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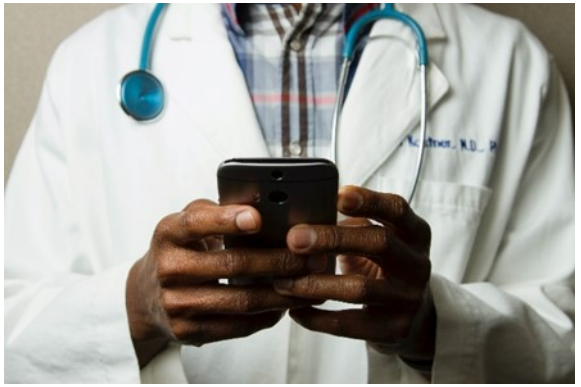
Showcase of Medical Discoveries

Cardiovascular Research



Wednesday
April 21, 2021
10:00 — noon

A Research & Innovation virtual event featuring UAMS Investigators discussing their research and discoveries

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Poster #20

Development of a Novel Extra-corporeal Cardio-pulmonary Support Device for the Immediate Treatment of Out-of-Hospital Cardiac Arrest

Jay K. Bhama, M.D.

Patients with cardiac arrest are managed with chest compressions until they can be transported to a hospital where extra-corporeal mechanical circulation is available. Among patients who survive transport, less then 10% survive to discharge due to organ damage during transport. There is significant need for technology that would allow immediate restoration of circulation in the field.

Current extra-corporeal mechanical circulation devices cannot be used outside the hospital as they require complicated equipment and specialized physicians to institute.

A novel concept for an artificial cardiopulmonary support device that could be utilized by medical first responders would create a disruptive technological advance in emergency medical care.

This proposal posits the development of such a device by applying an innovative, pulse-generating technology towards the development of a novel extra-corporeal cardio-pulmonary support device that would allow deployment by medical first responders. Ultimately, we envision this technology being highly portable for immediate field application in cardiac arrest patients.

Poster #19

The Sensitivity of Graphic Trends in Differentiating Sinus and Supraventricular Tachycardia

Hakan Paydak, M.D.

Telemetry is used to monitor inpatients with arrhythmias. While most of the focus is on the rhythm strip data, a significant utility remains in analyzing the graphic heart rate trends (rectangle or bell shaped curve) to differentiate supra-ventricular tachycardia (SVT) and sinus tachycardia (ST)

Methods: We gathered data from the medical student interpretation of 82 strips of in-hospital cardiac telemetry and asked them to differentiate SVT and ST based on the shape of the graphic trend.

Results: Without graphic trends, 73% of their answers were correct. Diagnostic accuracy improved to 96%, with the addition of the graphic trend. Depending on the telemetry rhythm strip alone, sensitivity to detect SVT was 75%, with 68% specificity. With the addition of the graphical trend, sensitivity improved to 98% and specificity to 100%.

Conclusion: Review of graphical trends allows novice ECG readers to improve the ability to distinguish between ST and SVT.

The UAMS division of Research and Innovation is pleased to sponsor the 30th Showcase of Medical Discoveries focused on cardiovascular research.

Check out the latest collaborative research by outstanding UAMS health professionals and researchers online! https://research.uams.edu

Susan Smyth, MD, Ph.D., Dean, College of Medicine and cardiovascular researcher introduces the CV Showcase.

To augment our efforts to bring you exciting up-to-date research discoveries via the Showcase format, please email Andrea McBryde (amcbryde2@uams.edu) with feedback, comments, and suggestions.

- Research | Innovation

Poster #1

Virtual Atrial Fibrillation Clinic- A Comprehensive Multidisciplinary Telemedicine Approach to Treatment of Atrial Fibrillation

Subodh Devabhaktuni, Khaled Khasawneh, Ming Hwei Yek, Madeline Sorensen, Irion Pursell, Samuel Sears, Hakan Paydak, and Paul Mounsey

Atrial Fibrillation (AF) is the most common heart arrhythmia. Patients with AF may experience distressing symptoms that can negatively impact quality of life. In many patients, symptoms can be managed through lifestyle and behavior modification in addition to medical management.

The primary objective of this research study is to evaluate the effectiveness of a 90 day, three-visit, multidisciplinary strategy to manage AF patients using the UAMS telemedicine platform. The team will include cardiac electrophysiologist, psychologist, dietician, sleep medicine physician, exercise physiologist and a pharmacist. For this pilot project, 50 patients will be identified and followed in a prospective manner. Outcomes will be measured by a battery of well-validated surveys and questionnaires which will be administered to patients at baseline (visit 1) and endpoint (at discharge).

Poster #18

Early Neurodevelopmental Outcomes of Children with Single Ventricle Physiology

Tara Johnson, M.D., Alexa Escapita, B.S., Kelsey Renard Lambou, M.S., Lawrence Greiten, M.D., Brian Reemtsen, M.D., Dala Zakaria, M.D., Heather G Raiees-Dana, B.S.N, R.N., and Kenneth Knecht, M.D.

Background: Congenital heart disease affects 1% of children in the United States. Children with single ventricle physiology (SV) are at some of the highest risks for neurodevelopmental disabilities such as developmental delay, autism, and ADHD.

Methods: As part of a larger study, we implemented a novel protocol using the Capute Scales and General Movement Assessment (GMA) to evaluate early language and motor development in infants with SV physiology.

Results: Over a one-year period, our team studied a patient cohort consisting of ten infants with SV physiology. At their initial visit, all ten infants had typical language development, as measured by the Capute Scales. All ten of the infants had gross motor delay and hypotonia. Four infants were evaluated with the GMA, and their results were normal.

Discussion: In future studies, we will track the neurodevelopment of each participant as they mature. The implementation of this novel protocol will provide early identification and intervention for these high-risk children, allowing access to proven treatments and therapies.

Poster #17

Recent Trends in Atrial Arrhythmia Hospitalizations and Procedure Utilization. Gender Differences in Catheter Ablation Utilization 2016-2018.

Dinesh Voruganti, MD MS; Subodh Devabhaktuni, MD;
Hakan Paydak, MD; and Paul J Mounsey, MD PhD.

Background: Atrial arrhythmias are the most common sustained rhythm disturbances .

Objective: We aim to provide epidemiological insight into atrial fibrillation/atrial flutter (AF/AFl) hospitalizations and the utilization of procedures.

Methods: The National Inpatient Sample (NIS) was used to identify AF hospitalizations (2016-2018). Primary diagnosis code of I480, I481, I483, I484 were used. Procedure codes were used for cardioversion and catheter ablation.

Results: 726,971 hospitalizations were identified (2016-2018) for AF. 72% were paroxysmal AF/AFl, 21.5% for persistent AF, 3.25% for typical AFl, 2.15% for atypical AFl. Hospitalizations continue to increase every year for all arrhythmias (Figure 1). 223,480 in 2016; 242,605 in 2017; 254,835 in 2018. The majority of hospitalizations were in the white race and 65-79 age group. Both males and female were equally represented in this cohort. Catheter ablation utilization slightly increased over three years. A lower catheter ablation rate was reported among females for both AF (5.31% vs. 4.13%) and AFl (46.55% vs. 40.70%), consistently over 3 years.

Conclusion: Gender differences in utilization of ablation requires further study.

Poster #2

Cardiac Fibrosis Following Myocardial Ischemia is Mitigated by Mesenchymal Stem Cell Exosomes

R.A. Kore, Xianwei Wang, Zufeng Ding, J.L. Mehta

There is activation of macrophages and fibroblasts leading to scar formation following an ischemic event in the heart. It is critical to limit the pro-fibrotic remodeling and activate the reparative, regenerative remodeling phase to limit cardiac dysfunction.

Mesenchymal stem cell (MSC) exosomes offer significant protection against ischemia-related systolic dysfunction. Here we studied if MSC exosomes would offer protection against pro-fibrotic events in mouse hearts subjected to acute ischemia (1 hr. left coronary artery occlusion [LCA]) or chronic ischemia (7 days LCA occlusion). Following acute ischemia, there was activation of inflammatory signals, more in the peri-infarct than in the infarct area, in the saline (vehicle)-treated mice. At the same time, there was expression of cardiac remodeling signals (vimentin, collagens-1 and -3, and fibronectin and CD197–the pro-inflammatory macrophage marker), more in the infarct area. MSC exosomes treatment suppressed inflammatory signals during acute as well as chronic ischemia. Exosome treatment promoted pro-regenerative cardiac ECM remodeling (increased CD206 expression), in both the infarct/peri-infarct areas by suppressing fibronectin secretion and by modulating collagen secretion to reduce fibrotic scar formation via altered cellular signaling pathways. Comparison of biological processes of exosome-treated vs saline-treated LCA ligated hearts showed suppression of fibrosis and interstitial fibrosis along with fibrogenesis. Proteomics study revealed intense expression of IL-1β and activation of pro-fibrotic signals in the saline-treated ischemia hearts and their suppression in MSC exosome-treated hearts.

This is the first report to our knowledge on the early molecular events deciphering the molecular and proteomics events to explain MSC exosome-mediated suppression of scar formation in ischemic mouse hearts.

Poster #3

Bleeding Cessation in a Mouse Jugular Vein Puncture Wound Model Is Caused by Extravascular Capping, Not Hole Infill

Brian Storrie, Ph.D.

Based on full 3D electron microscopic characterization of jugular vein puncture wound thrombi, we conclude that bleeding cessation in a true puncture wound occurs from the extravascular side of the thrombus rather than through the formation of a platelet plug that fills the hole. We propose an alternative model of bleeding cessation in which localized platelet aggregates are the starting pedestal upon which all subsequent steps in puncture wound thrombus formation builds, that we term "**Cap and Build**". The extent to which properties differ among systems remains an open question.

Poster #16

Subclavian Artery Thrombus: A Late Complication of COVID 19

Jack Xu, Kirby N Von Edwins, Fares Mashal, Yusuf Hassan

A 36-year-old male with no significant past medical history presented with left hand numbness and shortness of breath. He recovered from COVID 19 two months prior to admission during which time he developed a stroke and completed a five week course of apixaban. On this admission, he was found on computed tomography of his chest to have a nonocclusive filling defect of his left subclavian artery. He was started on apixaban and aspirin and his symptoms improved.

The etiology of the subclavian thrombus was thought to be related to his COVID 19 infection from which he had recovered. In combination with an inflammatory state and prolonged immobilization of critically ill COVID 19 patients, these mechanisms may be the etiology of arterial thromboembolisms.

We think that clinicians should consider a longer term post discharge thromboprophylaxis for high risk hospitalized patients with COVID 19 who have a low risk of bleeding.

Poster #15

Machine Learning and Deformable Model-Based 4D Characterization of Cardiac Dyssynchrony from MRI

Subhi Al Aref, M.D.

Cardiac function can be adversely affected by many diseases, including heart failure (HF) and dyssynchrony, which can worsen the symptom of HF. However, while imaging methods such as magnetic resonance imaging (MRI) can provide good images of the moving heart, conventional clinical quantitative analysis of cardiac function is largely limited to global function analysis, with only qualitative and subjective characterization of regional function. Recent advances in machine learning (ML) approaches to image analysis are promising as a new means to speed up the processing of cardiac images, as well as analyze the underlying regional motion patterns. In this research study, we seek to develop new ML-based methods which will incorporate information on the specific cardiac motion factors that lead to classification of different disease states in dyssynchrony. Our hypothesis is that with these new ML-based methods for cardiac motion analysis, we will discover and evaluate, significant quantitative correlations between types of cardiac dyssynchrony and cardiac resynchronization therapy (CRT) outcomes. The discovery of these correlations will allow us to prospectively validate them in future clinical studies.

Poster #4

CardioWellness in Communities

Pursell, I., Dugyala, S., Ha, Y., Sorensen, M., Terry, A., and Mounsey. J.

Reducing CVD outcome disparities in rural Arkansas requires expertise and capacity to 1) identify and address social, environmental, and other issues that contribute to CVD outcome inequality at the community-level, and 2) improve the access and quality of medical care, including CVD self-management in target communities. The UAMS Cardiology Division established Cardio–Wellness in Communities (CWC), the first-in-nation primary cardiovascular disease prevention program domiciled in an academic cardiology department, led by a public health practitioner, to design and implement a novel approach to CVD prevention. Integration of community-level prevention and CVD medical management allows project investigators to examine the tightly interwoven relationship between social determinants of health and CVD and deploy intervention measures that improve CVD outcomes in rural underserved populations. The funding for a CWC pilot project in three Eastern Arkansas counties is provided by the Office of the Assistant Secretary for Health, US Department of Health and Human Services.

Poster #5

Sentrin/SUMO, Seizure, and Sudden Death

Edward T.H. Yeh, MD, FACC, Hui-Ming Chang, MD, MPH

Sudden unexpected death in epilepsy (SUDEP) accounts for 1.16 death per 1000 individuals with epilepsy. The causes for SUDEP are not well understood and treatment options are limited. We have generated a new model of SUDEP caused by an abnormality in the post-translational modification of the Kv7.2/Kv7.3 potassium channel due to partial deficiency of Sentrin/SUMO-specific protease 2 (SENP2). The SENP2-deficient mice developed spontaneous seizure at 4 weeks of age and died by 8 weeks with 100% penetrance. SENP2 deficiency results in an increase of SUMO-modification in Kv7,2/Kv7.3 proteins, leading to reduction of M current, which increases neuronal membrane excitability. Furthermore, seizure triggers high-degree AV block and cardio-respiratory arrest. We have used multi-modality monitoring, including EEG, ECG, video recording, and plethys-mography, to assess brain activity, cardiac rhythm, and respiration following seizure in the SENP2-deficient mice to determine the cause of death and to identify new preventive strategy for SUDEP.

Poster #14

Creating a No Power Auscultation Device for Remote Patient Monitoring

Joseph Sanford, M.D., Kevin Sexton, M.D., Adria Abella Villafranca, Nikiya Simpson, and Fuad Habash, M.D.

Background: With COVID 19 **and the fact that 655,000 Americans are dying from heart disease** each year there is a need for an inexpensive and accessible stethoscope for remote auscultation. The IDHI Innovation team developed ClipBeat, an inexpensive mechanical stethoscope device that attaches to any smartphone or tablet.

Methods: A 3D printed stethoscope CAD model (ClipBeat) was developed along with a smartphone application for heart sound classification. Using an electronic Littman stethoscope and Clip-Beat, heart sounds were recorded from a SAM II Mannikin. The recorded sounds were added to a RedCap survey. Multiple physicians, and medical students listened to the sounds on the blind survey and submitted answers about sound quality and diagnosis.

Results and Conclusion: ClipBeat had better results on sound quality compared to the Littman stethoscope. ClipBeat sound performance was determined to be sufficient for physicians to use the device for remote auscultation on multiple platforms.

Poster #13

Vitamin D Receptor Signaling Prevents the Adverse Actions of Glucocorticoid Excess in Bone, Skeletal Muscle, and the Heart by Interfering with MuRF1

Amy Y. Sato, Meloney Cregor, David L. Halladay, Munro Peacock, Monte S. Willis, and Teresita M. Bellido

Glucocorticoid (GC) excess adversely affects the musculoskeletal system and heart. We found that GCs upregulate in bone, skeletal muscle, and left ventricles (LV) expression of proteasomal degradation inducer MuRF1, and that MuRF1 upregulation is prevented by $1,25D_3$ (calcitriol) *ex vivo*. These findings provide a targetable pathway to block GC actions. We then investigated whether Vitamin D Receptor (VDR) activation blocks GC-induced MuRF1 to prevent tissue loss and dysfunction. *In vivo*, $1,25D_3$ (50ng/kg/d 5x/wk) prevented the loss of bone and skeletal muscle, and prevented LV (systole and diastole) thinning induced by GC (2.1 mg/kg/d prednisolone, 8 wks, N=10-12 mice). GC increased LV volume at systole, reduced ejection fraction, and decreased fractional shortening, which was prevented by $1,25D_3$. GC or $1,25D_3$ did not alter heart mass or rate. GC increased MuRF1 expression, but not in $1,25D_3$ treated mice. These findings demonstrate that VDR activation blocks GC-induced MuRF1 upregulation, tissue loss, and dysfunction.

Poster #6

PCSK9 Regulates Cardiac Fibrosis in Chronic Myocardial Ischemia: Results of Preliminary Studies

Zufeng Ding, Xianwei Wang, Rajshekhar A Kore, and Jawahar L Mehta

PCSK9 degrades low-density lipoprotein cholesterol (LDL) receptors and subsequently increases serum LDL cholesterol. Clinical trials show that inhibition of PCSK9 efficiently lowers LDL cholesterol levels and reduces cardiovascular events, including myocardial infarction. We have recently shown that PCSK9 is secreted by hypoxic cardiomyocytes following left coronary artery (LCA) ligation and determines the extent of myocardial infarct. Cardiac fibrosis is an independent risk factor for heart failure and a leading cause of death in disability. Unfortunately, current therapies treating diastolic dysfunction have been of no avail. Based on this, we hypothesized that PCSK9 released during ischemia may be regulating cardiac fibrosis during chronic myocardial ischemia.

We studied PCSK9's role in regulating cardiac fibrosis *in vitro* (cultured human cardiac fibroblasts) and in *in vivo* (mice with chronic myocardial ischemia [CMI] created by LCA ligation for 1 week). *In vitro* studies showed recombinant PCSK9 (hrPCSK9) treatment significantly induced expression of $TGFb_1$ and fibrosis markers, such as fibronectin and collagen-1, in a dose-dependent manner. Further, hrPCSK9 treatment increased endoplasmic reticulum stress. Masson's trichrome staining of ischemic hearts showed intense fibrosis in the wild-type mice. The extent of fibrosis was substantially reduced in mice with PCSK9 gene deletion ($PCSK9^{-/-}$) despite LCA ligation (**Figure**).

Our data suggests that PCSK9 regulates cardiac fibrosis during CMI. Further studies will focus on the role of cardiac-secreted PCSK9 in regulating proteomics of cardiac fibrosis and cardiac diastolic dysfunction. These observations advance understanding of cardiac diastolic dysfunction during CMI.

Poster #7

Genome-wide DNA Methylation Signatures Predict the Early Asymptomatic Doxorubicin-induced Cardiotoxicity in Breast Cancer

Michael A. Bauer, Valentina K. Todorova, Ping-Ching Hsu, Jeanne Wei, L. Joseph Su, Annjanette Stone, Weleetka Carter, and Issam Makhoul

This study had two aims: Aim 1: to examine whether the DNA methylation profile of peripheral blood cells (PBCs) induced by the first cycle of DOX-based chemotherapy can predict the risk of cardiotoxicity; and Aim 2 to determine if there are pre-treatment methylation signatures at baseline that will predict the risk of cardiotoxicity. The results from this study provide evidence that the DNA methylation profile of peripheral blood cells has the potential to predict the risk of DOX-induced cardiotoxicity. The important finding was that the extent of methylation at baseline correlated with the post-DOX LVEF reduction, indicating that it may have the potential to predict the subsequent development of cardiotoxicity. This has the potential to further the goal of personalized medicine and tailoring individual treatment to reduce the chances of adverse effects.

Poster #12

Can Structural Abnormalities of Cardiac Amyloidosis be Reversed? The Arkansas experience

Srikanth Vallurupalli, M.D.

Cardiac amyloidosis, a restrictive cardiomyopathy due to abnormal protein deposition, carries a poor prognosis. While significant advances in treatment of this light chain dyscrasia have occured, conventional wisdom is that once cardiac structural abnormalities occur, they are irreversible. UAMS has been at the forefront of the fight against light chain dyscrasias such as amyloidosis with a multi-disciplinary team of oncologists, cardiologists and radiologists who have developed significant expertise in the diagnosis and treatment of this condition. Using state-of-the-art imaging techniques, we have observed structural and functional improvement in some patients with this condition. We will showcase imaging techniques, as well as data that illustrate these findings.

Poster #11

Early Feasibility Study aimed to Assess Safety and Performance of the Leaflex™ Performer in the Treatment of Symptomatic Severe Aortic Stenosis

Gaurav Dhar, Subhi Al'Aref, Srikanth Vallurupalli, Jay Bhama

Objective: To demonstrate the safety and performance of aortic valve treatment with the Leaflex™ Performer.

Primary efficacy endpoint – change in AVA measured by echocardiography before treatment with the Leaflex™ (within 7 days prior to index procedure) and after treatment with the Leaflex™ (within 3 days post index procedure).

Background: Calcific or degenerative Aortic Stenosis (AS) is characterized by a tricuspid aortic valve with fibrotic thickening of the valve leaflets and the formation of calcium deposits throughout the valve leaflets. This reduces leaflet's mobility and flexibility decreasing valve opening during systole.

Patients are not candidates for a permanent implant (SAVR or TAVR) due to either co-morbidities, age or short life expectancy. These patients are currently treated by Balloon Valvuloplasty but that is limited by short durability of its therapeutic effect.

The Leaflex™ is a 16Fr catheter, introduced trans-femorally, is designed to create scoring lines and score the calcific deposits within the leaflets causing the clinical syndrome of aortic stenosis.

The Leaflex™ increases leaflets pliability and mobility thereby increase aortic valve area. Treatment with this new device is potentially more effective and durable than BAV, which has not been associated with acceptable long-term clinical outcomes.

Poster #8

Prospective Evaluation of the Strategy of Functionally Optimized Coronary Intervention

Barry F. Uretsky, MD; Shiv K Agarwal, MD; Srikanth Vallurupalli, MD; Malek Al-Hawwas, MD; Rimsha Hasan, MD; Kristin Miller, RN; and Abdul Hakeem, MD

Background: Long-term outcomes after percutaneous coronary intervention (PCI) relate in part to residual ischemia in the treated vessel, as reflected by post-PCI fractional flow reserve (FFR). The strategy of FFR after PCI and treatment of residual ischemia— known as ***functionally optimized coronary intervention (FCI)***—may be feasible and capable of improving outcomes.

Methods and Results: Feasibility and results of FCI using an optical-sensor pressure wire were prospectively evaluated in an all-comer population with 50% to 99% lesions and ischemic FFR (≤0.80; ClinicalTrials.gov identifier NCT03227588). FCI was attempted in 250 vessels in 226 consecutive patients. The PCI success rate was 99.6% (249/250 vessels). FCI technical success—that is, performance of FFR before and after PCI and PCI itself using the FFR wire—was 92% (230/250 vessels). Incidence of residual ischemia in the treated vessel was 36.5%. Approximately a third of these vessels (34.5%, n=29) were considered appropriate for further intervention, with FFR increasing from 0.71±0.07 to 0.81±0.06 (P<0.001). Pressure wire pullback showed FFR ≤0.8 at distal stent edge was 7.9% and 0.7% proximal to the stent. FFR increase across the stent was larger in the ischemic than in the non-ischemic group (0.06 [interquartile range: 0.04–0.08] versus 0.03 [interquartile range: 0.01–0.05]; P<0.0001) compatible with stent underexpansion as a contributor to residual ischemia.

Conclusions: **FCI is a feasible and safe clinical strategy** that identifies residual ischemia in a large proportion of patients undergoing angiographically successful PCI. Further intervention can improve ischemia. The impact of this strategy on long-term outcomes needs further study.

Poster #9

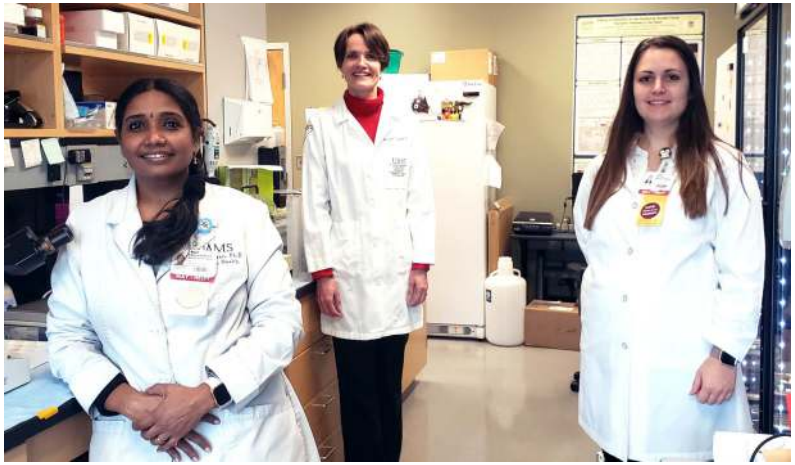
Inflammation and Platelets in Chronic Kidney Disease

Nishank Jain, MD, MPH, Adam Corken, PhD,
John M Arthur, MD, PhD and Jerry Ware, PhD

Platelets are capable of influencing the distribution of monocyte sub-groups in circulation. Cross-talk between the platelet surface receptor, glycoprotein (GP)Ib-IX receptor, and a counter-receptor on the leukocyte, integrin Mac-1 impacts monocyte populations, which in turn effects the release of cytokines and thrombogenic tissue factor; thus, a dynamic platelet-leukocyte axis modulates inflammatory response. In animal models with dysfunctional GPIb-IX, there is a heightened inflammatory response when induced with sepsis, including a higher proportion of nonclassical monocytes, reduced platelet-leukocyte aggregates and, increased release of inflammatory cytokines (e.g., TNF-α, IL-6and IL-1β). Chronic kidney disease (CKD) is a pro-inflammatory state. It remains unclear whether platelets play any role in modulating inflammation in CKD state. Our goal was to compare monocyte subcategorization, platelet-leukocyte aggregates and plasma TNF-alpha levels between CKD and controls. We compared the proportion of monocyte (CD14+/CD66b-) subpopulations in patients with CKD and controls; leukocytes with CD42b fluorescence (platelet-monocyte aggregates) not on antiplatelet therapy; and, plasma TNF- levels with 2 weeks of antiplatelet therapy with aspirin and a $P2Y_{12}$ inhibitor. CKD patients had a higher proportion of the non-classical monocytes ($CD14^{Low}/CD16^{High}$); reduced levels of platelet-leukocyte aggregates; and plasma TNF-α levels in each group were >50% lower than at baseline. Our preliminary findings suggest CKD patients bear striking similarities to previous work in mice wherein inflammatory dysregulation was attributed to the disruption of the GPIb-IX in the platelet-leukocyte axis that resulted in higher cytokine levels, reduce platelet-leukocyte aggregates and higher expression of the non-classical monocytes. Future studies need to investigate whether a pro-inflammatory state in CKD is a result of disrupted platelet-leukocytes interactions via the GPIb-IX/Mac-1.

Poster #10

Cardiovascular Effects of Exposure to Ionizing Radiation



Viji Mohanseenivasan, Ashley Nemec-Bakk, Kim Krager,
and Marjan Boerma
College of Pharmacy, Division of Radiation Health

During radiation therapy of tumors in the chest of some patients, part of the heart may be exposed to radiation which can have long-term effects on cardiovascular health. Moreover, accidental radiation exposure can lead to cardiovascular disease, and there is a concern about potential adverse effects of ionizing radiation when astronauts travel in deep space. Our laboratory uses animal models that mimic each of these three scenarios of radiation exposure with the goal of determining biological mechanisms by which radiation has adverse effects in the heart and test potential intervention countermeasures.