroid hormone secretion and urinary calcium wasting.

**Case Presentation:** We present the case of a 45-year-old man with polysubstance use, history of severe alcohol withdrawals, T2DM, COPD, schizophrenia who was admitted for psychiatric concerns. Early in hospitalization, the patient had kidney injury with peak sCr to 1.6 mg/dl, but now back to baseline after sufficient fluid repletion. The persistent problem during this hospitalization while receiving benzodiazepine taper for withdrawal was mild hypercalcemia and severe hypomagnesemia. The patient received aggressive repletion both PO and IV, with levels that continued to be low despite supplementation. On interview, the patient stated that he has had intermittent cramping of his bilateral lower extremities for years, even before heavy alcohol use. Also endorsed non-focal abdominal pain without nausea, vomiting. Denied chest pain, palpitations, syncope, cardiac complications in the past.

Patient seen by nephrology in the past. Based on 24-hour urine Magnesium studies at that time, there was increased renal magnesium excretion. Assessment at that time was that chronic alcoholism caused direct tubular damage and resultant chronic hypomagnesemia, suggested 800 mg TID Magnesium Oxide supplementation and follow up, but patient never returned to clinic.

Initial evaluation consisted of 24-hour urine studies for Mg, Ca, and creatinine. Additionally, hypercalcemia work up was obtained indicating a low PTH, normal 25-vitamin D, low 1,25-(OH)<sub>2</sub> Vitamin D. Studies returned with low 24-hour urine calcium and elevated 24 hour urine magnesium levels. The most likely diagnosis after these studies were performed was renal wasting of magnesium due to Gitelman's syndrome. Patient discharged on high doses of magnesium oxide, 800 mg three times daily.

**Discussion:** Here, the difficulty with determining alcohol-induced vs inherited channelopathy causing renal magnesium wasting is based on two factors: historical and parathyroid-calcium axis delinquencies. Using the history that the patient provided, which appears to lend itself towards the idea that this magnesium-wasting disease had been present outside of his heavy alcohol use, as well as the hypercalcemia that the patient was experiencing with inappropriate renal response, indicates that Gitelman's is the more likely diagnosis. This underlies the importance of obtaining calcium studies and paying close attention to renal calcium handling and whether it is impaired in the patient with persistent hypomagnesemia due to renal cause.

Poster #116

**Presenter:** Dale Oommen, MD

Clinical Vignette

**Authors:** Dale Oommen, MD; Mercy Ude, MD; David Johnson, MD

**Title:** A Case of Bilateral Adrenal Masses

**Abstract:**

**Case Presentation:** A man in his 50s with pertinent medical history of hypertension, no longer requiring medications, and kidney stones who presented to an urgent care center with a 2 month history of weight loss, poor oral intake and constant right lower quadrant abdominal pain associated with nausea and vomiting. He was treated for GERD. One month later, episodes of nausea and emesis increased precluding adequate food intake. This was accompanied by worsening right lower quadrant pain radiating to the back, chills and drenching night sweats. He presented to a local ED, where he was worked up for suspected cholecystitis, however a gallbladder ultrasound was negative. Days later, he presented to a local hospital for ongoing abdominal pain, nausea and emesis. At that facility, an abdominal CT scan revealed bilateral adrenal masses measuring 5.9 cm on left adrenal gland, and 11.5 cm on right adrenal gland that encased the right renal artery. He presented to our facility for expedited workup and management of his continued symptoms. On physical exam, the patient was well-appearing and in no acute distress. He was afebrile and normotensive with BMI of 28. He had mild right lower quadrant pain on deep palpation. Abdominal exam was otherwise benign. There was no hepatomegaly or splenomegaly. A renal artery bruit could be auscultated. He had no cervical, supraclavicular, axillary, or mediastinal lymphadenopathy. There were no cushingoid features or hyperpigmentation. CT scan and MRI of abdomen revealed right (10cm) > left (7cm) bilateral adrenal masses. Hormonal workup was significant for undetectable plasma aldosterone level, elevated ACTH level, and inadequate cortisol response to ACTH stimulation test. 17-hydroxyprogesterone levels were normal. Plasma and urine metanephrines levels were normal. Patient underwent left adrenal biopsy which supported a diagnosis of Diffuse Large B-cell lymphoma (DLBCL). Staging CT scans, LP, FISH were otherwise unremarkable. Patient was discharged on day after receiving the first cycle of R-CHOP. Seen by Onc and Endocrine follow up, currently on cycle 3 of R-CHOP with pegfilgrastim support. He was later switched to Pola-R-CHOP in the outpatient setting given its improved outcomes compared to R-CHOP. He was started and continued on adrenal replacement therapy, hydrocortisone 10 mg BID and fludrocortisone 0.1 mg daily. At time of writing, patient is pending PET before cycle 4 of chemotherapy.

**Discussion:** We described a case of primary adrenal diffuse large B cell lymphoma in a patient who presented with non-specific symptoms and bilateral AIs. While unilateral AIs are increasingly detected given radiologic advancements, bilateral AIs remain rare. The prognosis of primary adrenal lymphoma is poor with 1 year survival rates as low as 18%. Treatment has historically been chemotherapy with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone). Adrenalectomy is controversial and studies have shown no benefit. In April 2023, FDA approved Pola-R-CHOP for the treatment of diffuse large B cell lymphoma. Pola-R-Chop combines traditional R-CHOP with polatuzumab, an anti-CD79b monoclonal antibody. Data has show that addition of polatuzumab is associated with improved mortality compared to R-CHOP alone. Patient was initially started on R-CHOP while inpatient, but switched to pola-R-Chop in the outpatient setting. A learning point is the importance of an expedited workup once the masses are identified given the significant difference in OS in those started on chemotherapy and the poor prognosis given the median survival of 20 months in recent years. The presence of the above symptoms within the demographic of a male of advanced age should raise one's clinical suspicion of this disease and if bilateral masses are identified rapid workup is warranted.

Poster #117

**Presenter:** Dimitri Maamari, MD

Clinical Vignette

**Authors:** Dimitri J. Maamari, MD; Vivek Koshti, MD; Rafic F. Berbarie, MD

**Title:** A Curious Case of Clozapine Carditis with Cardiac Convalescence

**Abstract:**

**Case Presentation:** Clozapine is an antipsychotic used in treatment-resistant schizophrenia. Its use has been limited by adverse events, rarely including myocarditis. Here, we describe a rare case of clozapine-induced myocarditis and the improvement of cardiac function with avoidance of clozapine for one week and initiation of guideline-directed medical therapy (GDMT).

A 29-year-old man with schizophrenia on risperidone and paroxetine was admitted with schizophrenia decompensation and suicidal ideations. He was transitioned to clozapine with improvement in his psychiatric symptoms. Thirteen days after starting clozapine, he developed nausea, vomiting, tachycardia, and low-grade fever. He had leukocytosis but it was thought to be, in part, secondary to methylprednisolone before rituximab infusions for his multiple sclerosis. An electrocardiogram revealed sinus tachycardia, and troponin, which was taken in the setting of clozapine therapy, was 6.

Four days later, his fever and tachycardia with chills and dyspnea persisted; troponin was in the forties and increased to 235 within a few hours. Over the next 36 hours, troponin peaked at 3,600. C-reactive protein and erythrocyte sedimentation rates were elevated at 20.5 and 51, compared to 1.8 and 3 respectively upon initiation of symptoms a few days earlier. A respiratory viral panel, blood and urine cultures, human immunodeficiency virus, and an autoimmune workup were unrevealing. Clozapine was held. A transthoracic echocardiogram revealed a reduced systolic function with a left ventricular ejection fraction (LVEF) of 40%. A cardiac magnetic resonance imaging revealed acute myocarditis with LVEF 24%. He was started on GDMT and a repeat echocardiogram six days later revealed normalization of systolic function with LVEF 56% with clinical improvement. His last dose of clozapine was seven days earlier. He was discharged on GDMT and clozapine was added to his allergy list.

**Discussion:** Myocarditis is a serious and rare adverse event to clozapine therapy. Symptoms are non-specific and delays in diagnosis may lead to myocardial damage and fatal arrhythmias. In light of the patient's presentation, unrevealing workup, and improvement with avoidance of clozapine, we believe that the individual had clozapine-induced myocarditis. It is important to highlight the occurrence of this rare outcome to consider this toxicity and initiate treatment in time.

Poster #118

**Presenter:** Do Park, MD

Clinical Vignette

**Authors:** Do Park, MD; Elizabeth Hardin, MD

**Title:** Navigating Diagnostic Complexity: An Unusual Presentation of Cardiac Sarcoidosis

**Abstract:**

**Case Presentation:** A 19-year-old woman with no prior medical history presented after a pre-syncope episode. She was found to have sustained, monomorphic ventricular tachycardia and underwent electrical cardioversion with successful restoration of sinus rhythm. Workup was notable for large soft tissue “mass” in the right ventricle attached to the interventricular septum with extensive late gadolinium enhancement on cardiac magnetic resonance imaging with additional soft tissue mass encasing the inferior vena cava and in the right paratracheal region. PET-CT showed FDG avidity of the soft tissue abnormality in the interventricular septum and inferior vena cava with involvement of both the right atrium and right ventricle. Additionally, there were FDG avid lymph nodes in the thorax. Endomyocardial biopsy was pursued and notable for scattered interstitial T-cells and macrophages, negative for amyloid deposits, and overall non-diagnostic. Transbronchial biopsy of the mediastinal lymph nodes revealed non-caseating granulomas and multinucleated giant cells without evidence of malignancy or infection on extensive staining. The diagnosis of sarcoidosis with cardiac involvement was made.

**Discussion:** An enigmatic disease, sarcoidosis is a multi-system, granulomatous inflammatory disease that can involve any organ system but most commonly affects the lungs, eyes, and skin. Clinically manifest cardiac sarcoidosis (CS) is prevalent in only 5% of patients who have systemic sarcoidosis. However, based on autopsy and imaging studies, 25% of patients with sarcoidosis have subclinical or asymptomatic cardiac involvement. Cardiac involvement is a leading cause of morbidity and mortality in patients with sarcoidosis. The most common clinical manifestations of CS include heart block, malignant ventricular arrhythmias including sudden cardiac death, and heart failure.

CS presenting as cardiac tumor is atypical and can be challenging to diagnose definitively. The yield of endomyocardial biopsy for the definitive diagnosis of CS is highly specific but not sensitive with a yield of around 25%. Therefore, clinicians rely heavily on clinical criteria based on expert consensus guidelines. These guidelines recommend an extra-cardiac biopsy suggestive of sarcoidosis as well as evidence of underlying cardiac pathology. Experts emphasize the use of multimodal imaging as these have high diagnostic accuracy and can help differentiate between different types of cardiac masses through characteristic features.



Poster #119

**Presenter:** Jimin Hwang, MD, MPH

Clinical Vignette

**Authors:** Jimin Hwang, MD, MPH; Sanaa Tejani, MD; Jessica Abramowitz, MD; Darren K. McGuire, MD, MHSc; Justin L. Grodin, MD, MPH

**Title:** Severe Hypoglycemic Ketoacidosis in a Patient without Diabetes Concurrently Taking a Sodium Glucose Cotransporter-2 Inhibitor and an Anti-Obesity Incretin Analog

**Abstract:**

**Case Presentation:** Here is a case of a 39-year-old woman with no history of diabetes who presented with generalized weakness and shortness of breath. She had been taking the sodium glucose cotransporter-2 inhibitor (SGLT2i), empagliflozin for heart failure with reduced ejection fraction, and the glucagon-like peptide 1/glucose-dependent insulinotropic polypeptide receptor agonist (GLP-1/GIP RA), tirzepatide, for weight loss. Since starting tirzepatide 8 months prior, she had lost 23kg of body weight. She presented after two days of nausea and vomiting, during which time she had continued to take both medications. She was found to have severe hypoglycemia (33mg/dL) and severe ketoacidosis with incomplete respiratory compensation (anion gap=21; serum pH=7.30, bicarbonate=11, serum beta-hydroxybutyrate=3.0). The ketoacidosis was thought to be triggered by poor oral intake with starvation ketosis, exacerbated by empagliflozin. Her dyspnea was likely from respiratory response to the metabolic acidosis, and heart failure was ruled out with low NT-proBNP and no signs of volume overload. The metabolic acidosis, ketosis, and respiratory symptoms corrected rapidly with dextrose-containing isotonic fluids. Empagliflozin was discontinued on discharge.

**Discussion:** Mildly hyperglycemic diabetic ketoacidosis is a well-known adverse effect of SGLT2i use among persons with type 1 or type 2 diabetes, common in the former but rare in the latter; ketoacidosis as an adverse effect of SGLT2i has been scarcely reported in persons without diabetes.[1,2] In this patient, decreased carbohydrate intake due to GI illness superimposed on the continued use of empagliflozin and tirzepatide may have led to an increased glucagon-to-insulin ratio, thus ketogenesis. Mechanistically, SGLT2i can cause ketoacidosis by increasing glucagon secretion and decreasing renal excretion of ketone bodies. Although GLP-1 increases insulin secretion and protects against ketoacidosis, GIP agonism stimulates glucagon secretion, shifting the glucagon-to-insulin balance.[3] This ketoacidosis can be exacerbated in patients who develop a concomitant starvation ketosis due to gastrointestinal side effects of incretin analogues. Diabetes guidelines discourage use of SGLT2i when there is interruption in oral intake given the risk of ketoacidosis.[4] Likewise, patients receiving both SGLT2i and incretin therapy, even in the absence of diabetes, should be cautioned on the "sick-day" risk of ketoacidosis during periods of decreased nutrient intake and/or catabolic stress.

Poster #120

**Presenter:** Kristina Collins, MBBS

Clinical Vignette

**Authors:** Kristina D. Collins, MBBS; Peter A. Kentros, MD; Christine Manthuruthil, MD

**Title:** A Case of Unexplained Bilateral Ground Glass Opacity Leading to the Diagnosis of Metastatic Pulmonary Calcification

**Abstract:**

**Case Presentation:** A 63-year-old male with a history of ESRD on PD, HTN, and HIV presented to the hospital with six weeks of productive cough with associated shortness of breath. His peritoneal dialysis was ineffective in optimizing electrolytes and volume for 6 months, but he declined to transition to intermittent hemodialysis (iHD). Chest CT revealed bilateral ground glass and reticular opacities. Labs were notable for an NT-proBNP of >70,000, CBC with WBC count of 11.55, Ca 10.2, Phos 10, CD4 277, undetectable HIV viral load, and negative respiratory viral and autoimmune panel. He was started on empiric antibiotics and a trial of iHD. Bronchoscopy showed normal parenchyma grossly, and BAL cultures and cytology were negative with monocytosis. Bone Scan revealed diffuse radiotracer uptake in bilateral lungs consistent with metastatic calcification. His symptoms improved with optimal dialysis.

**Discussion:** Ground-glass opacities (GGO) are commonly found in chest CT scans. GGO refers to areas of increased lung density that preserve bronchial and vascular markings and can have many different causes. In our patient with end-stage renal disease (ESRD) who had a high calcium-phosphate product, metastatic pulmonary calcification (MPC) was the cause. MPC is caused by one or more pro-calcifying factors in combination with local or systemic hypercalcemia. Etiologies include renal failure, multiple myeloma, granulomatous disease, and vitamin D intoxication. Although the true incidence and prevalence of MPC are unknown, as many as 60-70% of patients undergoing hemodialysis are found to have MPC at autopsy. MPC is often asymptomatic but can sometimes present with chronic cough and dyspnea or with other radiological findings such as consolidation and pleural effusion. Identifying MPC as the cause of GGO can help avoid unnecessary diagnostic workup, serve as a marker for renal disease severity, and prevent further pulmonary complications, including restrictive lung disease. In cases where imaging and bronchoalveolar lavage (BAL) findings are inconclusive, bone scans can provide diagnostic clarity, as with our patients. Treatment usually involves correcting serum calcium and phosphate and may involve renal transplantation or parathyroidectomy in patients with ESRD. In our patient's case, optimizing his hemodialysis with the transition to iHD was chosen.

Poster #121

**Presenter:** Kristina Collins, MBBS

Clinical Vignette

**Authors:** Kristina D. Collins, MBBS; Peter A. Kentros, MD

**Title:** What Happened to MAC? A Case of Loss to Follow-up: How Could This Be Prevented?

**Abstract:**

**Case Presentation:** A 78-year-old Spanish-speaking woman from Mexico with a history of treated TB presented with worsening cough and dyspnea for four months. The initial history was challenging to ascertain due to the limited availability of interpreters, low health literacy regarding her previous clinical course, and no family present for collateral history. Initial vitals and investigations were notable for SPO<sub>2</sub> 88%, WBC 10.09, Hgb 6.5, and CT imaging demonstrating multiple large cavitary lesions, calcifications, nodules with consolidation. Infectious workup revealed mycobacterium avium complex (MAC) with negative MTB PCR. Prior outside medical records ultimately showed MAC pneumonia 20-months ago with incomplete treatment due to failure to afford medications and follow-up appointments. Through working with the hospital social services, she successfully applied for emergency Medicaid and the hospital's financial assistance program, covering her discharge medications, home oxygen, and follow-up appointments.

**Discussion:** Social Determinants of Health (SDOH) are the non-medical factors that influence health outcomes, and these comprise 80% of the factors that contribute to one's health. This patient was affected by health-related social needs, including language, social support, economic status, health literacy, and lack of insurance. This impacted her health negatively as she had a 20-month delay in treatment, which resulted in significant debility. It was paramount for her to receive timely treatment as pulmonary MAC is associated with a 25% all-cause mortality, which is even higher in patients with cavitary lung disease. Approximately 16% of the adult US population are immigrants, with 20% reporting difficulties with paying for health care and 22% skipping appointments because of cost. Moreover, 3 in 10 immigrant adults report difficulties in seeking medical treatment, including complaints being ignored, incomprehension of medical content provided, disrespectful treatment, and language barriers. To address these issues, a crucial step moving forward is for physicians to recognize the importance of their role in identifying specific patient health-related social needs and to direct them to appropriate resources. In addition to ongoing training to develop their skills in overcoming potential challenges for patients arising from SDOH. As in our patient's case, to also continue working with interdisciplinary teams that include social workers to provide equitable care.

Poster #122

**Presenter:** Patrick O'Hara, MD

Clinical Vignette

**Authors:** Patrick O'Hara, MD; Lauren K. Truby, MD, MS; Hadi Beaini, MD; Anas Jawaid, MD; Fizza Hussain, MD; Maryjane Farr, MD, MSc; Christopher Heid, MD; Peiman Lahsaei, MD; Sonia Garg, MD; Faris G. Araj, MD

**Title:** Catastrophic Bioprosthetic AV Thrombosis: An Unappreciated Complication of VA-ECMO Support in Cardiogenic Shock

**Abstract:**

**Case Presentation:** A 56-year-old male with a history of cardiac sarcoidosis with biventricular systolic heart failure (HF) and a bioprosthetic aortic valve presented with acute decompensated HF. Progressive cardiogenic shock and hemodynamic instability ensued, requiring urgent bedside placement of an intra-aortic balloon pump (IABP) which provided only marginal hemodynamic support. After extensive multidisciplinary discussion, emergent cannulation for veno-arterial ECMO (VA-ECMO) was performed at the bedside as a bridge-to-decision for advanced HF therapies. The IABP was left in place for LV venting. Within 72 hours, extensive bilateral pulmonary opacities had developed. It was later realized that true LV ejection (as evidenced by aortic pulsatility on the arterial line) was not present and had been masked by pseudo-pulsatility provided by IABP inflations and deflations. Compared to an echocardiogram done 7 days prior to VA-ECMO cannulation, the bioprosthetic leaflets were no longer opening, thrombosis of the AV had occurred, and thrombus formation along the ECMO venous drainage cannula was noted. Failure to achieve LV venting culminated in complete thrombosis of the entire LV and LA and the patient ultimately expired.

**Discussion:** Bioprosthetic valve thrombosis is a lesser-known complication of VA-ECMO support, with most reports involving bioprosthetic valves in the mitral position. Indeed, bioprosthetic valve thrombosis occurs at a higher rate than native valve thrombosis during VA-ECMO support. However, bioprosthetic AV thrombosis is an extremely rare complication of VA-ECMO support and arguably results in a more catastrophic scenario as most traditional approaches to LV unloading are contraindicated. The optimal LV unloading strategy for these patients (IABP, Impella, surgical apical unloading, etc) is unknown. Data from large retrospective analyses have demonstrated extremely poor outcomes when prosthetic valve thrombosis occurs, and it is thus critical to prevent this complication from developing. In contrast to IABP counter-pulsation, the benefit of upfront transvalvular LV venting with an Impella device safeguards the presence of a direct LV vent in the event of bioprosthetic AV thrombosis and eliminates the false reassurance of IABP pseudo-pulsatility. Further studies are needed to better elucidate the optimal LV unloading strategy in patients with bioprosthetic valves, particularly in the aortic position.

Poster #123

**Presenter:** Peter Kentros, MD

Clinical Vignette

**Authors:** Peter A. Kentros MD; Navid Manouchehri Ardestani, MD; Michael Burton, MD, MSPH

**Title:** An Uncommon Cause of STEMI: Nonbacterial Thrombotic Endocarditis

**Abstract:**

**Case Presentation:** A 69-year-old gentleman with metastatic pancreatic cancer and prior venous thromboembolism with inconsistent anticoagulation presented with worsening subacute chest pressure. He appeared cachectic and in pain. Troponin-T was flat in the 800s. There were new Q-waves as well as ST elevations in V2-V4. Ejection fraction was 50% with inferoseptal/apical akinesis; echodensities were attached to the chordal structure in the right ventricle (2.5 x 1.5 cm), anterior and posterior mitral leaflets (1.9 x 1.9 cm, 2.3 x 1.9 cm), and one in the right atrium. He was managed with aspirin, statin, and beta-blockade; revascularization was deferred due to completed infarction and poor prognosis. Approximately one week later he decompensated and died after three cardiac arrests and worsening anion gap metabolic acidosis with distributive shock.

**Discussion:** Nonbacterial thrombotic endocarditis (NBTE), also known as marantic endocarditis, is a rare form of endocarditis characterized by the deposition of sterile thrombi on the heart valves. It is most associated with hypercoagulable conditions, with cytokines including TNF and IL-1 leading to endothelial damage--one large single center study found that 41% had an underlying malignancy, 33% had lupus, and 36% had antiphospholipid antibody syndrome (1). The true incidence and prevalence of NBTE is not known. One autopsy series of 1,640 patients found NBTE occurred in 1.25% of patients with malignancy, compared to 0.2% without (2). Adenocarcinoma was the most common malignancy (2.70% vs 0.47%), with pancreatic adenocarcinoma more common than others (10.34% vs 1.55%). The second most common cause is SLE (3,4). Although it can be asymptomatic, stroke is the initial presentation in 60% of cases, along with other infarcts (1).

Diagnosis requires ruling out an infectious cause with several blood cultures, and potentially investigation for organisms known to cause culture-negative endocarditis. ACC 2012 guidelines recommend systemic anticoagulation; insufficient evidence was found to support using DOACs vs heparin/warfarin (5). Systemic anticoagulation and treatment of underlying disease is also recommended by oncology groups (6). Surgical treatment can be considered (7). The prognosis is grim, given the associated comorbidities and severe morbidity and mortality from thrombotic events.

Poster #124

**Presenter:** Sanaa Tejani, MD

Clinical Vignette

**Authors:** Sanaa Tejani, MD; Rachel Bonnema, MD

**Title:** Vitamin A Deficiency and Decompensated Cirrhosis: An Insightful Connection

**Abstract:**

**Case Presentation:** We present a case of a 53-year-old male with a past medical history of cirrhosis secondary to alcohol use, who presented to clinic with new onset vision changes. He noted several weeks of changes in nighttime vision, specifically, feeling like his vision would not adjust when going from brightly lit to dim spaces, and having difficulty seeing while driving at night. He was asymptomatic in daylight and had no changes in peripheral vision or visual acuity. He was unable to get ophthalmologic evaluation due to lack of financial coverage. Given his history of recently diagnosed cirrhosis and ongoing alcohol use, there was concern that vitamin deficiency, specifically vitamin A deficiency, was contributing to his vision changes. Nutrition labs were checked and resulted with undetectable vitamin A level. Intramuscular vitamin A was unavailable, thus oral vitamin A supplementation was started at 25,000 units twice daily. After three months of high-dose oral vitamin A supplementation, his vitamin A level increased to normal at 35.8 mcg/dL (reference range 32 – 78 mcg/dL) and he reported improvement in his nighttime vision.

**Discussion:** Vitamin A deficiency is predominantly seen in under resourced regions due to dietary insufficiency. It is rare in the United States, affecting less than 1% of the population, however, certain individuals are at increased risk of vitamin A deficiency despite adequate dietary intake, including those with chronic liver disease. Close to 70% of individuals with cirrhosis are estimated to have vitamin A deficiency. The etiology of this deficiency in cirrhosis is multifactorial, including impaired secretion of bile salts causing fat malabsorption in the small bowel, impaired vitamin A storage in the liver, and impaired vitamin A metabolism. Nyctalopia, or night blindness, is often the first clinical manifestation of vitamin A deficiency, though many patients with vitamin A deficiency are asymptomatic. Given the high prevalence of this vitamin deficiency in cirrhosis and its risk of causing worsening liver fibrosis, providers should have a low threshold to assess for vitamin A deficiency in patients with cirrhosis, especially those who present with associated clinical symptoms, such as vision changes.

Poster #125

**Presenter:** Sanaa Tejani, MD

Clinical Vignette

**Authors:** Sanaa Tejani, MD; Jessica Abramowitz, MD; Nicholas Tritos, MD, DSC; Oksana Hamidi, DO; Sasan Mirfakhraee, MD

**Title:** Prolonged Adrenal Insufficiency After Osilodrostat Exposure with Eventual Recovery of Adrenal Function

**Abstract:**

**Case Presentation:** A 41-year-old woman was noted to have an incidental pituitary macroadenoma on MRI brain obtained for upper extremity radiculopathy. In retrospect, she noted 8kg weight gain in a central distribution over the prior year associated with facial plethora and acne. Biochemical testing revealed elevated 24-hour urinary free cortisol of 71 µg (reference range, 4-50 µg/24 hr) and elevated serum cortisol of 8.1 µg/dL after 1-mg overnight dexamethasone suppression test (normal, ≤1.8 µg/dL). Despite transsphenoidal resection of adenoma and Gamma Knife radiosurgery, she continued to have elevated late night salivary cortisol. She was started on osilodrostat due to concern for active, persistent hypercortisolism. After 11 months on osilodrostat, she reported symptoms of adrenal insufficiency. Biochemical testing revealed low serum cortisol and high plasma ACTH. Osilodrostat was stopped, and given her inadequate serum cortisol response to ACTH stimulation (10.4 mcg/dL, normal, >14 mcg/dL), she was started on physiologic hydrocortisone. This was discontinued 23 months after last osilodrostat exposure when laboratory testing revealed recovery of endogenous cortisol production.

**Discussion:** Osilodrostat is an oral 11-beta-hydroxylase inhibitor used for treatment of Cushing disease in patients ineligible for pituitary surgery or with persistent disease after surgery. Prolonged adrenal insufficiency (AI) is a rare, but significant adverse effect of osilodrostat use. Recently published reports have documented 5 patients total with prolonged AI following osilodrostat use – none had complete recovery of adrenal function during the follow-up period. Our case is notable for prolonged primary AI following 11 months of osilodrostat, with eventual recovery of adrenal function 99 weeks after last exposure to osilodrostat. This is the first reported case of a patient developing prolonged AI after osilodrostat exposure with eventual full recovery of glucocorticoid production.

While the mechanism of prolonged AI after osilodrostat exposure is not well understood, prescribers should be cognizant of this potential adverse effect due to the severity of a missed diagnosis. Providers should have a low threshold to test for AI in patients recently treated with osilodrostat who develop AI-related symptoms. If AI is diagnosed, patients should undergo periodic reassessment of adrenal function since delayed recovery may be seen.

Poster #126

**Presenter:** Sanghoon Park, MD

Clinical Vignette

**Authors:** Sanghoon Park, MD; Sasan Mirfakhraee, MD; Raksha Jain, MD

**Title:** Single-Center Experience of Effect of GLP-1 Receptor Agonists in Adult Patients with Cystic Fibrosis

**Abstract:**

**Case Presentation:** Glucagon-like-peptide-1 (GLP-1) receptor agonists are commonly used to improve glycemic control and promote weight loss in individuals with type 2 diabetes mellitus (T2DM) and/or obesity. However, there is a paucity of evidence regarding GLP-1 agonist use in people with cystic fibrosis (CF). GLP-1 agonists present an attractive treatment option for people with CF who have gained excess weight (particularly with increased use of cystic fibrosis transmembrane conductance regulator [CFTR] modulator therapy) or in those with cystic fibrosis-related diabetes (CFRD) who prefer the convenience of once-weekly GLP-1 agonists over prandial insulin.

We present 11 CF patients (males: 3, females: 7; age range 24-47; BMI range 25.7-43.7) treated with GLP-1 agonists (semaglutide: 9, tirzepatide: 2) for variable duration (1-50 months). All experienced weight loss on GLP-1 agonist therapy (mean  $\Delta$  weight = -8.8 kg;  $\Delta$  BMI [kg/m<sup>2</sup>] = -0.9 to -8.1). 8 patients showed improvement in forced expiratory volume in 1 second (FEV1) [ $\Delta$  (%) = -5 to +18]. Of the 7 patients with CFRD, all reduced their insulin amount (mean, 28.3% decrease in total daily insulin dose), and glucose time in range improved for most (mean, +11% increase from baseline). 4 patients stopped using GLP-1 agonists: 2 due to severe nausea/vomiting, 1 due to lack of perceived benefit, and 1 due to change in insurance coverage. 2 patients with initial nausea/vomiting were ultimately able to tolerate GLP-1 agonist therapy: one by lowering the dose of semaglutide and another by switching from semaglutide to tirzepatide.

**Discussion:** Our data collection is the largest known to date of CF patients treated with GLP-1 agonist therapy. With the addition of GLP-1 agonists, all patients experienced weight loss and a reduction in daily insulin dose, and most had an improvement in pulmonary function. GLP-1 agonist tolerability was similar to that reported in non-CF patients with diabetes and/or obesity treated with these agents. In summary, we have shown that GLP-1 agonists can be safely used in CF patients, with notable improvement in weight, insulin dose, glycemic parameters, and lung function. Future studies can corroborate the efficacy and tolerability of these agents in the CF population.



Poster #127

**Presenter:** Aemen Zamir, MD

QI/High Value Care

**Authors:** Aemen Zamir, MD; Joad Eseddi, MD; Shannon Wishin; DeAnne Carmichael, RPh, CSP; Puneet Bajaj, MD, MPH

**Title:** Increasing Biosimilar Uptake in the Rheumatology Clinics Within a Large Academic Medical Center

**Abstract:**

**Background:** Biological drugs have revolutionized the treatment of rheumatic diseases, but the high costs have contributed towards higher prescription drug spending in the United States. The US Food and Drug Administration (FDA) has approved several biosimilars, medications that are like their reference biologics and have comparable safety and effectiveness, for the use of rheumatic diseases. We describe here a quality improvement project aimed at increasing the use of biosimilars for rituximab and infliximab among rheumatology providers within UTSW.

**Methods:** Patients aged 17 and above with rheumatologic conditions who were prescribed therapy plans for infliximab, rituximab, and their biosimilar equivalents (infliximab – dyyb and rituximab-abbs) were included in the study. A series of interventions were implemented between 2018 and 2020 to facilitate the use of the two biosimilars. These interventions involved education for rheumatology providers and changes to the electronic health record that would make the biosimilars for infliximab and rituximab the default order for their respective therapy plans. This project measured the percentage of biosimilar therapy plans prescribed amongst all rheumatology patients over time and the potential cost savings associated with increased use of biosimilars.

**Results:** By making infliximab – dyyb and rituximab-abbs the default orders in our EHR, the overall rate of use of these biosimilars medications increased from a baseline of < 5.0% to 49.6% for infliximab – dyyb and 51.3% for rituximab-abbs. We estimated a total of > \$3.2 million in cost savings solely through two biosimilar substitutions within one specialty clinic at our institution.

**Conclusions:** Through this project, we promoted an increase in biosimilar use amongst rheumatology providers at UTSW, potentially leading to institutional savings, while still providing patients with the same standard of care. Our project demonstrated a sustained upward trend in biosimilar prescribing practices for both infliximab – dyyb and rituximab-abbs more than six months after they were incorporated into the EHR as the default order.

Poster #128

**Presenter:** Paige Della-Penna, MD

QI/High Value Care

**Authors:** Paige Della-Penna, MD; Feroz James, BS; Nathan Sumarsono, BS; Aseel Dweik, MD; Hannah Lehrenbaum, MD; Franck H. Azobou Tonleu, MD; Kyle Geurink, MD; Hurst M. Hall III, MD; Sandeep Das, MD, MPH

**Title:** Use of Supplemental Lipid Lowering Therapies at One Year after MI Among Patients Not Meeting AHA/ACC LDL Goal Despite High Intensity Statin

**Abstract:**

**Background:** The 2018 ACC/AHA cholesterol guidelines defined LDL targets and recommended adjunctive non-statin therapies—ezetimibe and PCSK9 inhibitors—in selected patients to reach an LDL < 70 mg/dL. How effectively these additional lipid lowering therapies (LLT) are being employed in the highest risk patients is not well known.

**Methods:** Using an institutional quality improvement registry, we identified a cohort of patients at a large urban safety net hospital and a university hospital in Dallas, TX admitted for Type 1 MI between 2018-2021. Included patients had index LDL  $\geq$ 70 mg/dL despite being prescribed high intensity statin therapy (HIS) prior to admission. Using the hospital EHR, we extracted the prescribed LLTs at admission, discharge and 1 year follow-up. LDL values drawn during index admission or within 30 days prior to admission were reviewed. Patients lost to follow-up were excluded from the analysis.

**Results:** Of 504 patients with baseline LDL tested, 47 met inclusion criteria of LDL > 70 mg/dL with prior to admission HIS prescription. Ezetimibe was added to 5 (11%) of these patients at discharge and to a total of 8 (17%) at 1 year. No patients were prescribed a PCSK9 inhibitor. At discharge, 42 (89%) remained on HIS alone, with 39 (83%) remaining on HIS alone at 1 year.

**Conclusion:** In this cohort, 4 of 5 patients with MI were not prescribed additional LLT at 1 year, even though their LDL was above ACC/AHA recommended targets. These findings represent an important care gap in the secondary prevention of ASCVD.

Poster #129

**Presenter:** Paige Della-Penna, MD

QI/High Value Care

**Authors:** Paige Della-Penna, MD; Feroz James, BS; Nathan Sumarsono, BS; Aseel Dweik, MD; Chiatanya Malladi, MD; Hannah Lehenbaum, MD; Franck Azobou Tonleu, MD; Kyle Geurink, MD; Eizabeth Moss, PharmD; Sandeep Das, MD, MPH

**Title:** Comparative Rates of Post-Discharge LDL Testing After Myocardial Infarction in a University and Safety Net Health System

**Abstract:**

**Background:** AHA guidelines for patients hospitalized with MI recommend repeat LDL testing post-hospitalization at 4-12 weeks. In Dallas, TX a University Hospital (UH) and a county Safety Net Hospital (SNH) have cardiology services staffed by the same physician groups. We quantify rates of lipid testing among patients who follow up in this recommended timeframe and examine whether rates of testing differ by clinical practice site.

**Methods:** Using the hospital electronic medical record, we manually reviewed 3-month post-discharge LDL for all patients who were hospitalized with a type 1 MI between 2018-2021 at a SNH and UH. Patients who expired during the index admission or who did not follow up in one of these health systems were excluded from analysis. This analysis included 267 patients from the UH and 734 patients from the SNH.

**Results:** In our cohort, of the UH patients, 20% were Black, 15% Hispanic white, and 6% uninsured. In contrast, of the SNH patients 26% were Black, 48% Hispanic white, and 61% uninsured. No significant difference was found in 3-month LDL testing rates for SNH versus UH. Approximately 70% did not have LDL repeated by 3 months, an additional 10% had LDL tested and  $\geq 70$  mg/dL, with only the remaining 20% at LDL  $< 70$  mg/dL.

**Conclusion:** Despite guideline recommendations, rates of repeat LDL testing within 4-12 weeks post-discharge after MI were low. Although there were significant differences in burden of adverse social determinants of health between health systems, including race, language, and lack of insurance, the lack of significant difference in testing between the UH and SNH suggests care gaps may be driven more by provider factors rather than unique patient or health-system factors.

Poster #130

**Presenter:** Ruchi Desai, MD

QI/High Value Care

**Authors:** Ruchi Desai, MD; Nainesh Shah, MD; Ray Zhang, MD; Maria Bacalao, MD; Haidy Galous, MD; David Karp, MD; Puneet Bajaj, MD

**Title:** Reduction in the Concomitant Ordering of Erythrocyte Sedimentation Rate and C-Reactive Protein at an Academic Medical Center

**Abstract:**

**Background:** Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) are two laboratory tests often ordered simultaneously to assess for inflammation. Studies have shown that CRP is superior to ESR and co-ordering ESR and CRP increases expenditures and phlebotomy without any demonstrable benefit to patient care. The goal of this quality improvement project was to implement best practices to reduce ESR co-ordering with CRP at UTSW and Parkland.

**Methods:** Using the Plan, Do, Study, Act (PDSA) iterative methodology for continuous improvement, we developed a two-pronged approach of education and Electronic Medical Record (EMR) changes targeted first at the rheumatology department and then at the greater hospital system. Our interventions included inter-department discussions, general education to all rheumatology providers (February 2023), targeted education to a few rheumatology providers with high ESR/CRP co-orders (March 2023), removal of the ESR order from the rheumatology order set at UTSW (March 2023), implementation of a Clinical Decision Support Tool (CDS) at both UTSW and Parkland in which the ESR order was changed to recommend CRP (May 2023) and general education to internal medicine residents (July 2023). At Parkland, the ESR order was previously deselected as a default order in March 2021. We compared ESR and CRP co-orders and total ESR orders alone between the pre-intervention period (2/13/22-2/5/23) and the post-intervention period (2/6/23-2/3/24).

**Results:** At both hospitals combined, total ESR and CRP co-orders decreased from 33,739 to 22,767 and total ESR orders alone decreased from 8,012 to 4,391. At UTSW, average ESR and CRP co-orders per week decreased by 36% and average ESR orders alone per week decreased by 47%. Most change was seen within the rheumatology division although significant change was also seen for the EM, IM-Hospital and IM-General ordering groups. At Parkland, average ESR and CRP co-orders per week decreased by 25% and average ESR orders alone per week decreased by 27%. Using Medicare reimbursement rates for ESR, estimated payer savings at both hospitals combined was \$62,312.11.

**Conclusion:** Educational and EMR interventions can be particularly effective in reducing redundant laboratory testing to provide greater quality and higher value care for patients.