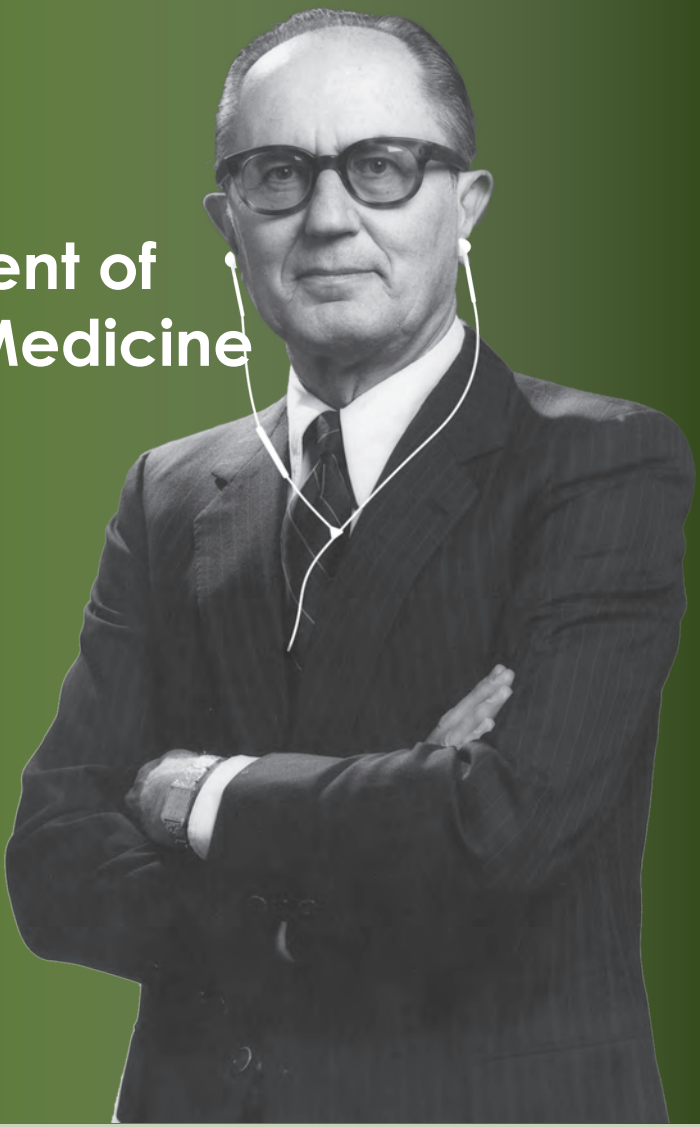
The

Department of Internal Medicine

Presents



The 5thAnnual

Donald W. Seldin, M.D. Research Symposium

May 21, 2020

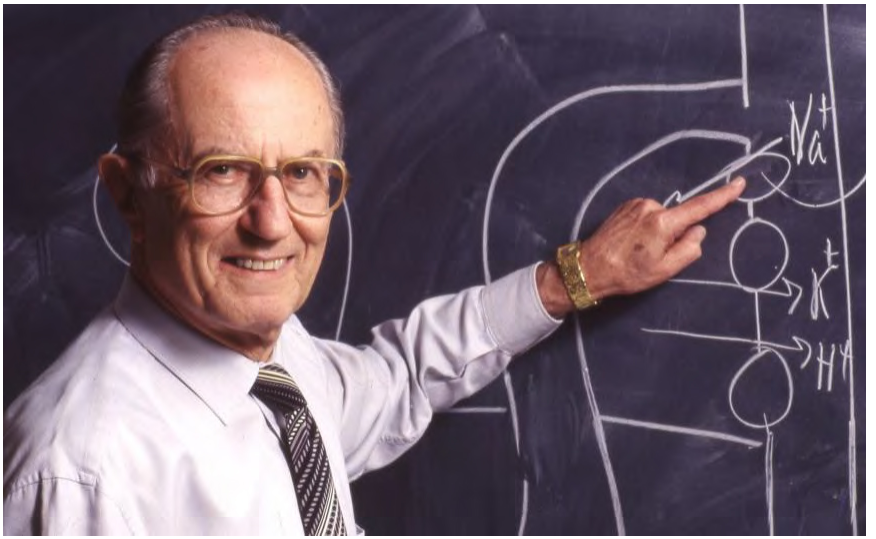
Message from Thomas J. Wang, M.D.

Dr. David Johnson and the Chief Residents launched the Donald W. Seldin Research Symposium in 2016. This conference has been a unique opportunity to highlight 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 will feature more than 100 poster presentations, spanning the entire range of research, from fundamental biology to quality improvement.

As we gather this year to celebrate the wonderful collaborations between trainees and faculty, we also mark the 100th anniversary of Dr. Seldin's birth. The beginning of Dr. Seldin's tenure at UT Southwestern is a tale that has been told frequently, but bears repeating. In 1951, Dr. Seldin arrived in Dallas to find that the entire campus consisted of a set of military barracks and a brick building in disrepair. By the middle of 1951, Dr. Seldin was the sole remaining full-time faculty member in the department, and thus its chair by default. He built the Department of Internal Medicine from those humble beginnings by emphasizing what he perceived as the institution's greatest resource: its trainees. By personally selecting the most promising talent and sending them across the country to study with the best scientific minds of the time, Dr. Seldin created a faculty of staggering distinction and accomplishment. The list includes Daniel Foster, Michael Brown, Joseph Goldstein, Jean Wilson, Floyd Rector, Norm Kaplan, and many others. As one example of his vision, he encouraged Dr. Goldstein to study genetics and supported his collaboration with Dr. Brown, leading to a legendary partnership that has changed science and medicine.

Throughout his 37-year tenure as Chair, Dr. Seldin never wavered in his advocacy for the clinician scholar. As academic medicine evolved with increasing clinical demands, Dr. Seldin ensured that research remained a cornerstone of the tripartite academic mission. 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."

While the symposium this year will be virtual, it will not be any less impressive in the quality and breadth of the work that will be presented. Indeed, Dr. Seldin would be proud of the resilience and determination our trainees in pursuing their scholarly activities even during these challenging times.



"An institution is The Lengthened Shadow of One Man."

-Ralph Waldo Emerson

The biomedical research pedigree of UT Southwestern Medical Center is as storied and accomplished as that of other prominent institutions more than twice our age. Those who lead UT Southwestern today can point to one figure who, more than anyone else, was the singular 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 endlessly throughout the years, but bears repeating. In 1951, Dr. Seldin arrived in Dallas from Yale 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, Dr. Seldin built the Department of Medicine upon the foundation that still underpins the strength of UT Southwestern today: its trainees. By personally selecting the most promising talent, sending them across the country to study with the best scientific minds of their time with the promise to return, Dr. Seldin's faculty tree blooms with staggering 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 suggestion of partnership with Michael Brown, culminated in their Nobel Prize in Physiology or Medicine.

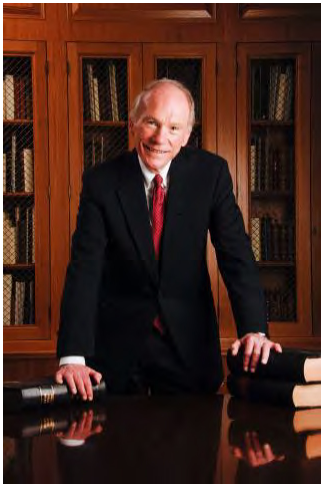
Throughout his 37-year tenure as Chair, Dr. Seldin never wavered in his advocacy that anchored the Department to the mission of the clinical scholar – advancing a fundamental understanding of human health, disease and its treatment via research. During the evolution of academic medicine and its increasing clinical demands, Dr. Seldin's leadership ensured that research flourished as a key emphasis in the tripartite academic 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 paradigm of professions is surely the medical profession. We, all of us, are inheritors of the activities of people who have proceeded us, and who have devoted themselves to the mitigation of suffering".

- *Donald W. Seldin*

Without his guiding hand, it is no stretch to believe that UT Southwestern would have neither achieved its lofty heights in world-renowned research, nor would have trained so many gifted and successful physicians still serving in Texas and across the United States. Simply put, there is and was no UT Southwestern Medical Center without Donald W. Seldin.

5th Annual Donald W. Seldin, M.D. Research Symposium



Daniel W. Foster, M.D.
1930-2018

The third of five chairs of the Department of Internal Medicine at UT Southwestern, 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 3-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 on his watch.

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. He served as Headmaster of the Academic Colleges at UT Southwestern, President of the Academy of Medicine, Engineering, and Science of Texas, and was 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.

Presentation #1

Title: Homotypic Fusion Generates Multinucleated Cardiomyocytes in the Postnatal Murine Heart

Presenter: Shah Ali

Authors: Shah Ali, MD; Ivan Menendez-Montes, PhD; Jane Warshaw, BA; Feng Xiao, PhD; Hesham Sadek, MD, PhD

Faculty Mentor(s): Hesham Sadek

Abstract:

Multinucleation is an important and prominent phenotype of postnatal mammalian cardiomyocytes, and its occurrence in early life correlates with the loss of regenerative potential in mice. This phenomenon is believed to be the result of mitosis followed by cytokinesis failure, although direct proof of this mechanism has not been provided for every single adult cardiomyocyte. Moreover, many multi-nucleated cells in other organs are formed after homotypic cell fusion. Although heterotypic cell fusion between myocytes and circulating cells has been described as a rare event, it is not known whether homotypic myocyte fusion occurs and if it can lead to bi- and multi-nucleation. We developed a novel mouse model wherein multi-color fluorescent protein reporter expression occurs stochastically only in cardiomyocytes (Myh6-MerCreMer;Rosa26-Confetti). Using pulse-chase experiments during development and at birth, we show that a small fraction of cardiomyocytes fuses with other myocytes to generate binucleated and multinucleated cells; we calculate a fusion rate of at least 2%, although this reflects the lower limit of the phenomenon due to technical limitations of our model. We reveal that this process occurs in the first week of life and is stable at one month of age. Our findings suggest a revision of the dogma in postnatal cardiac development by providing another mechanism for multinucleation of cardiomyocytes. Future experiments will address whether fusion is a reversible process and whether fused myocytes can undergo abscission in response to physiological or pathological cues.

Presentation #2

Title: Inhibition of Cbl-b prevents CD8+ T cell exhaustion and promotes CAR-T cell function

Presenter: Jitendra Kumar

Authors: Jitendra Kumar, PhD; Amir Singh, PhD; Ritesh Kumar, PhD; Mahesh Kathania, PhD; Elviche L. Tsakem, MS; Matthew J. Riese, PhD; Prithvi Raj, PhD; Marco Davila, MD; Venuprasad Poojary, PhD

Faculty Mentor(s): Venuprasad Poojary

Abstract:

Background: Chimeric antigen receptor (CAR)-T cell therapy is an emerging option for cancer treatment, but its efficacy is limited, especially in solid tumors. This is partly because the CAR-T cells become dysfunctional and exhausted in the tumor microenvironment (TME). Exhausted T cells exhibit progressive loss of effector function (expression of IFN-γ, TNF-α and tumor cell killing) and express inhibitory receptors (PD1, Tim3, LAG3 etc.). However, our understanding of the key pathways responsible for impaired function of exhausted cells remain unclear and their dissection will be necessary to overcome CAR-T cell exhaustion.

Methods: Published RNA-sequencing data of tumor infiltrated CD8+ lymphocytes(TILs) has led to identification of Cbl-b as a potential target. The sequencing data was validated using syngeneic MC38 colon cancer model. To analyze the in vivo role of Cbl-b in T cell exhaustion, we analyzed tumor growth, % PD1+Tim3+ cells, and expression of effector cytokine was analyzed in Cbl-b+/+ and Cbl-b-/- mice. To evaluate the therapeutic potential of Cbl-b depletion, we generated a new CAR construct, hCEAscFv-CD28-CD3ζ. GFP, that recognizes human carcinoembryonic antigen(CEA). Cbl-b+/+ and Cbl-b-/- CEA-CAR T cells were generated by retroviral transduction. Rag-/- mice bearing MC38-CEA cells were injected with Cbl-b+/+ and Cbl-b-/- CEA-CAR T cells, tumor growth, % PD1+Tim3+ cells, expression of effector cytokine was analyzed.

Results: Our results show that the E3 ubiquitin ligase Cbl-b is upregulated in exhausted (PD1+Tim3+) CD8+ TILs. CRISPR-Cas9-mediated inhibition of Cbl-b restores the effector function of exhausted CD8+ TILs. Importantly, the reduced growth of syngeneic MC38 tumors in Cbl-b-/- mice was associated with a marked reduction of PD1+Tim3+ CD8+ TILs. Depletion of Cbl-b prevented CAR-T cell exhaustion resulting in reduced MC38-CEA tumor growth, reduced PD1+Tim3+ cells and increased expression of IFN-γ, TNF-α and increased tumor cell killing.

Conclusions: Our studies demonstrate that deficiency of Cbl-b overcomes endogenous CD8+ T cell exhaustion and deletion of Cbl-b in CAR-T cells render them resistant to exhaustion. Our results could facilitate the development of efficient CAR-T cell therapy for solid tumors by targeting Cbl-b. This will be an attractive strategy as this would mimic the combination of check-point inhibitors (anti-PD1 and anti-CTLA4 antibodies) and CAR-T cells.

Presentation #3

Title: Gut microbiota contributes to spontaneous colitis in E3 ligase Itch-deficient mice

Presenter: Mahesh Kumar Kathania

Authors: Mahesh Kathania, PhD; Elviche L. Tsakem, MS; Arianne Thiess, PhD; and K. Venuprasad, PhD

Faculty Mentor(s): Venuprasad Poojary

Abstract:

Background: Inflammatory bowel diseases (IBDs) are associated with complex shifts in microbiota composition. However, it remains unclear whether specific subsets of commensal bacteria induce IBDs in genetically susceptible hosts. Our previous studies have shown that deficiency of the E3 ubiquitin ligase Itch leads to spontaneous colitis in mice and a loss of function mutation in Itch gene leads to enteropathy in humans. Here, we investigated if the gut microbes trigger colitis in Itch-/- mice.

Methods: 16S rRNA sequencing was performed using fecal pellets of Itch+/+ and Itch-/- mice to analyze alterations in the gut microbiota. The effect of depleting microbiota on spontaneous colitis in Itch-/- mice was analyzed by antibiotics treatment. Transferability of colitis via Itch-/- microbiota into Itch+/+ mice was analyzed by fecal transfer of antibiotic treated Itch+/+ mice with Itch-/- microbiota. To investigate if Bacteroides strains that are expanded in Itch-/- mice triggers colitis, antibiotics treated mice were reconstituted with these strains.

Results: Our results show that deficiency of the E3 ligase Itch, which leads to spontaneous colitis and rectal prolapse, is associated with alteration of the gut microbiota. 16S rRNA sequencing showed expansion of colitogenic Bacteroides sp. in Itch-/- mice. Treatment with broad-spectrum antibiotics substantially reduced colonic inflammation in Itch-/- mice. Microbiota of Itch-/- mice failed to induce spontaneous colitis upon transfer to Itch+/+ mice, but aggravated chemically induced colitis. Further, we found that B. vulgatus, which is expanded in Itch-/- mice, was sufficient to induce colon inflammation in Itch-/- mice.

Conclusions: Our results demonstrate that Itch has an essential role in shaping a protective assembly of gut bacterial communities and suggest that manipulation of dysbiosis is a potential therapeutic approach in the treatment of IBDs. This work was supported by grants from the National Institutes of Health (R01-DK115668-01), and Cancer Prevention Research Institute of Texas (RP160577, RP190527).

Presentation #4

Title: Brain Fibroblast Growth Factor Receptor 4 Activation Is Involved in High Phosphate Diet-Induced Skeletal Muscle Reflex Overactivation in Rats

Presenter: Han Kyul Kim

Authors: Han-Kyul Kim, PhD; Masaki Mizuno, PhD; Gary Iwamoto, PhD; Rie Ishizawa, PhD; Jere Mitchell, MD; Orson Moe, MD; Scott Smith, PhD; Wanpen Vongpatanasin, MD

Faculty Mentor(s): Wanpen Vongpatanasin

Abstract:

Background: An increasing number of studies have reported a deleterious role of inorganic phosphate (Pi), which is widely used as a preservative in processed foods, in increasing cardiovascular disease risk. Previously, our laboratory has demonstrated that dietary Pi excess induces exaggerated blood pressure and renal sympathetic nerve activity (RSNA) responses to muscle contraction (i.e. exercise) in otherwise normal rats. These abnormalities have been further shown to be mediated by an overactive skeletal muscle exercise pressor reflex (EPR). However, the mechanism underlying the hypertension and sympathetic overactivity generated by excess Pi consumption remains unclear. High Pi diet is known to induce release of Fibroblast Growth Factor (FGF) 23, a bone-derived phosphaturic hormone, to maintain normal Pi balance. Evidence suggests that FGF23 is present in the central nervous system, and FGF receptors (FGFRs) are expressed in the brainstem. Given that the EPR activates cardiovascular control centers within the brainstem during muscle contraction, we hypothesized that high Pi diet-induced EPR overactivation is mediated by brain FGFR stimulation.

Methods: We measured mean arterial pressure (MAP) and RSNA responses to EPR activation before and after intracerebroventricular administration of a selective FGFR4 inhibitor BLU9931 in decerebrate Sprague-Dawley rats fed either a normal Pi (NP) diet containing 0.6% Pi (n=6) or a high Pi (HP) diet containing 1.2% Pi (n=6) for three months.

Results: Compared to NP rats, HP rats showed markedly increased cerebrospinal fluid FGF23 levels (7.2±0.8 vs. 8.3±0.9 pM, $P<0.01$). In brainstem, level of calcineurin A involved in FGFR4-mediated downstream signaling was 31 % higher in HP animals than those in NP animals ($P=0.03$). Intracerebroventricular BLU9931 administration significantly attenuated the potentiated MAP (Δ=41±14 vs. 20±14 mmHg, $P<0.01$) and RSNA (Δ=112±70 vs. 65±46 %, $P<0.01$) responses to EPR stimulation by electrically-induced hindlimb muscle contraction in HP rats, but did not significantly affect the responses in NP rats (ΔMAP=11±3 vs. 7±4 mmHg and ΔRSNA=21±17 vs. 15±5 %).

Conclusions: Our findings suggest that activation of brain FGFR, particularly FGFR4, contributes significantly to high Pi diet-induced EPR overactivity. Importantly, the results implicate dietary Pi as a potential therapeutic target for improving/preventing the abnormally large blood pressure and sympathetic responses to exercise.

Presentation #5

Title: Effect of haptoglobin genotype on anacetrapib-mediated cholesterol efflux capacity in diabetics with coronary heart disease: a substudy of the DEFINE trial

Presenter: Mark Metzinger

Authors: Mark P. Metzinger, MD; Jaskeerat Gulati, BA; Suzanne Saldanha, PhD; Ayea El-Ghazali, MS; Colby Ayers, MS; Kershaw Patel, MD; Parag Joshi, MD; Anand Rohatgi, MD, MSCS

Faculty Mentor(s): Anand Rohatgi

Abstract:

Background: Macrophage Cholesterol efflux (CEC), the initial step of reverse cholesterol transport, is inversely associated with coronary heart disease (CHD). Anacetrapib, the only cholesterylester transfer protein (CETP) inhibitor to both increase high density lipoprotein cholesterol levels and reduce CHD, also increases CEC in those with CHD. Copy number variants (CNV) in haptoglobin (Hp) (specifically the "2-2" genotype) are linked to impaired CEC in diabetics. The objective of this study is to determine the effect of Hp CNV status on anacetrapib-mediated CEC in those with diabetes and CHD.

Methods: This study included 574 participants with CHD along with baseline and 24-week follow-up data (332 with diabetes) from the DEFINE trial, a randomized placebo-controlled trial of anacetrapib in participants with CHD on statin therapy. CEC was measured using J774 macrophages, BODIPY fluorescent cholesterol, and apolipoprotein B (ApoB)-depleted plasma and normalized to efflux elicited by pooled human plasma. Hp CNV status was determined using a commercially available ELISA assay. Each participant was identified as having the "1-1" (normal), "2-1" (heterozygous for abnormal "2" allele), or "2-2" (homozygous for abnormal "2" allele) CNV genotypes. Multivariable adjusted linear regression analyses were performed to evaluate the independent associations between CEC and Hp CNV status.

Results: Similar baseline characteristics were seen between haptoglobin CNV groups. Anacetrapib was associated with a significant increase in CEC in diabetics with the 1-1 genotype but not in those with the combined 2-1/2-2 genotypes after adjustment for baseline CEC with a significant interaction (p for interaction = 0.02). In those without diabetes, no significant interaction was seen (p for interaction = 0.36). The effect of anacetrapib on reducing levels of ApoB was greater in diabetics with the Hp "2" allele; no difference by Hp status was seen for the other lipids.

Conclusions: Among patients with diabetes and CHD, the effect of anacetrapib on CEC was significantly blunted in those with the Hp "2" allele whereas it was preserved among those homozygous for the normal "1" allele. The ApoB lowering effect of anacetrapib was enhanced in those with the Hp "2" allele.

Presentation #6

Title: Deubiquitination of NLRP6 by Cyld Critically Regulates Intestinal Inflammation

Presenter: Sandip Mukherjee

Authors: Sandip Mukherjee, PhD; Tsakem Lenou Elviche, MS; Ritesh Kumar, PhD; Fotis Loakeimidis, PhD; Dimitris L. Kontoyiannis, PhD; George Mosialos, PhD; Arianne L. Theiss, PhD; Richard Flavell, PhD; and K. Venuprasad, PhD

Faculty Mentor(s): K. Venuprasad

Abstract:

Background: NLRP6, which is a component of NLRP6-inflamamsome, is highly expressed in the intestine and plays critical roles in maintaining gut homeostasis. NLRP6 forms a complex with ASC and Caspase 1 and facilitates the cleavage of pro-IL-18 into biologically active mature IL-18. Since, increased IL-18 is strongly associated with bowel diseases (IBDs), a clear understanding of regulation of NLRP6 is essential to develop effective therapeutic strategies.

Methods: To gain new insights into regulation of NLRP6, we performed mass spectrometry analysis using the lysate of colonic mucosa of mice infected with Citrobacter rodentium. Cyld-NLRP6 association was analyzed by co-immunoprecipitation and GST-pull down assays. To investigate if Cyld deubiquitinates NLRP6, ubiquitination assay was performed using control and Cyld mutant that lacks enzymatic activity. To gain in vivo evidence for NLRP6-Cyld-IL-18 pathway we generated Cyld-/-NLRP6-/- and Cyld-/-IL-18-/- mice and analyzed colonic inflammation in these double deficient mice. Further, we performed correlation analysis between Cyld expression and active IL-18 level in ulcerative colitis patient's samples.

Results: Our results show that Cyld expression is downregulated in approximately two third ulcerative colitis patient's mucosal biopsies. Our results show that Cyld prevents excessive IL-18 in the colonic mucosa by deubiquitinating NLRP6. We show that deubiquitination inhibits the NLRP6/ASC complex and regulates the maturation of IL-18. Cyld deficiency in mice resulted in elevated levels of active IL-18 and severe colonic inflammation following gavage with Citrobacter rodentium. Further, in ulcerative colitis patients, the level of active IL-18 was inversely correlated with Cyld expression.

Conclusions: Our studies have uncovered a novel mechanism by which NLRP6-mediated IL-18 maturation is modulated to prevent colonic inflammation. Our data also suggest that K63-linked ubiquitination promotes NLRP6 inflammasome activation by facilitating NLRP6/ASC complex formation. A defect in the deubiquitination of NLRP6 results in elevated IL-18 and severe colitis. These new findings could pave the way to identify new therapeutic approaches for the prevention and treatment of IBDs. This work was supported by grants from the National Institutes of Health (R01-DK115668-01), and Cancer Prevention Research Institute of Texas (RP160577, RP190527).

Presentation #7

Title: Repeatability of hyperpolarized pyruvate metabolism measurement in human heart

Presenter: Katarina Yaros,

Authors: Katarina Yaros, MD; Jae Mo Park, PhD; Craig Malloy, MD; Jeffrey Algers, Tarique Hussain, and Vlad Zaha, MD,PhD

Faculty Mentor(s): Vlad Zaha

Abstract:

Background: Dissolution dynamic nuclear polarization (DNP) is a novel method that increases more than 10,000-fold the signal-to-noise ratio (SNR) allowing detection of molecules much less prevalent than water in human body. It permits study of metabolic changes within tissues, including flux via pyruvate dehydrogenase (PDH), which has been shown to play a role in adaptation to physical activity, energy sources, and various disease states. We employ DNP coupled to MR to detect hyperpolarized [1-13C] pyruvate and its metabolites within human heart in vivo and show that metabolite signal over time is well described by a single compartment first-order kinetic model and that out pipeline is highly repeatable.

Methods : HP[1-13C] pyruvate was infused intravenously into five human subjects. Dynamic spectroscopic data was acquired for 1-13C-labeled pyruvate, alanine, lactate, and bicarbonate at two consecutive times for each subject. Imaging data was exported into MATLAB. We employed a first-order kinetic model to fit the signal for the hyperpolarized metabolites assuming bidirectional flow between pyruvate and lactate as well as pyruvate and alanine. A gamma variate input function was used to model the initial pyruvate bolus. We also calculated non-parametric values to describe the signal for each metabolite, specifically area-under-curve (AUC) and time-to-peak (TTP). The repeatability analysis was performed using an ANOVA-based method.

Results: Forward rate constants derived from the kinetic model: kPL 0.016±0.008s-1, kPA 0.012±0.006s-1, kPB 0.024±0.0095s-1 were of similar in order of magnitude to prior studies. The reverse constant for lactate to pyruvate conversion (kLP) is relatively unchanged across the subjects (0.0099±0.0005), and reverse constant for alanine to pyruvate (kAP) conversion is almost negligible (0.0008±0.0012). The model well describes the pyruvate metabolites signal over time. Furthermore, we show high within subject repeatability of the processing pipeline for both non-parametric measures and for rate constants. Interestingly, lower SNR (with more dispersed data) affects rate constant calculation significantly more than AUC or TTP.

Conclusions: We present a real-time pipeline for analysis and modeling of pyruvate metabolism in the human heart, and confirm that it is reproducible, a finding crucial for the ability to detect variation in cardiac metabolism.

Presentation #8

Title: Idiopathic Hypokalemia inLupus Nephritis: A Previously Unrecognized Entity

Presenter: Emmanuel Adomako

Authors: Emmanuel Adomako, MD; Saira Bilal, MD; Yu-lun Liu, PhD; Ayesha Malik, MD; Kamalanthan Sambandam, MD

Faculty Mentor(s): Kamalanthan Sambandam,

Abstract:

Background: Hypokalemia in lupus nephritis (LN) has been described in the context of type 1 renal tubular acidosis (RTA). In the usual care of our very large population of LN patients, we encountered a phenomenon of unexplained hypokalemia that has never been previously described. Here we begin to phenotype this unique cohort.

Methods: From our population of 399 LN patients followed in the Parkland Health and Hospital System, we identified a cohort of 19 patients with idiopathic hypokalemia (HK). This cohort is compared to 63 LN controls (control-nml) and 10 LN patients with distal RTA (control-RTA). In contrasting the three groups, the Chi-squared test or Fisher's exact test was used for categorical data and the one-way ANOVA or Kruskal-Wallis test was used for continuous measures. For paired comparisons of continuous variables between the groups, the student's t-test was employed.

Results: The HK cases had lower mean serum potassium compared to control-nml and control-RTA (3.24 vs 4.07 vs 3.75 mmol/L, respectively; P< 0.001). The mean serum bicarbonate was normal in HK and control-nml but lower in control-RTA (25.95 vs 25.08 vs 19.28 mmol/L, respectively; P< 0.001). The urine pH was abnormally high only in the RTA group (6.12 vs 6.23 vs 6.68; P= 0.021). The mean serum magnesium was modestly lower in HK compared to control-nml and control-RTA (1.76 vs 1.96 vs 1.97 mg/dL; P= 0.004) There were differences in serologic markers of autoimmunity. Compared with control-nml, both HK and control-RTA were more likely to be seropositive for anti-SSA (P= 0.001 and 0.014, respectively). In contrast, compared to controls-nml, only HK expressed a higher rate of anti-RNP seropositivity (P= 0.002) and only control-RTA had a higher rate of anti-SSB positivity (P= 0.037).

Conclusions: A syndrome of idiopathic hypokalemia was revealed in 19/399 (5%) of patients within our lupus nephritis population and is distinct from the RTA that is known to rarely occur in lupus nephritis. This phenomenon has not been previously described. We speculate that idiopathic hypokalemia in lupus nephritis is the result of a novel target of autoimmunity affecting renal tubular potassium transport.

Presentation #9

Title: Telemedicine Assessment of Jugular Venous Pressure: Volume Status by Video Call

Presenter: Samuel Aidan Kelly

Authors: Samuel Kelly, MD, MBE; Kevin Schesing, MD; Jennifer Thibodeau, MD, MSCS; Colby Ayers, MS; Mark H. Drazner, MD, MSc

Faculty Mentor(s): Mark H. Drazner

Abstract:

Background: Assessment of jugular venous pressure (JVP) is considered vital to assessment of patients with heart failure. To date, JVP evaluation has required bedside examination by a clinician. Given increasing utilization of telehealth, we conducted a prospective observational study comparing bedside JVP estimates with those performed over video chat for detection of elevated right atrial pressure (RAP).

Methods: We enrolled 31 adults with reduced left-ventricular ejection fraction (LVEF≤40%) whose clinical care required right heart catheterization (RHC). Each underwent one bedside evaluation and up to 4 remote evaluations by separate cardiologists. 63 remote evaluations were attempted; two remote evaluators (3%) were unable to estimate the JVP. Remote assessments were completed using Google Duo©, Facetime© or WhatsApp©. A bedside housestaff member repositioned the smartphone and patient as directed by the remote evaluator. C-statistics were calculated for bedside and remote JVP estimates (multiplied by 0.74 to convert to mmHg) relative to RAP ≥10 mmHg, then compared by bootstrapping with 500 replications. Generalized estimating equations with a logit link function were applied to account for repeat remote assessments of individual subjects.

Results: The bedside and remote JVP estimates ($r=0.37$, $p<0.001$), bedside JVP and RAP ($r=0.57$, $p<0.0001$), and remote JVP and RAP ($r=0.62$, $p=0.0001$) were significantly correlated. Both remote [OR=2.9 (1.5,5.8)] and bedside [OR=3.7 (1.02,13)] JVP estimates were associated with RAP in logistic regression models. Both discriminated for an elevated RAP with comparable c-statistics ($p=0.6$). Remote evaluators reported lower confidence than bedside evaluators [3.3 (2.8,4.0) vs. 4.0 (4.0,5.0) respectively, $p<0.001$]. Confidence level was not associated with ability to identify RAP ≥10 mmHg ($p=0.6$).

Conclusions: We found that 1) both bedside and remote JVP estimates were significantly correlated with measured RAP; 2) both estimates demonstrated good discrimination of RAP ≥10 mmHg; and 3) remote evaluators, using commercially available smartphones, reported lower confidence levels but achieved similar discrimination of an elevated RAP versus bedside evaluators. To our knowledge, this is the first demonstration that the jugular venous pressure (JVP) can be assessed reliably over video. We believe that these data can be of particular value given the high use of telehealth during the COVID-19 pandemic.

Presentation #10

Title: Associaton of African Ancestry with Arterial Stiffness and Risk of Hypertension: Findings from the Dallas Heart Study

Presenter: Ezimamaka Ajufo

Authors: Ezimamaka Ajufo, BM BCh; Neela D. Thangada MD; Colby R. Ayers, MS; Julia Kozlitina, PhD; Michael E Hall, MD, MSc; Adam Bress, PharmD, MS; Sandeep Das, MD, MPH; Amit Khera, MD, MSc; Mark H. Drazner, MD, MSc; James A. de Lemos, MD; Ambarish Pandey, MD, MSCS

Faculty Mentor(s): Ambarish Pandey

Abstract:

Background: HTN and higher arterial stiffness are more common among self-reported black individuals compared to whites. The degree to which genetic African ancestry accounts for racial disparities in these phenotypes is not well known.

Methods: Self-identified black participants from the Dallas Heart Study (DHS) free from CVD with available genotyping (Infinium HumanExome, Illumina) and arterial stiffness assessment by cardiac MRI were included. Genetic ancestry proportions were quantified from genome-wide genotyping data. Multivariable linear regression models were used to assess the association of African ancestry with arterial stiffness parameters [aortic pulse wave velocity (PWV), proximal aortic impedance (Zc), pulse pressure (PP)]. Among participants free from HTN at baseline, the association of African ancestry with HTN at follow-up 7 years later was assessed using adjusted logistic regression models.

Results: The cohort included 1120 self-identified black participants (mean age 45y, 57% women) with a mean African ancestry proportion of 86%. In adjusted analyses, proportion of African ancestry was not significantly associated with arterial stiffness (PWV, Zc & PP). By contrast, among participants free from HTN at baseline, a higher proportion of African ancestry was significantly associated with higher odds of HTN on follow-up independent of age, sex, SES factors, and CV risk factors.

Conclusions: Among self-reported black participants, higher proportion of genetic African Ancestry was associated with higher odds of HTN independent of biological and SES factors. However, African ancestry was not associated with measures of arterial stiffness. Genetic ancestry accounts for at least part of the higher burden of HTN but not arterial stiffness in black individuals. Future studies are needed to confirm these observations and better understand the contribution of genetic factors toward racial differences in hypertension.

Presentation #11

Title: Association between Cardiac Variables and Cognitive Function in Middle-Aged Adults: Analysis from The Dallas Heart Study-2

Presenter: Richard Chia

Authors: Richard Chia, MD; Colby Ayers, MS; Heidi Rosetti, PhD; Ambarish Pandey, MD; Jarret Berry, MD; Julia Kozlitina, PhD; Mark H. Drazner, MD; Sonia Garg, MD; Ronald Peshock, MD; James A. de Lemos, MD; Rong Zhang, PhD; Wanpen Vongpatanasin, MD

Faculty Mentor(s): Wanpen Vongpatanasin

Abstract:

Background: Previous studies have demonstrated a relationship between subclinical cardiac dysfunction and cognitive impairment in older adults. However, associations between hemodynamic variables and cognitive function has not been determined in an ethnically diverse middle-aged population. Furthermore, previous studies have not accounted for physical activity, which may be reduced in the presence of cognitive or cardiac impairment.

Methods: We assessed the relationship between cardiac function (by MRI) with Montreal Cognitive Assessment (MoCA) and white matter hyperintensities (WMH) volume in the Dallas Heart Study phase 2 (N=2,670) using multivariable linear regression. We assessed time spent in moderate-to-vigorous physical activity (MVPA) using an accelerometer. To determine if the relationship between hemodynamic variables and cognitive function is dependent on genetic predisposition to Alzheimer's disease, we stratified by ApoE carrier status.

Results: In a middle-aged and ethnically diverse cohort (age, 49.4 ± 11.1 years; 60.4% female; 50.9% black), we found that lower LVEF and stroke volume (SV) were independently associated with lower total MoCA, after adjusting for age, sex, race, BMI, systolic BP, antihypertensive drug use, diabetes, smoking, eGFR, education, and MVPA (β=0.23 ± 0.11, p=0.04; β=0.42 ± 0.13, p=0.001, respectively). Similarly, lower LVEF was associated with higher WMH volume after adjusting for the same covariates and normalizing to total cranial volume (β = -0.050 ± 0.025, p=0.04). To determine if the relationship is dependent on genetic predisposition to Alzheimer's disease, we determined association in the ApoE carrier positive subgroup analysis (N=1,010). Lower LVEF and stroke volume were independently associated with lower MoCA in both ApoE carriers and non-carriers (interaction $p > 0.2$).

Conclusions: These data suggest that lower LVEF and SV are associated with lower cognitive function, which is independent of physical activity and ApoE carrier status. Additional studies are needed to determine if strategies that maintain optimal cardiac function preserve brain white matter integrity and prevent cognitive decline in middle-aged adults.

Presentation #12

Title: Decision Support Tool for Screening of Tuberculosis Exposed Individuals Seeking Care at a Public Academic Health System

Presenter: Stephanie Cobb

Authors: Stephanie Cobb, DO; Stephanie Nguyen, DO, MPH; Deepa Raj; Dena Taherzadeh; Pranavi Sreeramoju, MD, MPH

Faculty Mentor(s): Pranavi Sreeramoju

Abstract:

Background: Mycobacterium tuberculosis (TB) is one of the leading causes of morbidity and mortality worldwide. At our health system, 50-100 patients are diagnosed with tuberculosis every year. One risk factor for TB is residence within a homeless shelter. In response to an increased number of cases in local homeless shelters, the health department sought assistance with contact tracing of individuals potentially exposed to tuberculosis. We are reporting the results of contact tracing performed at our health system.

Methods: The setting is a 770-bed safety-net academic hospital with community clinics and a correctional health center. Name, date of birth and social security number of contacts potentially exposed during February 2009 to July 2013 were programmed into the electronic medical records to create a decision support tool upon entering the health system. The 'Best Practice Alert' (BPA) informed physicians of the exposure and offered a link to a screening test, T-spot.TB®, and a link to an information sheet. This was implemented from July 2013 to July 2015. After excluding patients with active TB, data on the magnitude of exposure in each homeless shelter and screening test results were analyzed with ANOVA using IBM SPSS for Windows® v26.

Results: Of the 8649 identified exposed contacts, 2118 entered our health system. Of those in which the BPA was triggered, 1117 had a T-spot.TB® done, with 313 resulted positive and 57 borderline. The table shows that Shelter 3 was correlated with a positive T-spot.TB®.

Conclusions: The BPA, which prompted physicians to evaluate an individual for TB, was effective at capturing high risk, exposed individuals. Clinical decision support tools enabled our safety-net health system to respond effectively to a local public health need.

Presentation #13

Title: Lung transplantation and donor-specific antigens: clinical and serologic factors associated with survival and allograft dysfunction.

Presenter: Daniel Guidot

Authors: Daniel G. Guidot, MD; S. Ghosh MD; N. Madala; J. Varghese, MD; Amit Banga MD, Sinivas Bollineni, MD; John O. Joerns, MD; Adrian Lawrence, MD; Manish Mohanka, MD; C. Zhu, Vaidehi Kaza, MD

Faculty Mentor(s): Vaidehi Kaza

Abstract:

Donor-specific antigens (DSA) acquired after transplantation are associated with allograft dysfunction and worse survival. Clearance of DSA is associated with improved survival. Less is known about clinical and treatment factors associated with DSA clearance. We did a retrospective review of patients receiving lung transplantation between January 1, 2010, and June 30, 2014 with follow up through September, 2019. We compared overall survival (OS) and bronchiolitis obliterans syndrome (BOS)-free survival stratified by DSA development and clearance, then multivariate analysis to assess clinical or demographic associated with spontaneous DSA clearance. Finally, among those without spontaneous DSA clearance, we compared OS and BOS-free survival among different treatment groups. We identified 194 patients, mostly male (59%), mostly white (75%), and transplanted ages 16-77 (median 60). 125 (64%) developed DSA, and 74 (59%) had clearance. OS and BOS-free survival were significantly different among patients stratified by DSA development and clearance. Median survival for patients who never developed DSA was 5.0 years, similar to patients who developed DSA with spontaneous clearance (6.5 years) and those with clearance after treatment (4.9 years). For those with persistent DSA, median survival was worse with treatment (2.6 years) and without treatment (2.6 years). BOS-free survival was also significantly different. In multivariate analysis of patients who developed DSA, no identified demographic or clinical variables were associated with spontaneous clearance. However, the degree of DSA as measured by cumulative mean fluorescence intensity (cMFI) was associated with spontaneous clearance, with those clearing having significantly lower cMFI values at onset of DSA ($p < 0.001$) and at peak ($p = 0.035$). Among those without spontaneous DSA clearance, multivariate analysis of treatment showed that OS and BOS-free survival was associated with patients who received IVIG/plasma exchange ($p = 0.034$, $p < 0.001$) or rituximab ($p = 0.031$, $p = 0.001$). Treatment with bortezomib, thymoglobulin, and eculizumab were not associated with improved OS or BOS-free survival. Patients who develop DSA but have clearance have survival curves similar to those who never developed DSA. Persistent DSA presence shows worse survival. Lower magnitude of DSA at onset and peak is associated with spontaneous DSA clearance.

Presentation #14

Title: Safety of Zoster Vaccine Recombinant, Adjuvanted Among Patients with Rheumatic Diseases

Presenter: Surbhi Gupta

Authors: Surbhi Gupta MD, Reuben Arasaratnam MD, Blair Solow MD, Puneet Bajaj MD

Faculty Mentor(s): Puneet Bajaj Reuben Arasaratnam, Blair Solow

Abstract:

Background: Zoster Recombinant Adjuvanted (ZRA) is a two-dose series subunit vaccine for prevention of herpes zoster (HZ). The CDC recommends ZRA for immunocompetent adults ≥50 years. Despite the increased risk in immunocompromised patients, there are no recommendations for this population. There is limited safety data of ZRA in patients with rheumatic diseases, who might be taking DMARDs. In addition, there is concern regarding its potential to trigger disease flares. This retrospective study aims to assess the safety of the ZRA vaccine in this population.

Methods: This retrospective study included patients with autoimmune rheumatologic diseases followed in UTSW clinics who had received at least one dose of the ZRA vaccine since 2018. The primary outcome was adverse event frequency, defined as described by Lal et al (1). Secondary outcome was disease flares three months following vaccination, as identified by a rheumatologist or an increase in prednisone. This was compared to six months before vaccination.

Results: The study included 39 patients, 33 of whom were women and the average age was 67 years. There were 11 diseases represented, of which the most common diagnoses were rheumatoid arthritis, polymyalgia rheumatica, and Sjogrens. There were 25 patients on DMARDs, 9 of whom were on biologics. Average time to follow-up was 52.18 weeks. Adverse events occurred in 4/39 participants (10.3); all were minor systemic events, and no major adverse events occurred. A flare occurred in only one patient (2.6%), 6.9 weeks after vaccine administration in the setting of self-stopping abatacept for 2 weeks, and was treated with a new prescription of 40 mg prednisone. There was no significant clinical difference in flare rate 6 months before and 3 months after vaccination.

Conclusions: In patients with autoimmune diseases, the rate of HZ is higher than the average population (2). However, the recombinant subunit ZRA vaccine is not currently recommended in this population due to lack of safety data. Our preliminary data suggests that the ZRA vaccine is well-tolerated with minor adverse events and disease flares that were not clinically significant. At the present we are expanding our database to further characterize the safety of this vaccine.

Presentation #15

Title: Hepatitis C Epidemiology at the Dallas County Jail: A Changing Demographic

Presenter: Emily Hoff

Authors: Emily Hoff, MD; Ank Nijhawan, MD, MPH, MSCS

Faculty Mentor(s): Ank Nijhawan

Abstract:

Background: People involved in criminal justice (CJ) are disproportionately infected with Hepatitis C (HCV) and nearly 1 in 3 people living with HCV pass through the CJ system each year. As a result, the CJ system is a crucial location for Hepatitis C screening, education and linkage to care. We aim to 1) identify the prevalence and incidence of HCV and 2) evaluate HCV demographic trends at a large urban jail.

Methods: Universal opt-out HCV testing was offered in four separate testing cycles from 2015 to 2019 to any individual undergoing a routine blood draw at the Dallas County Jail (N=14490). HCV antibody (Ab) assay (LabCorp) was used with reflex RNA testing added on in 2017. Demographic variables were extracted from the electronic medical record for all tested with risk factors collected from those who tested positive for HCV Ab (HCV Ab+), and multivariate logistic regression was performed.

Results: The prevalence of HCV Ab+ was 16.7% in the Dallas County Jail; 75.3% of those who tested HCV Ab+ were also HCV RNA+. The HCV Ab+ incidence rate was 13.5 cases per 1000 person-years. People who were HCV Ab+ were more frequently (adjusted odds ratio [95% confidence interval], p-value): older (47 v. 36, 1.07[1.06-1.07], $p< 0.001$), female (26% v. 25%; 1.24[1.07-1.44], $p=0.004$), white (56% v. 43%, 2.12[1.83-2.45], $p< 0.001$), in the birth cohort 1945-65 (41% v. 10%, 1.79[1.44-2.23], $p< 0.001$) and released to prison (43% v. 35%; $p< 0.001$). In earlier birth cohorts (1940s), black men were proportionately more likely to be HCV Ab+; in more recent birth cohorts (1990s), white and Hispanic females were proportionately more likely to be HCV Ab+. Over half of those who were HCV Ab+ identified injection drug use (IDU) as a risk factor. Among individuals who tested HCV Ab+, IDU was more frequently reported by white individuals, particularly women, compared to black individuals ($p<0.001$).

Conclusions: The high prevalence and incidence of HCV at the Dallas County Jail argues for routine, universal testing and linkage to treatment. Additionally, demographic trends mirror the IDU epidemic and shed valuable insight into designing risk reduction and treatment interventions.

Presentation #16

Title: Effects of Sex Hormones on Markers of Health in Women with Cystic Fibrosis

Presenter: Melanie Holtrop

Authors: Raksha Jain, MD; Melanie Holtrop, MD; Veronika Shabanova, PhD; Ashley Keller, MPH; Lauren Schumacher, MS; Sonya Heltshe, PhD

Faculty Mentor(s): Raksha Jain

Abstract:

Background: A host of epidemiologic data suggests that women with cystic fibrosis (CF) have worse outcomes than men, including higher mortality rates and earlier colonization with respiratory pathogens. These differences become apparent after puberty. In addition, women with CF demonstrate an increased rate of exacerbations near ovulation. The basis for these differences has not been established, but existing data suggests estrogen may play a role. In this study, we sought to elucidate how inflammatory markers, sputum cytology, respiratory parameters, and symptoms change throughout the ovulatory cycle in women with CF.

Methods: This was a single center, prospective, observational study with a treatment sub-study designed to assess the impact of estrogen on lung function and inflammation in CF. Enrollees were stable women with CF who were not on hormonal contraception or oral corticosteroids. Data was collected during study visits that corresponded to menses, ovulation, and the luteal phase of the ovulatory cycle. A subset of patients were then given the oral contraceptive pill (OCP) ethinyl estradiol/norethindrone and assessed during a fourth visit. At each visit, lung function (FEV1%), respiratory symptoms, sweat chloride, sputum bacterial density, sputum inflammatory markers, and serum cytology were assessed. The primary outcome was relative change in percent FEV1. Secondary outcomes included change relative to menses and ovulation in respiratory symptom scores, sweat chloride levels, sputum bacterial density, sputum inflammatory markers, and cytology.

Results: Hormone levels fluctuated throughout the ovulatory cycle as expected. The inflammatory markers IL-8, TNF-alpha, and neutrophil elastase trended higher during ovulation. When placed on oral contraceptive pills (OCP), the levels of these inflammatory markers were significantly lower relative to levels during ovulation. Similarly, FEV1% was significantly higher when on OCP as compared to during ovulating. When placed on an OCP, women also reported a trend toward higher scores on the respiratory domain of the Cystic Fibrosis Questionnaire-Revised Application (CFQ-R).

Conclusions: Our study demonstrated a trend toward increased inflammation during ovulation; this corresponded with lower FEV1% and symptoms scale. Inflammatory markers, FEV1% and symptoms improved when placed on OCP. Larger studies to understand the implications of sex hormones on health in CF are needed.

Presentation #17

Title: Symptom Differences and Health Perceptions Between Men and Women with Cystic Fibrosis

Presenter: Melanie Holtrop

Authors: Raksha Jain, MD; Melanie Holtrop, MD; Veronika Shabanova, PhD; Ashley Keller, MPH; Lauren Schumacher, MS,; Sonya Heltshe, PhD

Faculty Mentor(s): Raksha Jain

Abstract:

Background: Multiple epidemiologic studies have shown outcome differences between men and women with CF with regards to rate of CF exacerbations and survival. In terms of symptoms and perceptions of health, data suggests that women report better perception of body image but worse perception of physical health; however, this has not been evaluated in a randomized prospective fashion. As part of a study to evaluate the effect of temporal changes in sex hormones on inflammation and disease, we evaluated differences in patient reported symptoms between men and women with CF while at baseline health status.

Methods: Women who had regular ovulatory cycles and were not on hormone contraception were enrolled. Males were recruited as controls at a 1:1 ratio in an age and FEV1% matched fashion. The Cystic Fibrosis Questionnaire-revised was administered at time points corresponding to menses, ovulation, and luteal phase of the ovulatory cycle. In addition, data regarding lung function, sputum inflammatory markers, and serum hormone levels and cytology was collected. Differences between men and women at different time points in the ovulatory cycle were assessed by linear or negative binomial regression adjusting for BMI and age.

Results: Men and women were similar in age, BMI, and degree of airflow obstruction. Hormone levels were as expected throughout the ovulatory cycle. Compared to men, women showed higher levels of IL-8 and TNF-alpha at ovulation. There were no other differences in inflammatory markers, bacterial density, or sputum cytology at any point throughout the ovulatory cycle. In contrast, women reported decreased scores related to physical health and eating throughout the ovulatory cycle when compared to men. Additionally, during menses and the luteal phase, women reported decreased vitality and total symptom burden. There were no differences noted in respiratory scores.

Conclusions: Despite equal health status, there are potentially important differences in self-reported outcomes and health perceptions between men and women with CF. How this plays a role on their mental and emotional health, adherence to therapies and physical activities requires further investigation. Larger studies evaluating sex disparities and the impact of sex hormones on patient reported outcomes warrants further investigation.

Presentation #18

Title: Hypertension attenuates the association of coronary artery calcification with CVD events in individuals with and without CKD

Presenter: Geoffrey Huntley

Authors: Geoffrey D. Huntley, MD; L. Parker Gregg, MD; Beverley Adams-Huet, Xilong Li, James de Lemos, MD; and Susan Hedayati, MD

Faculty Mentor(s): Dr. Susan Hedayati Dr. L. Parker Gregg

Abstract:

Background: The prognostic value of coronary artery calcification (CAC) is limited in high-risk individuals, such as with chronic kidney disease (CKD), perhaps due to higher prevalence of traditional CVD risk factors. Hypertension (HTN), a major CVD risk, is present in up to 85% of CKD patients. We sought to examine whether HTN presence attenuates the association between CAC and CVD events in patients with CKD.

Methods: We analyzed 2,288 participants of the Dallas Heart Study, a community-based longitudinal cohort. Cox proportional hazards regression determined associations of CAC with global CVD events (composite of CV death, myocardial infarction, stroke, CV revascularization, and hospitalization for heart failure or atrial fibrillation) over 12.5 years, adjusted for age, diabetes, HTN (blood pressure >140/90 mmHg or on antihypertensive therapy), and CKD (eGFR<60 mL/min/1.73m2 or urine albumin-to-creatinine ratio ≥17 mg/g in men or ≥25 in women). Interactions for CKD and HTN were tested at various CAC cutoffs (>0, ≥10, ≥100, and ≥400 Agatston units), with significant interaction P<0.10.

Results: There were 170 (7.4%) participants with CKD and 811 (35.4%) with HTN. CAC prevalence was highest in the CKD/HTN and lowest in the non-CKD/non-HTN groups. Of 232 events, the proportion with events was highest in the CKD/HTN (43.5%), similar between the CKD/non-HTN (21.0%) and non-CKD/ HTN (16.2%), and lowest in the non-CKD/non-HTN groups (4.1%), P<0.001. CAC was associated with CVD events at each CAC cutoff among the non-CKD groups. However, CAC was not associated with CVD events at CAC >0 for the CKD/HTN group, aHR 2.05 (0.70, 5.98), or at CAC ≥10 for the CKD/non-HTN and CKD/HTN groups, aHR 3.48 (0.86, 14.07) and 1.44 (0.78, 2.65), respectively. There was a CKDxCAC interaction for CAC ≥10, aHR 3.31 (2.34, 4.67) in non-CKD and 1.64 (0.93, 2.89) in CKD, interaction P=0.001, but no CKDxCAC interaction for higher CAC cutoffs. CAC was less predictive of CVD events in those with HTN, with a significant HTNxCAC interaction at all CAC cutoffs.

Conclusions: The presence of HTN attenuated the association between CAC and global CVD events. The prognostic ability of CAC in CKD may be limited by the high prevalence of HTN.

Presentation #19

Title: Sex, Racial and Ethnic Disparities in HCC Clinical Trial Enrollment

Presenter: Jenny Jan

Authors: Jenny Jan, MD; Caitlin C. Murphy, PhD; Amit G. Singal, MD; Nicole E. Rich, MD

Faculty Mentor(s): Nicole Rich and Amit Singal

Abstract:

Background: Disparities in clinical trial enrollment have not been investigated in hepatocellular carcinoma (HCC). While women and minorities are historically underrepresented in clinical trials overall, men and minorities are disproportionately affected by HCC. Our aim was to quantify the enrollment of women and minorities in HCC clinical trials in the U.S.

Methods: We queried ClinicalTrials.gov to identify enrollment data from all therapeutic HCC clinical trials reported as "completed" from 1998 to 2019. We included phase II or III trials with any degree of enrollment within the U.S. Trials involving cancer prevention, cancer diagnosis, surgical intervention, non-hepatobiliary cancers, and cancers metastatic to the liver were excluded. We calculated enrollment fraction (EF) as the number of trial enrollees divided by the estimated number of HCC cases in each subgroup, using data from the U.S. Cancer Statistics database matched to the time period of trial enrollment. We used Chi-square test to compare the relationship between EFs by sex and in various racial/ethnic groups and estimated crude odds ratios (ORs) within each subgroup.

Results: Of 2571 clinical trials, 63 (0.6%) met inclusion criteria; 30 (47.6%) trials were sponsored by an academic institution, 21 (33.3%) by a pharmaceutical company and 12 (19.1%) by the NIH/NCI. There were 9843 total trial participants, including 7939 (80.7%) men and 1904 (19.3%) women. Information on race/ethnicity was available for 28/63 (44.4%) trials; among these, there were a significantly higher proportion of non-Hispanic whites (48.1%; n=2448) enrolled compared to non-Hispanic blacks (3.2%; n=162) and Hispanics (2.7%; n=135). Women had a lower EF compared to men (2.2% vs 3.2%, p <0.001; OR 0.67 95% CI 0.64 - 0.70). Compared to a 1.2% EF among white patients with HCC, only 0.34% of black (OR vs whites, 0.28; 95% CI 0.24 - 0.33) and 0.27% (OR vs whites, 0.23; 95% CI 0.19 - 0.27) of Hispanic patients participated in trials, respectively.

Conclusions: Clinical trial enrollment is exceedingly low among all groups of HCC patients, with larger disparities observed among women and minorities. Future efforts should focus on interventions to improve clinical trial enrollment in underrepresented groups to reduce disparities and improve HCC care for all.

Presentation #20

Title: Comparison of Antiplatelet Regimens after Endovascular Revascularization of Infrainguinal Peripheral Artery Disease: Insights from the XLPAD Registry

Presenter: Ryan Kabir

Authors: Ryan Kabir, MD; Kunal Patel, MD; Yulun Liu, PhD; Suchith Vuppala, MD,; Ishita Tejani, BDS, MS, MSPH; Chris Metzger, MD; Peter Monteleone, MD; Khusrow Niazi, MD; Emmanuouil Brilakis, MD, PhD; Ehrin Armstrong, MD; Subhash Banerjee, MD

Faculty Mentor(s): Subhash Banerjee

Abstract:

Background: The optimal antiplatelet therapy regimen after endovascular revascularization of infrainguinal arteries remains uncertain.

Methods: Using the ongoing multicenter Excellence in Peripheral Artery Disease (XLPAD) registry (NCT01904851), we analyzed antiplatelet prescription trends and outcomes of 2412 patients undergoing endovascular revascularization to compare patients who were prescribed antiplatelet monotherapy to those who were prescribed dual-antiplatelet therapy (DAPT). The primary outcomes assessed over a 12-month period were major adverse limb events (MALEs; a composite of death, repeat endovascular revascularization, surgical revascularization, and target limb amputation) and major adverse cardiovascular events (MACEs; a composite of death, myocardial infarction (MI), and stroke).

Results: Out of 2412 patients in the study, 47.7% (n=1151) were treated with DAPT (1078 received aspirin and clopidogrel, 35 received aspirin and ticagrelor, and 38 received aspirin and prasugrel). Patients who were prescribed DAPT had a significantly ($p<0.05$) higher incidence of preexisting coronary artery disease (CAD)(64.1% vs. 44.7%) and prior MI (26.0% vs. 16.5%). Kaplan-Meier analysis showed no significant difference at 12 months between the DAPT group and antiplatelet monotherapy group in freedom from MALE (87.2% vs. 85.3%, p=0.10) or MACE (96.4% vs. 95.9%, p=0.47). After adjusting for age, sex, race, and cardiovascular risk factors (diabetes, hypertension, dyslipidemia, smoking) in the DAPT group compared with the antiplatelet monotherapy group, the hazard ratios for MALE and MACE at 12 months were 0.86 (95% CI 0.68-1.11, p=0.24) and 0.88 (95% CI 0.55-1.40, p=0.58), respectively.

Conclusions: After infrainguinal endovascular revascularization, patients with underlying CAD were more likely to be prescribed DAPT as opposed to antiplatelet monotherapy. Adverse limb and cardiovascular events were similar in patients treated with DAPT and antiplatelet monotherapy.

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Presentation #21

Title: Trends in Utilization and Cost of LDL-lowering Therapies Among Medicare Beneficiaries: An Analysis from the Medicare Part D Database (2014 - 2018)

Presenter: Hussain Lalani

Authors: Hussain Saleem Lalani, MD, MPH; Andrew Sumarsono, MD; Muthiah Vaduganathan, MD, MPH; Ann Marie Navar, MD, PhD; Gregg C. Fonarow, MD; Sandeep R. Das, MD, MPH, MBA; Ambarish Pandey, MD

Faculty Mentor(s): Ambarish Pandey

Abstract:

Background: Low-density lipoprotein (LDL)-lowering therapies are the cornerstone of primary and secondary prevention of atherosclerotic cardiovascular disease. The economic burden of these therapies is evolving with the increasing availability of generic formulations of older medications, such as statins and ezetimibe, and the introduction of new, expensive therapies such as Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK-9) inhibitors.

Methods: We used the Medicare Part D Prescription Drug Event Dataset to analyze prescription drug utilization and cost trends for LDL-lowering therapies from January 2014 to December 2018 and estimated the potential savings if all beneficiaries on brand-name drugs were switched to available generic formulations. All calculations were adjusted for inflation and reported in 2018 US Dollars.

Results: This analysis included 11 drugs with 25 formulations (16 brand-name, 9 generic). Over the study period, the number of Medicare beneficiaries on LDL lowering therapies increased by 23% (20.5 million in 2014 to 25.2 million in 2018) while the associated Medicare expenditure decreased by 46% ($6.3 Billion in 2014 to $3.3 Billion in 2018). Lower expenditure was driven by greater uptake of generic statin and ezetimibe with a concurrent rapid decline in the use of respective brand-name formulations. Medicare spent $9.6 Billion on brand-name statins and ezetimibe during the study period, and could have saved $4.3 Billion if brand-name formulations were switched to therapeutically equivalent generic versions when available. Since their introduction in 2015, the number of beneficiaries using PCSK9 inhibitors has been modest, increasing by 144% (25,569 in 2016 to 62,476 in 2018) while total spending increased by 199% ($164 Million to $491 Million).

Conclusion: Between 2014 and 2018, LDL lowering therapies were used by 4.8 million more Medicare beneficiaries per year with an associated decline in Medicare spending of $3.0 billion. This cost reduction was driven by the rapid transition from brand name to lower-cost generic formulations of statins and ezetimibe. Switching the remaining eligible brand-name formulations to generics could have saved an additional $4.3 Billion over the five-year study period. PCSK9 inhibitor use remained low but increased rapidly and could have large implications on future Medicare spending.

Presentation #22

Title: Physician Voting Practices in California, New York, and Texas from 2006-2018

Presenter: Hussain Lalani

Authors: Hussain Lalani, MD MPH; Arthur Hong, MD MPH

Faculty Mentor(s): Arthur Hong

Abstract:

Background: From 1996 to 2002, physicians voted 17% less frequently in elections than the general population. Since then, the practice and delivery of health care has changed dramatically with the passage of the Affordable Care Act. However, it remains unclear how physician voting practices have changed over the last decade.

Methods: We characterized physician voting practices from 2006 to 2018 in the three states with the largest numbers of physicians (CA, NY, TX). We merged the National Physician Identifier (NPI) Registry from Centers for Medicare & Medicaid Services with state voter files from L2, a private non-partisan company, using a matching algorithm based on names, NPI enumeration dates, birth dates, and occupation data from credit reports provided by L2. We excluded physician trainees. Our primary outcome was voter participation: the proportion of voting eligible physicians (VEP) who voted in general elections from 2006 to 2018. VEP was calculated based on the Association of American Medical Colleges state physician workforce profiles. We compared this to general voter participation rates from publicly available data using chi-square analysis. We used logistic regression to determine the odds of physician voter turnout, proportion of registered physicians who voted, compared to the general population, adjusting for age, gender, ethnicity, education, income, and household size.

Results: We identified 117,478 physicians registered to vote - 50,854 in CA, 39,046 in NY, and 27,578 in TX. Two-thirds (66%) were male, median age 42 in 2006 (IQR: 31 - 52). Internal Medicine was the most represented specialty (16%). Overall, 36% of eligible physicians voted in general elections from 2006-2018 compared to 46% of the general population ($p<0.001$). Physician voter participation was lowest in 2006 (25%) and highest in 2016 (44%). Registered physicians voted between 4% less often to 6% more often than general population (2018 adjusted OR 0.97, 95% CI: 0.96-0.98; 2006 aOR 1.06, 95% CI: 1.05-1.06).

Conclusions: Eligible physicians in CA, TX, and NY voted 22% less than the general population from 2006-18, while registered physicians voted closer to general population trends, varying based on the year. This highlights the need to identify and reduce underlying barriers to physician.

Presentation #23

Title: Evaluation of Head and Neck Soft Tissue Sarcoma 8th Edition Pathologic Staging System and Proposal of a Novel Staging System

Presenter: Nicholas Lee

Authors: Nicholas Lee, MD; Antoine Eskander, MD, ScM; Henry Park, MD, MPH; Chirag Shah, MD; Michael Rutenberg, MD, PhD; Ali Hosni, MBBCh, MSc, PhD; and Zain Husain, MD

Faculty Mentor(s): Zain Husain

Abstract:

Background: The 8th edition AJCC American Joint Committee on Cancer (AJCC) issued a dedicated staging system for soft tissue sarcomas (STS) based on the body site of origin. For the head and neck (HN), this led to 2 and 4cm T classification cut-points, as well as a T4 cut off based on invasion of adjacent structures. However, stage groupings were not provided due to a paucity of data by which to evaluate the HN-STS staging system. Using large national databases, we sought to evaluate the new staging cutoffs, to derive a novel staging system for HN Sarcoma and to validate this in an independent dataset.

Methods: The Surveillance, Epidemiology, and End Results (SEER) database was used to identify patients 18 and older with non-metastatic HN-STS, who underwent primary surgery without neoadjuvant therapy. Pathologic tumor stage (pT), nodal stage (pN), and grade (G) were evaluated along with continuous tumor size. A risk-stratification scheme was established using recursive partitioning analysis with the SEER cohort. The newly identified groupings were validated in the National Cancer Database (NCDB). Survival analysis was performed with Kaplan-Meier methods and Fine-Gray competing risk method where applicable. Multivariable analysis was performed with Cox proportional hazards analysis.

Results: The most prognostic pathologic factors on multivariable analysis in the SEER cohort (N = 546) were structurally invasive tumors ($P < 0.001$) and increasing de-differentiation ($P < 0.001$). We identified 5cm as a proposed tumor size cut-point using recursive partitioning analysis, and generated three distinct risk-stratification groups with the following five-year overall survival: A (non-structurally invasive, <5cm, pN0-1M0G1-2 and >=5cm, pN0-1M0G1) 77.2%, B (non-structurally invasive, <5cm, pN0-1M0G3-4 and >=5cm, pN0-1M0G2-4) 54.3%, and C (structurally invasive, pN0-1M0G1-4) 17.5%. Differences in prognoses by these risk groups were validated in the NCDB ($P < 0.001$).

Conclusions: As the first study to evaluate AJCC 8 HN-STS pathologic staging, we confirm the importance of structural invasion and grade. We identify a new, unique tumor cut-point at 5cm not proposed in AJCC 8. We utilize these factors to propose the first, novel pathologic staging system that could be utilized currently and for future staging editions.

Presentation #24

Title: Cardiomyopathy and left ventricular structural remodeling in Duchenne muscular dystrophy carriers

Presenter: Hannah Lehrenbaum

Authors: Hannah Lehrenbaum, MD,; Michinari Hieda MD, PhD, MSc; Pradeep Mammen, MD

Faculty Mentor(s): Pradeep Mammen

Abstract:

Background: Duchenne muscular dystrophy (DMD) is an X-linked neuromuscular disorder, and DMD-associated cardiomyopathy is the primary mode of premature death in the majority of male DMD patients. However, the prevalence of cardiomyopathy and its clinical significance in female DMD carriers is less well characterized. We hypothesize that a significant proportion of DMD carriers develop a cardiomyopathy associated with maladaptive left ventricular structural remodeling over time.

Methods: A cross-sectional study was undertaken comparing cardiac magnetic resonance imaging (cMRI) and cardiopulmonary stress test (CPX) parameters between DMD carriers and healthy age- and sex-matched controls from the Dallas Heart Study (DHS). Demographic data, cMRI parameters, and CPX parameters were collected retrospectively on 30 consecutive DMD carriers and 26 control DHS subjects.

Results: The overall demographic data were similar between DMD carriers and DHS controls. The DMD carriers had a significantly lower LVEF compared to DHS controls (58+8% vs 70+7%, p<0.0001). The overall prevalence of reduced LVEF in DMD carriers (defined as LVEF <62%) was 63% compared to 8% in DHS controls. The volumetric variables indexed to body surface area (LVEDVi and LVESVi) were significantly higher in DMD carriers compared to control subjects (72+14 (ml/m2) vs 58+7, p<0.0001; 31+10 (ml/m2) vs 17+5, p<0.0001; respectively). LV concentricity was also significantly lower among DMD carriers compared to DHS controls (0.73+0.11 (g/mL0.67) vs 0.88+0.12, p<0.0001). We further analyzed differences in concentricity between DMD carriers with reduced LVEF (defined as LVEF <62%), DMD carriers with normal LVEF (LVEF > 62%), and DHS controls. LV concentricity was lower in DMD carriers independent of LVEF when compared to DHS controls.

Conclusions: Collectively, the data suggest that middle-aged female DMD carriers are at greater risk of developing left ventricular systolic dysfunction and cardiomyopathy. Our study suggests that a possible mechanism driving development of cardiomyopathy is a progressive, maladaptive left ventricular dilatation and cardiac atrophy leading to overall reduced LV mass and increased LV cavity volume. The presence of reduced concentricity in DMD carriers with normal LVEF suggests that these maladaptive structural changes are occurring before any clinically detectable LV systolic dysfunction develops.

Presentation #25

Title: Thrombocytosis is Associated with Worse Survival in Patients with Hepatocellular Carcinoma

Presenter: Po-Hong Liu

Authors: Po-Hong Liu, MD, MPH; Chia-Yang Hsu, MD, MPH; Nicole E. Rich, MD; Naoto Fujiwara, MD, PhD; Yujin Hoshida, MD, PhD, Amit G. Singal, MD, MS; Teh-Ia Huo, MD

Faculty Mentor(s): Amit Singal and Teh-Ia Huo

Abstract:

Background: Thrombocytosis is associated with more aggressive tumor biology in many malignancies, however, there are limited data in patients with hepatocellular carcinoma (HCC), which often occurs in patients with cirrhosis and portal hypertension. We aimed to explore the prognostic value of thrombocytosis in two cohorts of patients with HCC.

Methods: We included 3,561 patients from Taiwan and 1,145 patients from the United States. Thrombocytopenia was defined as platelet count < 150x109/L and thrombocytosis as ≥ 300x109/L at HCC diagnosis. We used multivariable Cox proportional hazard models to identify independent predictors of survival.

Results: Thrombocytosis was present in 9.0% and 6.9% of the Taiwan and U.S. patients, respectively. Compared to patients with normal platelet counts and those with thrombocytopenia, patients with thrombocytosis had larger tumors, increased vascular invasion and a higher proportion had extra-hepatic metastases in both cohorts. In multivariable analysis, thrombocytosis was associated with worse survival (aHR 1.40, 95% CI 1.23-1.60) after adjusting for age, gender, liver disease etiology, Child-Pugh score, maximal tumor size, tumor nodularity, vascular invasion, lymph node or distant metastasis, performance status, and alpha-fetoprotein level. Thrombocytopenia was also associated with worse survival (aHR 1.13, 95% CI 1.04-1.23). Patients with thrombocytosis had a median survival of 6 and 4 months in the Taiwan and U.S. cohorts, compared to 32 and 14 months for those with normal platelet counts, and 38 and 16 months for thrombocytopenic patients.

Conclusion: Thrombocytosis is independently associated with increased tumor burden and worse overall survival among HCC patients.

Presentation #26

Title: Changes in the epidemiology of acetaminophen overdoses in an urban county hospital after 20 years.

Presenter: Apple Long

Authors: Apple Long, MD, PhD; Melissa McGrath, MD,; Meredith Mihalopoulos, BA; Jody Rule, PhD; Deepak Agrawal, MD; Robert Haley, MD; William M. Lee MD

Faculty Mentor(s): William M. Lee

Abstract:

Background: Acetaminophen (APAP) toxicity is the most common cause of acute liver injury and acute liver failure in the US and Europe. In a previous paper, 71 cases of APAP toxicity were identified by ICD-9 code and chart review at Parkland Memorial Hospital, Dallas TX, (PMH), the safety net hospital for Dallas County, over a 40-month period (1992-1995). We analyzed the incidence and outcomes of APAP toxicity over a 5-year time span (2011-2015), and compared our findings to 20 years ago, in the same hospital with a different search strategy.

Methods: Utilizing a database search of all APAP levels drawn followed by chart review, we classified patients as having risk of or actual APAP toxicity using similar established criteria and reviewed clinical details of those meeting criteria.

Results: 27,143 APAP levels were obtained during 25,952 distinct hospital encounters; 328 (1.26%) patients had potential or actual APAP toxicity: 140 required hospital admission with mean length of stay (LOS) of 4.2 days; 35 required intensive care, five developed hepatic encephalopathy and none died.

Conclusions: APAP level testing, performed widely with very low yield, may not be cost-effective ($4.8 million spent for testing over 5 years). After 20 years, we continue to find many APAP toxicity cases (average 66/year), but improved outcomes. There was a lower incidence of encephalopathy and death, and shorter length of stay, but overall higher (3-4X) hospitalization costs despite adjusting for inflation. Improved outcomes may reflect an increase in public awareness and medical staff alertness in managing APAP toxicity.

Presentation #27

Title: Hepatocellular Carcinoma Surveillance Process Failures in Patients with Cirrhosis

Presenter: Patrick Marquardt

Authors: Po-Hong Liu, MD; Joshua Immergluck, MD

Faculty Mentor(s): Amit Singal

Abstract:

Background: A better understanding of barriers to HCC surveillance is important to inform intervention strategies. We aimed to identify points of failure in the HCC surveillance process in a cohort of patients with cirrhosis.

Methods: We conducted a multi-center retrospective cohort study of patients with cirrhosis diagnosed with HCC at an academic tertiary care hospital and a safety-net health system between 2011 and 2017. Patients without HCC surveillance were classified into four mutually exclusive categories that could have contributed to surveillance failure: failure of healthcare providers to recognize liver disease, failure to recognize cirrhosis, failure to order surveillance, and failure of the patient to complete HCC surveillance despite orders. We used univariable and multivariable logistic regression to identify predictors of surveillance failure.

Results: We identified 889 patients with HCC, of whom 298 had cirrhosis and at least 2 years of preceding care within either health system. Only 148 (48.0%) had received any surveillance during the two-year period and only 113 (37.9%) had their HCC diagnosed via surveillance. Although the vast majority (91.3%) had recognized liver disease, 77 (25.8%) did not have cirrhosis recognized by a healthcare provider prior to HCC presentation. Failure of providers to order HCC surveillance in at-risk patients was the most common reason for surveillance process failure, being observed in nearly one-third (33.0%) of the 221 patients with recognized cirrhosis. In contrast, patient adherence was the least common reason for surveillance failure, with only 3.4% of patients with orders not completing any testing. In multivariable analysis, completion of surveillance was more likely among men (OR 1.89, 95%CI 1.11-3.21) and among patients seen by hepatologists (OR 3.35, 95%CI 2.04-5.50).

Conclusions: HCC surveillance continues to be underutilized, with only 1 in 2 patients undergoing any surveillance over a two-year period and only 1 in 3 being detected by HCC surveillance. The least common reason for surveillance underuse was lack of patient adherence, while the most common reason was providers not ordering HCC surveillance in patients with known cirrhosis; the latter step serves as an ideal initial target for interventions to improve HCC surveillance utilization in patients with cirrhosis.

Presentation #28

Title: Soluble Fms-like tyrosine kinase-1 (sFlt-1) is associated with subclinical and clinical ASCVD: the Dallas Heart Study

Presenter: Rina Mauricio

Authors: Rina Mauricio, MD; Kavisha Singh, MD; Monika Sanghavi, MD; Colby R. Ayers, MS; Anand Rohatgi, MD; Wanpen Vongpatanasin, MD; James de Lemos, MD; Amit Khera, MD

Faculty Mentor(s): Amit Khera

Abstract:

Background: Soluble Fms-like tyrosine kinase-1 (sFlt-1) plays a role in angiogenesis, atherogenesis, and preeclampsia. The relationship between sFlt-1, subclinical atherosclerosis, and future atherosclerotic cardiovascular disease (ASCVD) events in a generally healthy population is unknown.

Methods: Participants from the Dallas Heart Study with s-Flt-1 measured were included (n=3932). Abdominal aortic atherosclerosis was measured by MRI and coronary artery calcium (CAC) by CT. The cohort was also followed for subsequent ASCVD events (CV death, MI, stroke, revascularization). Multivariable linear and logistic regression analyses and Cox regression analysis were performed for s-Flt-1, analyzed by quartile (Q4 vs. Q1), adjusting for demographics and traditional cardiac risk factors.

Results: sFlt-1 levels were higher in older individuals, males, and African Americans, and tracked with most traditional risk factors. sFlt-1 was significantly associated with aortic wall thickness and plaque area ($p<0.05$ each, 4th vs. 1st quartile sFlt-1) in multivariable models. Similarly, s-Flt-1 was also independently associated with prevalent aortic plaque [OR 1.32 (1.02-1.72)]. sFlt-1 was not associated with CAC. There were 336 ASCVD events over 12 years of follow-up. Higher sFlt-1 levels associated with increased ASCVD events in unadjusted (16.7% vs. 8.8%, $p<0.001$, Q4 vs. Q1) and adjusted analyses [HR 1.58 (1.14-2.18)]. Findings were unchanged when analyzing sFlt-1 as a continuous variable or when excluding those with a history of ASCVD.

Conclusion: In a population-based cohort, sFlt-1 is associated with measures of subclinical aortic atherosclerosis and clinical ASCVD events. Future studies are warranted on the therapeutic potential of targeting sFlt-1 for atherosclerotic disease.

Presentation #29

Title: Dipstick urinalysis can identify patients with early CKD who lack a quantified proteinuria measurement

Presenter: Meredith McAdams

Authors: Meredith McAdams, MD; DuWayne Willett, MD; Yu-Lun Liu, PhD; Vaishnavi Kannan, MS; L. Parker Gregg, MD, MSCS; S. Susan Hedayati, MD, MSc

Faculty Mentor(s): Susan Hedayati and Parker Gregg

Abstract:

Background: Urine protein-to-creatinine ratio (UPCR)>0.15 g/g or albumin-to-creatinine ratio (UACR)>30 mg/g is the gold standard for identifying patients with stages 1-2 CKD with eGFR>60 mL/min/1.73m2, but not routinely obtained. Dipstick urinalysis semi-quantitative protein (DSP) is widely available and very commonly measured.

Methods: To develop a pragmatic EHR tool to identify patients with stages 1-2 CKD, we investigated diagnostic utility of various DSP cutoffs (negative/trace, 30, 100, 300, or ≥500 mg/dL) against gold-standard proteinuria (UPCR>0.15 g/g or UACR>30 mg/g) using logistic regression. Since urinary protein concentration may vary with specific gravity (SG), we also investigated whether addition of SG improved the diagnostic utility of DSP by comparing areas under the receiver-operating characteristic curves (AUC) with and without addition of SG. DSP was obtained from UTSW EPIC in 3,897 individuals with UPCR or UACR measured on the same date. A development model was created in a random sample of 2,728 (70%) using a bootstrap method and validated in the remaining 1,169 individuals.

Results: Mean age was 57.6±16.9 years, 51.7% were female, 58.5% Caucasian, 25.6% Black, and 42.8% had an eGFR≤60 mL/min/1.73m2. Gold-standard proteinuria was present in 1,775 (45.5%). In the development cohort, combination of DSP and SG performed better than DSP alone, AUC (95% CI) 0.674 (0.653, 0.695) vs. 0.657 (0.640, 0.675), P=0.005. DSP cutoff=30 had the best diagnostic accuracy vs. all cutoffs (P<0.001), specificity 81.1 (79.0, 83.1), +LR=2.43 (2.15, 2.75), -LR=0.67 (0.63, 0.71), with AUC=0.673 (0.652, 0.693) after incorporating SG. In the validation cohort, addition of SG to DSP also yielded a higher AUC=0.650 (0.623, 0.687), than DSP alone, AUC=0.634 (0.608, 0.660), P=0.03. A DSP cutoff of 30 had an AUC of 0.652 (0.621, 0.684), P<0.001 vs. a cutoff of 300 or 500, but P=0.09 vs. a cutoff of 100. Using DSP≥30 identified an additional 141 individuals with CKD than use of eGFR<60 alone.

Conclusions: Combining DSP and SG from a dipstick urinalysis can identify patients with early CKD who do not have a measured UPCR or UACR to quantify proteinuria. These results will be validated in Parkland EPIC, and an EHR tool developed to identify patients with early CKD.

Presentation #30

Title: Early Experiences with COVID-19 at Clements University Hospital in Dallas - A Case Series

Presenter: Mridula Nadamuni

Authors: Mridula Nadamuni, MD; Sadaf Khan, MD; DuWayne Willett, MD; Catherine Chen, MD; Yu-Lun Liu, PhD; Susan Hedayati, MD, MSc

Faculty Mentor(s): Susan Hedayati

Abstract:

Background: The novel coronavirus, SARS-CoV-2, causes COVID-19, and is implicated in a global pandemic, causing over 1.6 million deaths to date. This case series describes the experience with COVID-19 at Clements University Hospital in Dallas from 03/13/20 to 04/09/20.

Methods: After IRB approval, we identified patients admitted with COVID 19, confirmed by polymerase chain reaction (PCR) testing. Demographic and clinical variables, obtained using chart review, were compared between patients based on ICU admission status. Continuous variables were compared using T-tests and categorical, using Chi-square or Fisher's exact tests. P-value<0.1 was considered significant.

Results: There were 24 patients with confirmed COVID-19, of which 15 (62.5%) were admitted to the ICU for ≥1 day(s). Mean age did not differ and was 61.6±15.8 years in ICU vs. 61.4±18.3 years in non-ICU patients. The majority, 60% of ICU and 66% of non-ICU patients, were male. There were no differences in race or ethnicity, with 33% of all being Black and 33% Hispanic. All except two presented with infiltrates on CXR. Though not statistically significant, twice as many patients in the ICU were smokers (47%) compared to only 22% of non-ICU. Hypertension was more prevalent among ICU (73%) vs. non-ICU (56%) patients, though not statistically significant. A similar percentage were on ACEI or ARB (40% vs. 33% ICU vs. non-ICU). The average WBC count on admission was lower (6,190) in ICU patients vs. non-ICU patients (9,140), p=0.047. There was no statistically significant differences between the groups in IL-6, ferritin, or LDH levels. A higher percentage of ICU patients received COVID-19-targeted therapies: IL-6-blockers (Tocilizumab or Sarilumab), 53% vs. 11% non-ICU, p=0.08; steroids, 47% vs. 11%, p=0.18; hydroxychloroquine, 67% vs. 56%, p=1.0). Of ICU-admitted patients, 67% (10/15) were intubated and 40% (6/15) proned. One ICU patient had ESRD and received hemodialysis and one had AKI and received CRRT. Only one patient expired.

Conclusions: During the first 3 weeks of the COVID-19 outbreak in our hospital, more than half were admitted to the ICU, but only one expired. The majority received immune-modulatory therapies. A lower WBC count correlated with ICU admission.

Presentation #31

Title: Hepatocellular Carcinoma Tumor Volume Doubling Time: A Systemic Review and Meta-analysis

Presenter: Piyush Nathani

Authors: Piyush Nathani, MD; Purva Gopal, MD; Nicole E. Rich, MD; Adam Yopp, MD; Takeshi Yokoo, MD. PhD; Binu John, Jorge A Marrero, MD; Neehar D. Parikh, Amit G. Singal, MD

Faculty Mentor(s): Amit Singal and Nicole Rich

Abstract:

Background: Tumor growth patterns have important implications for surveillance intervals, prognostication, and treatment decisions but have not been well described for hepatocellular carcinoma (HCC). The aim of our systematic review was to characterize HCC doubling time and identify correlates for indolent and rapid growth patterns.

Methods: We performed a systematic literature review of Medline and EMBASE databases from inception to December 2019 and national meeting abstracts from 2010 to 2018. We identified studies reporting HCC tumor growth or tumor volume doubling time (TVDT), without intervening treatment, and abstracted data to calculate TVDT and correlates of growth patterns (rapid defined as TVDT <3 months and indolent as TVDT >9 months). Pooled TVDT was calculated using a random-effects model.

Results: We identified 20 studies, including 1198 HCC lesions in 1158 patients. The pooled TVDT was 4.6 (95%CI 3.9 - 5.4) months, with 36.2% classified as rapid, 22.7% intermediate, and 41.1% indolent growth. In subgroup analysis, studies from Asia reported shorter TVDT than studies elsewhere (4.1 vs. 5.8 months). Imaging modality did not affect the TVDT (4.7 months for studies using ultrasound vs. 4.5 months for studies using CT or MRI). Shorter TVDT was noted in studies done after 2000 (5.2 months for studies published prior to 2000 vs. 4.1 months for those published after 2000) and studies with a higher sample size (4.8 months for studies with <50 patients vs. 4.3 months for studies with >50 patients). The most consistent correlates of rapid tumor growth included hepatitis B etiology, small tumor size, AFP trajectory during follow-up, and poor tumor differentiation. Studies were limited by small sample sizes, potential measurement bias, and inherent selection bias.

Conclusion: The tumor volume doubling time of HCC is approximately 4-5 months; however, there is marked heterogeneity in tumor growth patterns, including more indolent patterns in non-hepatitis B Western populations. Identifying correlates of tumor growth patterns is important to better individualize HCC prognostication and treatment decisions.

Presentation #32

Title: Patient Outcomes and Safety of Dual Biologic Therapies

Presenter: Rory Nicolaides

Authors: Rory Nicolaides, MD; David Khan, MD

Faculty Mentor(s): David Khan

Abstract:

Background: Patients with multiple allergic/immunologic diseases may require simultaneous biologic therapies. However, there is a paucity of literature regarding patient safety and outcomes while receiving dual biologic therapies. Objective: To characterize clinical and safety outcomes of patients receiving treatment with more than one biologic therapy.

Methods: A search of the electronic medical record was performed to identify patients over 18 years old treated with a biologic from our allergy, asthma, and immunology specialty clinics at 2 large urban hospitals, and a second biologic for any other indication within the last 10 years. The first biologic was required to be one commonly used in allergy and immunology practices (omalizumab, mepolizumab, benralizumab, reslizumab, dupilumab, canakinumab). Dual therapy was subcategorized into either a period of overlap (at least one dose of each biologic within 30 days), or ongoing therapy (simultaneous treatment with both biologics beyond 30 days).

Results: A total of 314 patients in our clinics have been treated with a biologic, 26 (8.3%) of whom received dual biologic therapy. Twelve patients received ongoing simultaneous biologic therapy while 14 had a period of overlap with a second biologic. 11/12 patients receiving ongoing therapy had a positive clinical response to the "allergy"-based biologic. Dual biologic therapy was not associated with serum sickness-like reactions, infusion related or injection site reactions , or any other significant adverse reaction. There was no evidence of increased immune suppression or frequency of infections reported by patients.

Conclusions: This report of patients on dual biologic therapy adds to the literature suggesting that dual biologics may not increase risk or impair clinical response

Presentation #33

Title: Performance of the Video-Assisted Pre-Participation Evaluation in Adolescent Athletes

Presenter: Gary Parizher

Authors: Gary Parizher, MD; Dermot M. Phelan, MD, PhD, FACC; Colby Ayers, MS; Russell Goodwin, BA; Benjamin D. Levine, MD, FACC, FAHA, FACSM

Faculty Mentor(s): Benjamin D. Levine

Abstract:

Background: We developed and previously published a video-enhanced pre-participation evaluation symptom questionnaire (the V-PPE), intended to help screen athletes by enriching the content and improving the understanding of key symptoms associated with increased risk of sudden cardiac arrest. We now report results of a pilot study evaluating V-PPE questionnaire's performance, conducted using an established electronic PPE network operated on a commercial basis by PRIVIT, Inc.

Methods: In a prospective before-and-after study, approximately 5700 high-school athletes in 16 high schools in Ohio, United States, who had already submitted their standard-of-care PPE questionnaires electronically using PRIVIT's commercially available software, were prompted to voluntarily fill out the V-PPE questionnaire. We compared symptom frequencies on standard PPE to those on V-PPE.

Results: Out of 5700 athletes, 46 (0.8%), 117 (2.0%), 33 (0.6%), and 101 (1.8%) reported syncope, angina, palpitations, and dyspnea, respectively on routine screening. 492 (8.6%) voluntarily filled out the V-PPE, 7 of which were excluded for submitting blank V-PPE questionnaires; there was no difference in reporting frequency between these 492 athletes and the 5700 of the entire cohort. Athletes were more likely to report palpitations and syncope on V-PPE than PPE, but not angina, dyspnea, or at least one symptom.

Conclusion: Symptom frequencies on electronic PPE questionnaires are lower than recent reports based on paper forms suggest. Embedded educational videos can alter athletes' symptom reporting and thereby change screening yield. More research is necessary to evaluate the predictive value of the V-PPE for clinically relevant cardiac pathology in adolescent athletes.

Presentation #34

Title: Association between surgical margins and Crohn's Disease recurrence: A systematic review and meta-analysis

Presenter: Roshni Patel

Authors: Roshni Patel, MD; Tasneem Ahmed, MD; Purva Gopal, MD; Amit G. Singal, MD

Faculty Mentor(s): Amit G. Singal, Tasneem Ahmed, and Purva Gopal

Abstract:

Background: Despite advances in medical therapy, nearly three-fourths of Crohn's disease (CD) patients require surgery in their lifetime. However, post-operative recurrence (POR) is common, with clinical recurrence reported in over one-third of patients within 5 years. Conflicting data exists as to whether histologically positive resection margins are a risk factor for POR, leading to variable reporting by pathologists and inconsistent treatment patterns by gastroenterologists in patients with positive margins. Therefore, this meta-analysis aims to characterize the association between positive histologic margins in CD resection specimens and POR risk.

Methods: We performed a systematic literature review of Medline and EMBASE databases from 1998 to May 2019. We identified studies reporting the association between histologic disease activity at CD surgical resection margins and POR. Pooled estimates were calculated and compared using the DerSimonian and Laird method for a random effects model.

Results: We identified 18 studies, comprising 1862 patients (708 with positive margins, 1154 with negative margins). Studies represented contemporary CD practice after availability of anti-TNF agents, with only six published between 2000-2010. Most studies defined CD recurrence clinically or endoscopically although two limited their evaluation to surgical recurrence. Definitions for positive margins were variable, with most studies using any CD-associated inflammation although nine focused on particular patterns such as lymphocyte infiltration or submucosal plexitis. Finally, half of studies assessed recurrence within 1 year whereas the rest examined recurrence over a time frame of 5-10 years. Overall, the pooled odds of CD POR were higher in patients with positive surgical margins (OR 1.30, 95%CI 1.00 - 1.68), although there was notable heterogeneity. The pooled risk of CD recurrence was 37.9% among patients with a positive surgical margin compared to 36.7% with a negative margin.

Conclusion: Current studies suggest presence of histologic activity at CD resection margins is associated with a statistically significant, albeit likely clinically insignificant, increased risk of POR. These data suggest positive margins likely should not change post-surgical surveillance or management. However, there is substantial heterogeneity in histologic assessments, definition of CD recurrence, and time frame for assessing recurrence, highlighting a need for consistent measures and standardized reporting across studies.

5th Annual Donald W. Seldin, M.D. Research Symposium

Presentation #35

Title: Effects of exercise training on cardiac biomarkers among patients with type 2 diabetes: the HART-D study

Presenter: Amit Saha

Authors: Amit Saha, MD; Kershaw Patel, MD; Colby Ayers, MS; Jarett Berry, MD; Neil Johannsen, PhD; Christopher deFilippi, MD; Timothy Church, MD; MPH, PhD; James de Lemos, MD; Ambarish Pandey, MD, MSCS

Faculty Mentor(s): Ambarish Pandey

Abstract:

Background: Cardiorespiratory fitness (CRF) is a modifiable predictor of heart failure (HF) risk. Identifying mediators of improvement in CRF would provide new opportunities for HF prevention. Cardiac biomarkers provide valuable insight into HF risk and may interact with CRF to determine HF risk.

Methods: We investigated the relationship between cardiac biomarkers and CRF in 166 participants enrolled in the Health Benefits of Aerobic and Resistance Training in Individuals with Type 2 Diabetes (HART-D) trial. Patients were divided into control (n = 31) and exercise (n = 135) groups. Biomarkers of interest were high-sensitivity cardiac troponin T (hs-cTnT), N-terminal prohormone of brain natriuretic peptide (NT-proBNP), and growth differentiation factor-15 (GDF-15). Peak oxygen uptake (VO2peak) and biomarkers were assessed at baseline and at 9-month follow-up. The exercise group was subdivided into tertiles of ΔVO2peak.

Results: Baseline characteristics were similar between control and exercise groups. Age ($P = 0.0245$) and mean systolic blood pressure ($P = 0.0210$) decreased across increasing tertiles of ΔVO2peak. Follow-up measurements of hs-cTnT and NT-proBNP did not differ between control and exercise groups. However, GDF-15 increased in controls ($P = 0.0258$) and was elevated on follow-up compared to the exercise group ($P = 0.0072$). There were no differences in baseline or follow-up biomarkers across ΔVO2peak tertiles. On multivariable linear regression, the strongest factor affecting each follow-up biomarker was its respective baseline measurement ($P < 0.0001$). Each exercise regimen (aerobic, resistance, and combination training) was associated with decreased follow-up GDF-15 ($\beta = -0.27$ [95% CI -0.44-(-0.090)], $\beta = -0.18$ [95% CI -0.35-(-0.01)], and $\beta = -0.20$ [-0.37-(-0.02)], respectively). ΔVO2peak was not associated with follow-up levels of any biomarker. On multivariable linear regression, baseline hs-cTnT negatively predicted ΔVO2peak ($\beta = -0.18$ [95% CI -0.31-(-0.05)]), while baseline GDF-15 was positively associated with ΔVO2peak ($\beta = 0.08$ [95% CI 0.01-0.15]).

Conclusions: This analysis describes the bidirectional relationship between cardiac biomarkers and exercise training. Baseline hs-cTnT negatively predicts ΔVO2peak. Prior data suggests this may represent a high-risk phenotype of cardiac remodeling. Exercise negatively predicted follow-up GDF-15, which may reflect decreased HF risk. Change in CRF was not reflected in follow-up measurement of biomarkers.

Presentation #36

Title: A Spatial Exploration Relating Healthcare Coverage and Medical Crowdfunding in the United States

Presenter: Sameh Saleh

Authors: Sameh Saleh, MD; Richard Medford, MD

Faculty Mentor(s): Richard Medford

Abstract:

Background: Americans have increasingly turned to medical crowdfunding to finance rising personal healthcare-related costs. This growing reliance is primarily attributed to the lack of a publicly funded healthcare system and resultant gaps in healthcare coverage and access. We explore the relationship between healthcare coverage and medical crowdfunding in the United States.

Methods: We conducted a cross-sectional spatial analysis of all active GoFundMe (the largest charitable crowdfunding platform) campaigns under the "Medical" subheading in the United States between September 1, 2018 and August 30, 2019. Through web scraping, we extracted all text and numerical data available from each campaign's webpage and used the listed location of each campaign to label state-level healthcare provision characteristics including Medicaid expansion status and uninsured rate. We explored descriptive statistics for numerical variables extracted and evaluated spatial representations of medical crowdfunding by state.

Results: We studied 120,310 campaigns, of which only 11.3% met their funding goal at the time of data extraction. Campaigns raised approximately $474 million in total over the course of the last year with a mean of $3,946 (standard deviation [SD], $9,132) and a median of $1,500 (interquartile range [IQR], $610-$3,865). While 36.1% of the American population lives in non-Medicaid expansion states, 39.1% of campaigns were in non-Medicaid expansion states ($p<0.001$). The number of Facebook shares also favored non-Medicaid expansion states (median [IQR] 126 [44-291] vs. 123 [41-297]) ($p<0.001$). However, campaigns in non-Medicaid expansion states raised substantially less (median [IQR] $1,325 [$565-$3,310]) than those in Medicaid expansion states (median [IQR] $1,636 [$655-$3,895]) ($p<0.001$). They also attained less of their funding goal (median [IQR] 24.4% [9.5%-55.7%] vs. 30.2% [11.5%-67.0%]) ($p<0.001$). Campaigns in states with higher uninsured rate tended to meet less of their funding goal as well.

Conclusions: These findings support concerns that medical crowdfunding does not adequately bridge gaps in healthcare coverage, but further maligns those with less socioeconomic privilege. We plan to further explore differences by county and by metropolitan area and evaluate other socioeconomic and demographic factors by location. Further research is needed to understand the social, ethical, and economic implications of medical crowdfunding in the United States.

Presentation #37

Title: An "Infodemic": Leveraging High-Volume Twitter Data to Understand Early Public Sentiment for the COVID-19 Outbreak

Presenter: Sameh Saleh

Authors: Sameh Saleh, MD; Richard Medford, MD; Andrew Sumarsono, MD; Trish Perl, MD; Christoph Lehmann, MD

Faculty Mentor(s): Richard Medford and Christoph Lehmann

Abstract:

Background: Twitter has been used to track trends and disseminate health information during viral epidemics. On January 21, 2020, the CDC activated its Emergency Operations Center and the WHO released its first situation report about Coronavirus disease 2019 (COVID-19), sparking significant media attention. How Twitter content and sentiment has evolved in the early stages of any outbreak, including the COVID-19 pandemic, has not been described.

Methods: We extracted tweets matching hashtags related to COVID-19 from January 14th to 28th, 2020 using Twitter's application programming interface. We measured themes and frequency of keywords related to infection prevention practices, vaccination, and racial prejudice. We performed a sentiment analysis to identify the emotional valence and predominant emotions in tweets and conducted topic modeling to identify and explore discussion topics over time.

Results: We evaluated 126,049 (of which 123,407 were unique) containing 2,877,816 words and 15,955,720 characters from 53,196 unique users during the study period. The hourly number of COVID-19-related tweets starkly increased from January 21, 2020 onward and closely tracked the number of newly confirmed cases. The frequency of racially charged tweets closely paralleled the number of newly diagnosed cases of COVID-19 and were present in 0.54% of all tweets. Nearly half (49.5%) of all tweets expressed fear and nearly 30% expressed surprise. Tweets with a negative sentiment were more common than neutral and positive tweets and increased at a faster rate over time. The economic and political impact of COVID-19 was the most commonly discussed topic, while public health risk and prevention were among the least discussed. Topic clusters that included themes of transmission, public health risk, and index cases were discussed from the start of the study period, while discussion of quarantine effects, economic and political impact, and government response increased significantly in the second week of the study period.

Conclusion: Twitter is a rich medium that can be used to understand and track public sentiment and thoughts in real-time. It can be leveraged to potentially target individualized public health messages for education and appropriate information dissemination based on user interest and emotion.

Presentation #38

Title: Ultrasound Quality for Hepatocellular Carcinoma Surveillance in Patients with Cirrhosis

Presenter: Haley Schoenberger

Authors: Haley Schoenberger,; MD; Nicolas Lugon, MD; David Fetzer, MD; Nicole E .Rich, MD; Adam C. Yopp, MD; Takeshi Yokoo, MD, PhD; Gaurav Khatri, MD; Mobolaji Odewole, BS; Megan Carugati, BS; Ana Arroyo, BS; Amit G. Singal, MD, MS

Faculty Mentor(s): Amit Singal MD MS

Abstract:

Background: Abdominal ultrasound fails to detect over one-fourth of hepatocellular carcinoma (HCC) at an early stage in patients with cirrhosis. Identifying patients in whom ultrasound is inadequate to exclude the presence of HCC lesions can inform interventions to improve surveillance effectiveness. We aimed to evaluate and identify correlates of inadequate ultrasound quality in patients with cirrhosis undergoing HCC surveillance.

Methods: We performed a retrospective cohort study of patients with cirrhosis who underwent ultrasound examination at Parkland Health & Hospital and UT Southwestern between July 2016 and July 2019. Ultrasound exam adequacy was defined by interpreting radiologists using LI-RADS visualization score (A=no/minimal limitations, B=moderate limitations, C=severe limitations). For patients with >1 ultrasound exam, we characterized change in visualization scores over time. We performed multivariable logistic regression to determine characteristics associated with inadequate visualization (LI-RADS score B or C).

Results: We identified 411 patients with ≥1 ultrasound exam, with most having an outpatient exam (78.6%) for surveillance indication (73.5%). Most (78.8%) had Child A cirrhosis, with only 17.5% having ascites or hepatic encephalopathy. Overall, 355 (86.4%) were classified as score A, 43 (10.4%) score B, and 13 (3.2%) score C, with the most common limitation being heterogeneous echotexture. In multivariable analysis, inadequate visualization was associated with Child B or C cirrhosis (OR 2.80, 95%CI 1.33-5.91) and presence of obesity (OR 2.80, 95%CI 1.04-7.53 for overweight; OR 2.36, 95%CI 0.81-6.83 for obesity; OR 11.0, 95%CI 3.69-32.7 for morbid obesity). Among 318 patients with >1 ultrasound, 250 (78.6%) had the same visualization score (234 score A, 13 score B, 3 score C). However, 44 (15.8%) of 278 patients with score A had inadequate visualization on repeat exam (42 score B, 2 score C) and 18 (45%) of 40 patients with initial inadequate visualization had score A when repeated. Changes in visualization were consistent across subgroups including patients with obesity or Child B-C cirrhosis.

Conclusions: Over 10% of ultrasound exams are inadequate quality for HCC surveillance, particularly among patients with obesity or Child Pugh B-C cirrhosis. However, ultrasound quality can change between exams, including improvement noted in half of patients with an initial inadequate ultrasound.

Presentation #39

Title: Optimal Phenomapping Strategy to Identify Novel Subgroups of Patients with Type 2 Diabetes Based on Long-term Cardiovascular Risk: An Analysis from the ACCORD and LookAHEAD Cohort

Presenter: Matthew Segar

Authors: Matthew Segar, MD; Kershaw Patel, MD; Muthiah Vaduganathan, MD; Melissa Caughey, PhD; Byron Jaeger, PhD; Mujeeb Basit, MD; Duwayne Willett, MD; Javed Butler, MD; Partho Sengupta, MD; Darren McGuire, MD; Ambarish Pandey, MD

Faculty Mentor(s): Ambarish Pandey

Abstract:

Background: Type 2 diabetes mellitus (T2DM) is a heterogeneous disease process with variable trajectories of cardiovascular disease (CVD). In this study, we aimed to evaluate three phenomapping strategies to identify distinct subgroups of individuals with T2DM and high CVD risk and determine the optimal clustering method.

Methods: Participants with T2DM and free of baseline CVD in the ACCORD trial were included in this study (n = 6,466). Informed variable selection method with optimization of the Wald index was used to select the top 20 covariates associated with CVD-free survival. Gaussian mixture models (GMM), latent class analysis (LCA), and finite mixture model-based clustering (FMM) were performed to identify mutually exclusive phenogroups. Bayesian information criterion (BIC), Dunn index, and model discrimination (C-index) were calculated for each method and compared. The association between the phenogroup and risk of the primary outcome [composite of fatal myocardial infarction (MI), non-fatal MI, or unstable angina] was evaluated using adjusted Cox models. The performance of the optimal phenomapping strategy was assessed in an external validation cohort (Look AHEAD trial: n = 4,211).

Results: Over 9.1 years of follow-up, 789 (12.2%) participants had a primary outcome event. FMM phenomapping method with three phenogroups was the optimal clustering strategy as determined by the BIC, Dunn index, and improvement in model discrimination. Phenogroup 1 (10.3%) had a higher burden of comorbidities and diabetes complications, phenogroup 3 (52.8%) had fewer comorbidities, and phenogroup 2 (36.9%) was older with an intermediate comorbidity burden. Compared with phenogroup 3, phenogroups 1 [adjusted hazard ratio (aHR), 1.80; 95% CI, 1.23-2.65] and 2 were at higher risk for the primary outcome (aHR, 1.28; 95% CI, 1.03-1.64). There were significant interactions between phenogroup and intensive glycemic control (P-interaction = 0.047) as well as combination lipid therapy (P-interaction = 0.005) for the risk of the primary outcome. Similar risk patterns among phenogroups were observed in the validation cohort.

Conclusion: Semi-supervised clustering using FMM was the optimal phenomapping strategy to identify replicable subgroups of patients with T2DM with distinct clinical characteristics, CVD risk, and response to therapies.

Presentation #40

Title: Machine learning-based and race-specific models to predict 10-year risk of incident heart failure

Presenter: Matthew Segar

Authors: Matthew Segar, MD; Byron Jaeger, PhD; Vijay Nami, MD; Chiadi Ndumele, MD; Adolfo Correa, MD; Javed Butler, MD; Christie Ballantyne, MD; Michael Hall, MD; Robert Mentz, MD; James De Lemos, MD; Ambarish Pandey, MD

Faculty Mentor(s): Ambarish Pandey

Abstract:

Background: Heart failure (HF) disproportionally affects African Americans compared to other racial/ethnic groups, however, current risk prediction methods do not account of unique pathophysiologic differences between races. In this analysis, we aimed to develop race-specific machine learning-based models to predict the risk of incident HF in black and white adults.

Methods: Race-specific 10-year models for risk of incident HF were derived and validated from patient-level data from large community-based cohorts. Participants with HF at baseline and age less than 40 years were excluded. A total of 7 machine learning and traditional statistical methods were assessed with the top performing model externally validated in 3 additional cohorts and compared to previously published risk prediction models.

Results: Among 1,217 and 8,274 individuals in the black and white derivation cohorts, HF occurred in 118 and 179 participants, respectively. The most important variables associated with incident HF in blacks included age, natriuretic peptide and troponin levels, renal dysfunction, and markers of diabetes while natriuretic peptide levels and markers of hypertension (Cornell Voltage on ECG, blood pressure), metabolic syndrome (BMI, heart rate), and atherosclerotic disease (CVD history and HDL-c levels) were most importance in whites. Random survival forest (RSF) was the best performing machine learning model with an overall C-index of 85.7 and 83.6 in the black and white cohorts, respectively. Among 6,452 black and 5,810 white participants in the external validation cohorts, the RSF models displayed good discrimination (C-indices ranging from 80.4 - 83.2) and calibration. The RSF model also showed improved performance compared to previously derived methods.

Conclusion: We designed, implemented, and validated race-specific machine learning-based clinical models to predict the risk of 10-year incident HF in the community. This tool can be implemented across a wide range of websites, mobile devices, and electronic health record systems to help facilitate clinical application.

Presentation #41

Title: cMRI vs. ECHO in identifying DMD-associated cardiomyopathy

Presenter: Rahul Sheth

Authors: Rahul Sheth, MD; Daniel Cheeran, MD; Faris G. Araj, MD; Alpesh A. Amin, MD; Mark H. Drazner, MD, MSc; Ronald M. Peshock, MD; and Pradeep P.A. Mammen, MD

Faculty Mentor(s): Pradeep P.A. Mammen, MD

Abstract:

Background: Duchenne muscular dystrophy (DMD) is an X-linked neuromuscular disorder with progressive muscle degeneration resulting in premature death, primarily due to complications related to the development of DMD-associated cardiomyopathy. The majority of DMD patients have scoliosis making cardiac assessment by echocardiography (ECHO) challenging. Although cardiac magnetic resonance imaging (cMRI) is the gold standard imaging tool to assess cardiac function, the vast majority of DMD patients still undergo ECHO rather than cMRI. We hypothesize that cMRI is able to assess cardiac function with more precision and provide valuable cardiac data to better assist the cardiologist in initiating guideline-directed medical therapy.

Methods: We undertook a retrospective study involving DMD patients referred to the UTSouthwestern Adult Neuromuscular Cardiomyopathy Clinic, who had undergone an ECHO as well as a cMRI within 15 months of each other. We assessed the proportion of left ventricular (LV) dysfunction [normal cardiac function: cMRI LVEF≥62% and ECHO Fractioning Shortening (FS)≥25] and technically difficult images by both techniques. In addition, we assessed the proportion of cMRIs with late gadolinium enhancement (LGE), a marker of myocardial fibrosis and associated with increased mortality.

Results: Out of 70 DMD patients who have established long-term cardiovascular care within the UTSouthwestern Adult Neuromuscular Cardiomyopathy Clinic, 20 patients met the inclusion criteria. Amongst these patients 10% of patients had technically difficult images by cMRI, while 85% of ECHO images were challenging to assess. By cMRI, 30% of the studies were normal (LVEF: 66±4%), while 70% were considered reduced cardiac function (LVEF: 44±12%). On the other hand, 75% of the ECHOs were considered normal (FS: 32±5), while 25% were abnormal (FS: 15±8). Finally, 61% of cMRI studies identified LGE (50% amongst normal LVEF and 67% with depressed LVEF).

Conclusions: Collectively, our study demonstrates that cMRI more accurately assessed cardiac function in DMD patients as compared to ECHO. In addition, cMRI was able to identify a large number of patients with LGE, irrespective of cardiac function. Earlier utilization of cMRI will enable the diagnosis of DMD-associated cardiomyopathy to be made and thus enable the cardiologist to initiate aggressive guideline-directed medical therapy at an earlier age.

Presentation #42

Title: Different Barriers to Linkage and Treatment in HCV Care Cascade

Presenter: Joslyn Strebe

Authors: Joslyn Strebe, MD; Abby Lau, MD; Teena Sura, MPH; Laura Hansen, MA; Mamta Jain, MD

Faculty Mentor(s): Mamta Jain and Abby Lau

Abstract:

Background: Among persons living with HIV, 15-30% have chronic hepatitis C (HCV) coinfection. In these patients, the progression to hepatic fibrosis and cirrhosis is accelerated, correlating to a more aggressive course of HCV. It is important that these coinfected patients achieve sustained virologic response (SVR) to HCV; however, barriers in both linkage to care (LTC) and access to treatment remain. Our goal is to evaluate predictors to SVR in coinfected patients along separate steps of the HCV care cascade.

Methods: We retrospectively evaluated all adults with HIV/HCV coinfection from 2014-2017, which included high rates of homelessness, cirrhosis, IV drug use (IDU), and other drug use, within one healthcare system. Univariate and multivariate logistic regression models evaluated for predictors of the LTC and treatment initiation steps of the HCV care cascade.

Results: Among our cohort of 655 HIV/HCV coinfected patients (34% homeless, 18% AIDS, 20% cirrhosis 49.6% IDU, 42.9% other drug use), 286 (44%) had LTC. Positive predictors to LTC were cirrhosis (OR 3.12, CI 1.95-5.14) and HIV viral load (VL) suppression (OR 1.6, CI 1.08-2.34), while a negative predictor was AIDs (OR .36, CI .21-.62). Of those patients that had LTC (25.9% homeless, 11.2% AIDS, 31.5% cirrhosis, 50.3% IDU, 37% other drug use), 136 (57%, 25% of total cohort) were started on treatment. A positive predictor to patients receiving treatment was HIV VL suppression (OR 2.11, CI 1.18-3.78) and negative predictors were homelessness (OR .39, CI .21-.74), IV drug use (OR .19, CI .05-.71), and other drug use (OR .29, CI .16-.54).

Conclusions: Different predictors to achieving SVR were revealed when separately evaluating the steps in the HCV care cascade in HIV/HCV coinfected patients. Those with cirrhosis and HIV VL suppression were more likely to have LTC, while those with AIDs were less likely. Those with HIV VL suppression were also more likely to receive treatment, but patients experiencing homelessness, and/or using IV or other drugs were less likely. Cirrhosis and AIDs were no longer significant factors in determining if a patient received treatment. These differences in predictors along the HCV care cascade indicate that using different strategies to target

Presentation #43

Title: Prognostic Value of Hypochloremia in Critically Ill Patients with Decompensated Cirrhosis

Presenter: Andrew Sumarsono

Authors: Andrew Sumarsono, MD; Jiexin Wang, MD, PhD; Luyu Xie, PharmD; Giuliana Cerro Chiang, MD; Thomas Tielleman, MD; Sarah E Messiah, PhD; MPH; Amit G Singal, MD, MS; Arjmand Mufti, MD; Catherine Chen, MD; Matthew Leveno, MD

Faculty Mentor(s): Matthew Leveno

Abstract:

Background: Cirrhosis is frequently complicated by electrolyte disturbances, with prior studies primarily focused on the importance of hyponatremia. Emerging evidence on patients with chronic heart failure and chronic kidney disease has identified hypochloremia as an independent predictor for mortality. This study aimed to investigate the prognostic value of serum chloride and its association with mortality in cirrhotic patients.

Methods: We conducted a retrospective cohort study on adult patients with cirrhosis admitted to the medical intensive care unit (ICU) at Parkland Memorial Hospital between March 2015 and March 2017. We performed Kaplan-Meier analysis and multivariable cox proportional hazard ratio models to determine the impact of hypochloremia on 180-day mortality.

Results: Of the 389 enrolled patients, 133 (34.2%) died within 180 days of ICU admission. Patients with hypochloremia had higher 180-day mortality than those with normochloremia (45.2% vs. 26.7%; $p < 0.0001$). Cumulative survival via the Kaplan-Meier method was significantly lower in the hypochloremic group. Serum chloride was independently associated with 180-day mortality with multivariable adjustment (HR: 0.95; 95% CI: 0.93 - 0.98; $p = 0.001$); or after adjusting for MELD or SOFA. Contrarily, the inverse association between serum sodium and mortality no longer existed in all multivariable models.

Conclusions: Serum chloride is independently and inversely associated with short-term mortality in critically ill cirrhotic patients. Hypochloremia, but not hyponatremia, remained associated with mortality with multivariable analyses, suggesting that hypochloremia may account for the mortality risk previously attributed to hyponatremia. Our findings signify the prognostic value of serum chloride and potential inclusion of chloride into future cirrhosis prognostic scores.

Presentation #44

Title: National and State Patterns of Cardiovascular Drug Prescriptions following Medicaid Expansion

Presenter: Andrew Sumarsono

Authors: Andrew Sumarsono, MD; Hussain Lalani, MD MPH; Ambarish Pandey, MD MSCS

Faculty Mentor(s): Ambarish Pandey

Abstract:

Background: On January 1, 2014, the Affordable Care Act (ACA) permitted states to expand Medicaid eligibility for all nonelderly citizens and permanent residents with an income up to 138% of the federal poverty level. Though early studies demonstrated increases in overall prescriptions post Medicaid Expansion, how the Medicaid expansion impacted cardiovascular prescription volume and spending has not been described.

Methods: Data were obtained from the Medicaid State Drug Utilization dataset from 2009 to 2018. We quantified the quarterly number of prescriptions and overall spending of 7 classes of antihypertensives, antiplatelets, and statins between 2009 and 2018. We employed a quasi-experimental difference-in-difference design to isolate the effect of the Medicaid expansion on statin prescriptions among states that did and did not expand Medicaid.

Results: In 2009, Medicaid beneficiaries received 6.3 million prescriptions of statins, 1.1 million prescriptions of anti-platelets, and 20.7 million prescriptions of antihypertensives. By 2018, prescriptions use of statins had increased by 183% (to 17.8 million), antiplatelets by 73% (to 1.9 million) and antihypertensives by 160% (to 53.9 million). The total number of total Medicaid beneficiaries increased from 50,567,554 to 67,604,061 over the study period. Following the Medicaid Expansion, early-expander states saw average quarterly increases in prescriptions/1000 beneficiaries of 2.45%, 1.13%, and 1.17% for statins, antiplatelets, and antihypertensives, respectively. In comparison, non-expander states saw quarterly changes of +0.01%, -0.37%, and 0.36%% in prescriptions/1000 beneficiaries of statins, antiplatelets, and antihypertensives.
Conclusion: Overall national use of statins, anti-platelets, and anti-hypertensives grew significantly between 2009-2018. States that expanded Medicaid noted significantly greater increases in use of statins, anti-platelets, and anti-hypertensives compared with states that did not.

Presentation #45

Title: Prevalence and Prognostic Implications of Depression in Patients With Heart Failure With Preserved Ejection Fraction

Presenter: Neela Thangada

Authors: Neela Thangada, MD; Vijay Agusala, BS; Colby Ayers, MS; Ambarish Pandey MD, MSCS

Faculty Mentor(s): Ambarish Pandey

Abstract:

Background: One in four individuals with HFpEF are diagnosed with depression. The prognostic implications of prevalent and new onset depression in patients with HFpEF are unknown.

Methods: Participants from the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist Trial (TOPCAT) with available PHQ-9 Depression Scale data at baseline were stratified according to depression severity: minimal (score: 1-4), mild (5-9), moderate (10-14), and severe (>15). Depression status at 1-year follow up was also determined in the subgroup with available follow up data using the PHQ-9 Depression Scale. The association of prevalent depression, change in depression status with risk of all-cause mortality and HF-hospitalization was evaluated using multivariable adjusted Cox models.

Results: The study included 1431 participants, of which 15.9% had moderate depression and 10.8% had severe depression at baseline. Participants with severe depression at baseline had higher BMI, were more commonly women, and had higher burden of diabetes, and worse NYHA functional status. In adjusted Cox models, there was a significant graded association between depression severity and risk of mortality, with the highest risk noted among those with severe depression. Among participants with 1-year follow up data, participants with new-onset depression on follow-up had significantly higher risk of all-cause mortality [HR (95% CI) = 2.00 (1.27 - 3.14), ref group: no depression at baseline and follow up]. Prevalent depression at baseline or new onset depression on follow up was not significantly associated with risk of HF-related hospitalization in the study cohort.

Conclusions: Prevalent and new onset depression is associated with higher risk of all-cause mortality in patients with HFpEF. Future studies are needed to determine if early identification and treatment of depression may modify the risk of all-cause mortality in patients with HFpEF.

Presentation #46

Title: Inflammation mediates the association of depression severity with SSRI treatment response in patients with CKD

Presenter: Stephanie Torres Rodriguez

Authors: Stephanie Torres Rodriguez, MD; L. Parker Gregg, MD, MSCS; Thomas Carmody, PhD; Madhukar Trivedi, MD; S. Susan Hedayati, MD, MHSc

Faculty Mentor(s): Susan Hedayati and Parker Gregg

Abstract:

Background: Patients with chronic kidney disease (CKD) are at high risk for depression, which is associated with death, dialysis initiation, and hospitalization. Depressive symptoms correlate with inflammatory biomarkers in patients with chronic diseases. We investigated whether depression severity is associated with response to treatment with sertraline and whether inflammation mediates this relationship in CKD patients with major depression (MDD).

Methods: We conducted the Chronic Kidney Disease Antidepressant Sertraline Trial (CAST), a randomized double-blind trial of 193 participants with stage 3-5 non-dialysis CKD and MDD randomized to sertraline or placebo for 12 weeks. Depressive symptoms were assessed using the Quick Inventory of Depressive Symptomatology (QIDS). High sensitivity C-reactive protein (hsCRP) was measured at baseline. Logistic regression determined associations of QIDS and hsCRP with treatment response (≥50% decrease) or improvement (≥3-point decrease) in QIDS. Models were controlled for baseline QIDS, age, sex, race, eGFR, diabetes mellitus, and study site. Interaction $P<0.10$ was considered significant.

Results: Fifty-five (28.5%) participants achieved treatment response. Baseline depression severity by QIDS correlated positively with hsCRP, rho=0.162, $P<0.05$. Median (IQR) hsCRP was 5.0 (2.0, 14.6) mg/L in sertraline responders and 2.7 (0.8, 6.0) mg/L in non-responders, P=0.03. Higher baseline QIDS was associated with increased odds of response in the sertraline group, OR (95% confidence interval) per 1-point increase 1.26 (1.04, 1.53) but lower odds in the placebo group, 0.77 (0.61, 0.97), interaction P=0.002. Higher baseline QIDS was also associated with 3-point improvement in the sertraline group, OR 1.27 (1.04, 1.56) but not in the placebo group, 1.04 (0.86, 1.27), interaction P=0.17. Higher baseline hsCRP was associated with higher odds of response, OR per log-unit increase 1.52 (1.06, 2.19), and improvement, 1.66 (1.11, 2.48), in the sertraline group, but not in the placebo group, interaction P=0.08 for response and 0.03 for improvement, even after controlling for baseline depression severity by QIDS score.

Conclusions: Higher depression severity was associated with improvement in depressive symptoms and response to treatment with sertraline in CKD patients. This may be explained by elevated baseline inflammation. Future studies should test whether sertraline is more effective than placebo in CKD individuals with higher plasma hsCRP.

Presentation #47

Title: Association of Statin Therapy With Risk of Thyroid Disease in 2 Propensity Score-Matched Cohorts

Presenter: Lakshya Trivedi

Authors: Lakshya U Trivedi, MD; Ethan A. Halm, MD, MPH; Ishak Mansi, MD; Laurette Femnou Mbuntum, MD

Faculty Mentor(s): Ishak Mansi

Abstract:

Background: Studies have suggested both beneficial and harmful effects of statin use on thyroid disease, however, data is limited and conflicting. Given the prevalence of various thyroid diseases, understanding predisposing factors, including medication-related exposures, deserves further attention. Objective: To examine the association between statin use and thyroid disease in a general population and in a healthy population (individuals with no severe comorbidities).

Methods: Patients were Tricare beneficiaries from October 2003 to March 2012. Based on patients' characteristics during baseline phase (fiscal year [FY] 2004-2005), 2 propensity score (PS)-matched cohorts of statin users and nonusers were formed: (1) a PS-matched general cohort and (2) a PS-matched healthy cohort. Our outcomes were defined using inpatient or outpatient ICD-9 codes for thyroid cancer, thyrotoxicosis, goiter, and thyroiditis during the follow-up phase (FY 2006 to March 2012) in statin users and nonusers.

Results: The study included a total of 43,438 patients (13,626 statin users and 29, 812 nonusers). The PS-matched general cohort matched 6342 statin users to 6342 nonusers. In the PS-matched general cohort, thyroid cancer occurred in 0.4% of statin users and 0.7% in nonusers (OR 0.048; 95% CI = 0.39-0.99). There was no significant difference between statin users and nonusers in thyrotoxicosis (OR 0.88, 95% CI = 0.71-1.09), goiter (OR 0.13; 95% CI = 0.77-1.03), or thyroiditis (OR 0.20; 95% CI = 0.53-1.15). The PS-matched healthy cohort matched 3351 statin users to 3351 nonusers; there was no difference between statin users and nonusers in thyroid cancer (OR 0.55; 95% CI = 0.36-1.73), thyrotoxicosis (OR 0.73, 95% CI = 0.75-1.50), goiter (OR 0.53; 95% CI = 0.75-1.16), or thyroiditis (OR 0.44; 95% CI = 0.69-2.38).

Conclusions: This study did not demonstrate any harmful effects of statins on examined thyroid diseases. Moreover, statin use was associated with a decreased risk of thyroid cancer in some populations.

Presentation #48

Title: Lipoprotein(a) and Coronary Artery Calcium Score for Predicting Atherosclerotic Cardiovascular Disease Risk

Presenter: Nestor Vasquez

Authors: Nestor Vasquez MD; Anurag Mehta MD, Colby Ayers MS, Jaideep Patel MD, Ananya Hooda MBBS, Michael J. Blaha MD MPH, Roger S. Blumenthal MD, Michael Tsai PhD, Michael Shapiro MD, Laurence S. Sperling MD, Salim Virani MD PhD, Amit Khera MD MSc, Parag H. Joshi MD MHS

Faculty Mentor(s): Parag H. Joshi

Abstract:

Background: Lipoprotein(a) [Lp(a)], and coronary artery calcium score (CAC) score are individually associated with an increased atherosclerotic cardiovascular disease (ASCVD) risk. The independent and joint association of these two risk markers for predicting incident ASCVD is unknown.

Methods: ASCVD-free participants from the Multi-Ethnic Study of Atherosclerosis (MESA) and the Dallas Heart Study (DHS) with Lp(a) and CAC measurements at baseline were pooled and followed for ASCVD events. The independent and joint associations of elevated Lp(a) (race-specific quintile 5 vs. quintiles 1-4) and CAC score (>100 and 1-100 vs. 0) were assessed using Cox models. Models were adjusted for traditional ASCVD risk factors, and multiplicative interaction of Lp(a) with CAC was tested. The 10-year cumulative ASCVD incidence for participant groups was compared.

Results: Among 5,862 participants (55.5 years, 3663 from MESA, 54% female, 36% Black, 21% Hispanic, 7% Chinese), 32% had CAC 1-100 and 17% had CAC >100. During 11.9 years follow-up, a total of 440 ASCVD events were observed. High Lp(a), CAC 1-100, and CAC >100 were independently associated with ASCVD risk (HR 1.37, 95% CI 1.09-1.71; 1.93, 95% CI 1.48-2.53; 2.96, 95% CI 2.24-3.90, respectively) and no Lp(a) x CAC interaction was observed (p>0.40). The 10-year ASCVD incidence among participants with CAC >100 was higher in those with Lp(a) quintile 5 vs. quintiles 1-4 (p=0.049). For participants with CAC score 0 there was no difference in the 10-year ASCVD incidence in those with Lp(a) quintile 5 vs. quintiles 1-4 (p=0.184); similar results were found in participants with CAC score 1 - 100 (p=0.169).

Conclusion: In this pooled sample of two ASCVD-free population-based cohorts, both Lp(a), and CAC were independently associated with incident ASCVD. A possible additive association of elevated Lp(a), and CAC score > 100 with increased ASCVD risk was found. However, for individuals with CAC score 0 the ASCVD risk does not appear higher when having concomitant elevated Lp(a) levels, further supporting the "power of zero" CAC.

Presentation #49

Title: ERAS® and Erase: Social Media Use by Internal Medicine Residency Applicants and Program Directors

Presenter: Joseph Vento

Authors: Joseph Vento, MD; Neil Keshvani, MD; Udit Dhal, MD; Reeni Abraham, MD; Salahuddin Kazi, MD; Arjun Gupta, MD

Faculty Mentor(s): Arjun Gupta and Salahuddin Kazi

Abstract:

Background: The role of social media screening in residency applicant evaluation is largely unknown. We aim to investigate the role of social media during the internal medicine residency application process and adjustments made by applicants prior to the start of application process.

Methods: We surveyed residents and program directors from 2017-2018 on their social media experience during the residency application cycle. We distributed the resident survey to internal medicine residents at the University of Texas Southwestern and Cleveland Clinic Akron (response rate 103/214, 48.1%). In addition, we sent an online survey to all Texas Internal Medicine program directors (PDs) (response rate: 15/24, 62.5%).

Results: 69.6% of surveyed residents believed PDs use Facebook® in evaluating applicants, and 13.3% of PDs responded that they or someone involved in ranking applicants look at applicants' Facebook® pages. Of resident responders, 89.3% had Facebook® accounts at the time of residency applications, and 57.6% changed their Facebook® accounts in some way during residency application season, most frequently by changing their name (31.5%), hiding pictures (29.3%), and/or changing their profile pictures (21.7%).

Conclusions: We discovered a significant proportion (70%) of internal medicine residents believed PDs review Facebook® during the residency application process and alter their profiles prior to applying; however, only a slim minority of surveyed PDs actually review and utilize Facebook® during the application process. We believe the robust alterations of social media by applicants is an overreaction to perceived program director screening but do recommend upholding of social media posting to a professional standard.

Presentation #50

Title: Hospital Medicine Physician Electronic Health Record Utilization: Efficiency, Variation and Opportunities

Presenter: Joseph Vento

Authors: Joseph Vento, MD; Nainesh Shah, MD, Maryam Warsi, MPH, Brett Moran, MD; Anita Hegde, MD and Eugene S. Chu, MD

Faculty Mentor(s): Eugene Chu Nainesh Shah

Abstract:

Background: Physicians increasingly utilize electronic health records (EHR) to deliver healthcare, and the EHR has been identified as leading source of physician burnout and frustration. However, there is no data to inform how hospital medicine physicians spend their time in EHRs. We sought to understand how hospital medicine physicians partition their time within the EHR as well as the variability between physicians.

Methods: We conducted a retrospective cohort study of 44 full time equivalent, day shift hospital medicine physicians performing direct patient care at Parkland Memorial Hospital. We obtained each hospitalist's Epic activity logs for six non-consecutive months between March 2017 and March 2019. We ranked physicians and divided them into quartiles of efficiency, then examined the distribution of EHR use by hour of day.

Results: We found that hospital medicine physicians at our institution spend a mean of 4.3 hours (± 66.9 minutes) a day in the EHR with a range of 2.2 hours/day to 7.4 hours/day in the EHR. Physicians in the top quartile spent a mean of 3.0 hours ± 31.3 minutes/day in the EHR while physicians in the bottom quartile spent a mean of 5.7 hours ± 57.6 minutes/day in the EHR, with nearly twice as much time in note writing and clinical review. Physicians spent the most time in the EHR writing notes (mean 86.6 ± 39.9 minutes) and in clinical review (49.0 ± 18.6 minutes), followed by time writing orders (32.8 ± 10.0 minutes) and navigating patient lists (23.8 ± 7.6 minutes). Physician time in the EHR showed a bimodal distribution with a sharp peak at 0800 and a second, flatter peak between 1300 and 1600.

Conclusions: For the same tasks, there is large intragroup variation amongst hospital medicine physicians in EHR usage and efficiency. It is not clear whether those who spend less time in the EHR do so at the cost of quality. Identifying physicians who are able to minimize time in the EHR and maintain high quality documentation and care will allow us to optimize the value of time spent in the EHR and minimize burnout associated with the EHR.

Presentation #51

Title: Thyroid dysfunction and immune checkpoint inhibitor outcomes

Presenter: Mitchell von Itzstein

Authors: Mitchell S. von Itzstein, MD; Rong Lu, PhD; Sadia Ali, MD; Donglu Xie, MS; Jennifer Cai, MSc MSCS; Yang Xie, MD PhD; David E. Gerber MD

Faculty Mentor(s): David Gerber

Abstract:

Background: Immune checkpoint inhibitors (ICI) frequently cause thyroid dysfunction. We performed a longitudinal analysis of thyroid function tests in a large, single-center cohort of patients with multiple cancer types receiving ICI.

Methods: We performed a retrospective medical records review of consecutive patients treated with ICI from 1/1/2005 to 12/31/2018. We collected demographic and clinical data, including serial thyroid function tests. We compared overall survival between patients with normal and abnormal thyroid stimulating hormone (TSH) at baseline and after ICI initiation using Kaplan-Meier curves, log-rank tests, and multivariate Cox proportional hazards model.

Results: A total of 910 patients were included: 63% male, 82% white, median age 67. The most common cancer types were lung (26%), kidney (18%), and melanoma (17%). ICI types were anti-PD1/L1 (78%), anti-CTLA-4 (7%), and combination ICI (15%). Normal baseline TSH and abnormal post-treatment TSH was associated with longer overall survival (median survival 26 months) compared to all other TSH permutations (median survival <10 months) (P<0.001). This finding persisted after multivariate Cox regression adjustment for age, gender and cancer type (P<0. 001), and also after sensitivity analysis censoring patients who died within 2 months after starting ICI. Conversely, abnormal TSH at baseline was associated with lower overall survival (median 8 months) compared to normal TSH at baseline (median 18 months) (P<0.001), which also persisted in multivariate analysis (P<0.001). Kidney and head and neck cancers (71% and 69%) were associated with increased development of thyroid dysfunction compared to melanoma, lung and other urological cancers (52%, 50% and 35%) (P<0.01).

Conclusion: Although abnormal thyroid function after ICI initiation was associated with improved overall survival, pre-treatment thyroid abnormalities were associated with worse overall survival. Given the prevalence of thyroid abnormalities in the general population, further research into these observations is warranted.

Presentation #52

Title: Identification of rare genetic variants in Dallas Heart Study participants with high cardiovascular risk burden but low coronary artery calcium scores

Presenter: Suchith Vuppala

Authors: Suchith Vuppala, MD; Julia Kozlitina, PhD

Faculty Mentor(s): Julia Kozlitina, PhD

Abstract:

Background: Coronary Artery Calcium (CAC), a measure of subclinical atherosclerosis, is an independent marker for cardiac events. CAC correlates with traditional risk factors (TRF) for atherosclerotic diseases. However, some individuals have low CAC despite high TRF burden. The Dallas Heart Study (DHS) is a multiethnic population-based probability sample of 6101 adults from Dallas County. The current study includes DHS participants who provided DNA samples for genetic analysis and completed clinical visits, including measurements of CAC (n=2682).

Methods: The objective was to test whether individuals with extremely low CAC carry genetic factors contributing to protection from atherosclerosis. In Dallas Heart Study participants (n=2682), frequency of single nucleotide variants (SNVs) was compared between individuals with CAC scores below expected CAC based on TRF-based regression model, and matched controls. Risk factors used to develop predicted CAC were age, gender, ethnicity, systolic blood pressure (SBP), total cholesterol, Diabetes Mellitus (DM II), smoking, and BMI. Individuals below the 3rd percentile of observed vs expected CAC were defined as low CAC cases. Selecting for the lowest 3 percentiles in terms of deviation of real CAC from expected CAC yielded a sample of 81 individuals.

Results: The high TRF-low CAC group (n = 81, mean age 54, 62% male, body mass index (BMI) 31, total cholesterol 192, 64% smokers, 52% DM II, systolic blood pressure (SBP) 139) had a mean CAC of 0. The remainder of DHS participants (n = 2601, mean age 45, 45% male, BMI 30, total cholesterol 181, 47% smokers, 25% DM II SBP 126) had a mean CAC of 62. As expected, mean age, cholesterol, SBP, percentage of smokers, men, and diabetics are all statistically significantly elevated in the (high TRF and low CAC) group. No SNVs reached genome-wide significance. The study identified a variant in the P2RX1 gene (P=9.82x10-4) that may confer genetic protection via apoptosis in the calcification pathway.

Conclusions: It is unclear whether genetic factors protect individuals with low CAC and high TRF burden from atherosclerosis. Some individuals with low CAC carry rare variants in a gene regulating apoptosis, suggesting it may contribute to protection from atherosclerosis.

Presentation #53

Title: Utilization of hepatocellular carcinoma surveillance in patients with cirrhosis: A systematic review and meta-analysis

Presenter: Erin Wolf

Authors: ErinWolf, MD; NicoleERich, MD MS; JorgeAMarrero, MD MS; NeeharParikh MD MS; AmitGSingal, MD MS

Faculty Mentor(s): Amit Singal

Abstract:

Hepatocellular carcinoma (HCC) surveillance is associated with early tumor detection and improved survival; however, it is often underused in clinical practice. We aimed to characterize surveillance utilization among patients with cirrhosis and the efficacy of interventions to increase surveillance. We performed a systematic literature review using the MEDLINE database from January 2010 through August 2018 to identify cohort studies evaluating HCC surveillance receipt, or interventions to increase surveillance, in patients with cirrhosis. A pooled estimate for surveillance receipt with 95% confidence intervals was calculated. Correlates of surveillance utilization were defined from each study and pre-specified subgroup analyses. Twenty-nine studies, with a total of 118,799 patients, met inclusion criteria, with a pooled estimate for surveillance utilization of 24.0% (95%CI 18.4 - 30.1). In subgroup analyses, the highest surveillance receipt was reported in studies with patients enrolled from subspecialty

Gastroenterology/Hepatology clinics and lowest in studies characterizing surveillance in population-based cohorts (73.7% vs. 8.8%, p<0.001). Commonly reported correlates of surveillance included higher receipt among patients followed by subspecialists and lower receipt among those with alcohol- or NASH-related cirrhosis. All eight studies (n=5229) evaluating interventions including patient/provider education, inreach (e.g. reminder and recall systems), and population health outreach strategies reported significant increases (range 9.4% - 63.6%) in surveillance receipt.

Presentation #54

Title: Risk factors of immune checkpoint inhibitor-induced colitis in patients with renal cell carcinoma

Presenter: Jianyi Yin

Authors: Jianyi Yin, MD, PhD; Roy Elias, MD; Hans Hammers, MD, PhD

Faculty Mentor(s): Hans Hammers

Abstract:

Background: Immunotherapy has become a standard of care in advanced renal cell carcinoma (RCC). However, data are limited with regard to immune checkpoint inhibitor (ICI)-induced colitis in RCC. This study aimed to describe the characteristics of ICI-induced colitis and determine its potential risk factors in patients with RCC.

Methods: We performed a retrospective study of adult patients who were treated with immunotherapy for advanced RCC between 2016 and 2018 at two tertiary care centers. Patients who developed ICI-induced colitis were identified and their clinical presentations and outcomes were noted. Univariate and multivariate logistic regression analyses were conducted to assess risk factors associated with ICI-induced colitis.

Results: A total of 176 patients who received immunotherapy for RCC were considered, of which 16 (9.1%) had ICI-induced colitis, including 7 patients with grade ≥3 colitis. Patients with colitis were not significantly different from those without colitis in age, gender, RCC histologic subtype, Fuhrman grade, previous cancer treatment, IMDC score, and overall survival. Initial immunotherapy regimen using combotherapy of nivolumab and ipilimumab, exposure to ipilimumab, and exposure to proton pump inhibitor (PPI) within 12 months after immunotherapy were significantly more frequent in patients with ICI-induced colitis than those without. Patients with ICI-induced colitis presented with significantly increased neutrophil-lymphocyte ratio (NLR) and absolute neutrophil count (ANC) from baseline, and a wide range of endoscopic and histologic findings. Exposure to ipilimumab and PPI were significantly associated with ICI-induced colitis in univariate and multivariate logistic regression analyses.

Conclusions: Exposure to PPI and anti-CTLA4 therapy may be risk factors of ICI-induced colitis in patients with RCC. Further studies are needed to verify these findings in other types of cancer.

Presentation #55

Title: Patient Utilization and Cost Effectiveness of Shared Medical Appointments for Diabetes Management at Community Clinic

Presenter: Christiana Beveridge

Authors: Christiana Beveridge, MD, MBA

Faculty Mentor(s): Kavita Bhavan

Abstract:

Background: Shared medical appointments (SMAs) increase access to care and improve outcomes by increasing patients' exposure to health care providers and others with similar health conditions. Diabetes is often targeted for management with SMAs because of its long asymptomatic phase, many complications, and personal management of medications and lifestyle behaviors. A recent systematic review of SMAs in diabetes showed improved clinical outcomes, but few studies have evaluated the cost-effectiveness of SMAs.The objective of this study is to evaluate the utilization and cost-effectiveness of SMAs for diabetes at a community clinic.

Methods: Retrospective chart review was completed on patients who attended the Garland COPC diabetes SMA from January 2017 - July 2019 for demographic and clinical characteristics. Data were collected about no-show rates. Time-driven activity-based costing (TDABC) was used to assess the cost of an SMA versus individual medical appointments. This method uses direct observation and interviews with staff to determine the amount of time required to perform specific activities.

Results: Between January 2017 and July 2019, 209 patients completed 636 SMA encounters. These encounters were completed in Spanish and English; 63% were female; 73% were between 41-64; 72% speak Spanish as their primary language. The average HgbA1c at the first visit was 10.03 and average BMI was 31.7. 56% of patients' HgbA1c improved, and 35% of patients' BMI improved over the time period of this study. Preliminary analysis using TDABC shows that SMA cost effectiveness is dependent on the number of patients seen during one shared visit. If similar no-show rates are assumed for SMAs vs regular outpatient appointments, TDABC analysis shows SMAs are more cost-effective than individual appointments.

Conclusions: This study re-affirms that SMAs have the potential to improve patient outcomes with the majority of patients improving their HgbA1c. This study also shows that SMAs are less costly than individual appointments. Shared Medical Appointments appear to be a cost-effective tool for managing diabetes.

Presentation #56

Title: Penicillin Allergy Testing by Allergy Trained Pharmacists in Hospitalized Patients

Presenter: Whitney Blackwell

Authors: Whitney Blackwell, MD; Felicia Diloreto, PharmD; Kristin Alvarez, PharmD; and David Khan, MD

Faculty Mentor(s): David Khan

Abstract:

Background: Penicillin is the most common reported drug allergy, although greater than 90% of patients labeled allergic can tolerate it. Hospitalized patients with reported penicillin allergy have been found to have longer hospital stays and increased rates of Clostridium difficile, vancomycin-resistant Enterococcus, and methicillin-resistant Staphylococcus aureus infections. Our goal of this program is to reduce inaccurate penicillin labels, increase patient education of drug allergy, and reduction of beta-lactam alternatives.

Methods: In September 2014, we implemented a protocol for clinical trained pharmacists to perform penicillin skin testing and challenges for inpatients at Parkland Hospital initiated by either physician consult or pharmacists screening of patients labeled with penicillin allergy.

Results: From November 2014 to June 2019, a total of 1926 consults were ordered and 850 patients underwent testing. Approximately one-third of consults were ordered secondary to electronic medical record best practice advisories or use of aztreonam order set. Of the patients tested, we removed penicillin allergy for 754 patients (89%). Positive testing occurred at skin prick for 55 patients (6.5%), intradermal for 15 patients (1.8%), and oral challenge for 11 patients (1.3%). Ninety-one patients (12%) were relabeled and through intervention 75 of these patients were delabeled.

Conclusions: A clinical trained pharmacist performing penicillin allergy testing inpatient is effective in removing penicillin allergy label, in addition, to retaining this label.

Presentation #57

Title: Improving Documentation of Smoking Cessation Counseling Among Spondyloarthropathy Smokers

Presenter: Yusuf Chao

Authors: Yusuf Y. Chao, MD; Elena K. Joerns, MD; Jake Hutto, MD; Rashmi Arora, MD; Swathi Reddy, MD; Una E. Makris, MD, MSc.

Faculty Mentor(s): Una Makris and Swathi Reddy

Abstract:

Background: Smoking is prevalent among patients with spondyloarthropathies and is associated with higher disease activity and dampened response to biologic therapy. Despite the strong recommendation for smoking cessation in the 2018 American College of Rheumatology guidelines for management of psoriatic arthritis, physicians do not routinely counsel spondyloarthropathy smokers in the context of their disease. The Dallas Veteran Affairs Medical Center (VA) is an ideal location for smoking cessation quality improvement (QI) given the robust tobacco cessation modalities already integrated into primary care. Our QI project will evaluate whether modification of the rheumatology clinic note template with prompts to address tobacco use will increase physician documentation of smoking cessation counseling.

Methods: For baseline pre-intervention data, we conducted a chart review of patients diagnosed with ankylosing spondylitis, inflammatory bowel disease-associated arthritis, and psoriatic arthritis who were current smokers seen for follow-up at the VA rheumatology clinic from 8/01/2017 to 6/30/2018. We assessed disease activity and documentation of smoking status, quantity and duration of cigarette use, and smoking cessation counseling. We modified the assessment and plan section of the clinic note template by including smoking cessation counseling prompts, effective 1/27/2020. Additional interventions include physician education on template use, awareness of tobacco cessation referrals, and equipping the clinic site with patient brochures on cessation resources. Since post-intervention data are not yet available, we present baseline data in this abstract.

Results: We reviewed 498 charts and identified 50 spondyloarthropathy smokers, including 21 patients with psoriatic arthritis, 23 with ankylosing spondylitis, and six with inflammatory bowel disease-associated arthritis. Smoking status was documented in rheumatology clinic notes for 46 (92%) patients. Only six (12%) smokers had documentation of smoking cessation counseling by rheumatology providers, while 16 (32%) had documentation of counseling by non-rheumatology providers (13 by primary care, two by gastroenterology, and one by endocrinology). There was no documentation of counseling by any provider for 29 (58%) smokers.

Conclusions: The baseline tobacco cessation counseling documentation rate for spondyloarthropathy smokers is low among rheumatology providers. In the next phase of our project, we will continue educating rheumatology providers and obtain post-intervention data.

Presentation #58

Title: Trainee Understanding of and Interaction with Out-of-Pocket Costs

Presenter: Jeffrey Chidester

Authors: Jeffrey Chidester, MD; Rebecca Vigen, MD, MSCS; Sandeep R Das, MD, MPH

Faculty Mentor(s): Sandeep Das and Rebecca Vigen

Abstract:

Background: Out-of-pocket costs (OOPC) are a significant barrier to care and drive suboptimal medical therapy. Despite this, there is minimal attention paid to these costs in post-graduate education. To define a potential knowledge gap, we surveyed trainee understanding of OOPC.

Methods: We surveyed Internal Medicine residents at a large academic program comprised of a large county safety-net hospital, a VA, and a private tertiary care hospital, about knowledge and practices surrounding patient OOPC. Residents rotate on services at all sites and the vast majority have primary care clinic at the county or VA hospital. Participants answered questions considering their most recent inpatient panel and their clinic patient panel. Familiarity was ranked on a 5-point Likert scale, and for the purposes of presentation, was divided into "Poor" and "Moderate or Better". Non-parametric analysis was used to test differences between outpatients v inpatients and by year of training.

Results: Of 159 residents, 106 (67%) responded. Familiarity with patient insurance status was moderate or better in 135 of 159 (85%). Moderate or better understanding of costs associated with medications (52%), testing (19%) and clinic visits (30%) was less common. Respondents had higher familiarity with OOPC for clinic patients compared with their most recent inpatient panel: clinic visits (39% v 21% $p < 0.005$), testing (25.7% v 12.4% $p = 0.002$), and medications (62% v 42% $p < 0.005$) Knowledge of cost of care was not an often-considered factor in decision making (27% "Often" or "Always"). There was no significant difference in response by year of training.

Conclusions: Our survey demonstrates that trainee familiarity with OOPC was low overall but modestly higher for established clinic patients, perhaps reflecting longitudinal experience with them or the heterogeneity of admitted patient funding status. Familiarity with patient OOPC was not an often-considered factor in decision making and did not significantly improve over years of training. This suggests an important gap in trainee education. Teaching greater familiarity with patient OOPC during residency can increase awareness of the financial realities of patients, enabling more patient-centered care.

Presentation #59

Title: Incidentalopathy: An Unintended Epidemic in Hospital Medicine

Presenter: Niraj Madhani

Authors: Anita Hegde, MD; Niraj Madhani, MD; Preetha Nair, MD; Bryan Block, MD; Lindsay Ripley, MD; Eugene S. Chu, MD

Faculty Mentor(s): Eugene Chu and Anita Hegde

Abstract:

Although incidental findings (IFs) are common, as a whole they are an unstudied phenomenon. This creates the possibility of adverse clinical events due to lack of recognition and follow up. We sought to determine the prevalence of IFs as well as to characterize the provider's assessment and plan for those findings. We reviewed a random sample of 153 patients discharged between January 1 and June 30, 2018 from Parkland Hospital. X-ray (XR), computed tomography (CT), ultrasound (US), magnetic resonance (MR), and nuclear medicine (NM) studies were included. We defined IFs as any finding within the radiology impression unrelated to the reason for imaging or patient's principal diagnosis. Progress notes one day after imaging result date (NDPN) and discharge summaries (DS) were assessed for IF documentation. Follow up, patient adherence, and progression or complications were also assessed up to one year post-discharge. There were 246 IFs out of 550 radiologic studies with an average of 3.6 imaging studies and 1.6 IFs per patient. XR was the most common (1.63/patient) with an IF prevalence of 35.0% while CT was the second (0.82/patient) with an IF prevalence of 74.5%. While only 2% of imaging was MR, its IF prevalence was 50.0%. AA's were the most prevalent (42.8% on CT, 53.4% on XR, 54.5% on US), followed by medical conditions (33.3% on CT, 14.4% on XR, 34.5% on US) and masses (22.2% on CT, 4.5% on XR, 10.9% on US). 20.6% and 23.5% of masses were on the NDPN and DS respectively. Of the non-masses, 16.4% and 14.5% were on the NDPN and DS respectively. Nine patients showed progression of an IF, though none were deemed preventable. There were no deaths related to missed IFs. IFs are common in hospitalized patients. The majority were not specifically documented or followed up on. However, the clinical relevance of many of the IFs is unclear and the "signal to noise" ratio may be diminished. Risk stratifying IFs may help to increase the signal to noise ratio and call notice to IFs that are high risk and require close and reliable follow up.

Presentation #60

Title: Empowering Telemetry Technicians to Call Code Blue

Presenter: Cody McCoy

Authors: Cody McCoy, MD; Neil Keshvani, MD, Maryam Warsi, Eugene Chu, MD, Anita Hegde, MD

Faculty Mentor(s): Anita Hegde

Abstract:

Background: In-hospital cardiac arrest (IHCA) events are common, and delays in treatment are associated with lower survival and poor neurologic outcomes. Many hospitals utilize centralized telemetry monitoring in the general inpatient setting, allowing for monitoring of higher patient volumes by specialized staff physically away from the patient's care unit. Delays in identification and verification of arrhythmias can lead to delays in code activation, which can lead to increased morbidity and mortality. We sought to assess the impact of telemetry technician driven activation of code blues on IHCA mortality rate, survival to discharge, time to cardiopulmonary resuscitation (CPR), and inappropriate code activation.

Methods: We implemented a quality improvement protocol at Parkland Memorial Hospital, a 900-bed, urban, safety-net hospital, in Dallas, Texas to empower telemetry technicians to call code blue directly for certain life-threatening arrhythmias (ventricular fibrillation, sustained ventricular tachycardia of greater than 30 seconds, asystole, or bradycardia less than 30 beats/minute) starting September 1, 2016. We then performed a retrospective chart review of all IHCA in patients on centralized telemetry at Parkland for one year prior to the intervention and two years post intervention looking at the primary outcome of survival to discharge. Secondary outcomes included code survival, time to CPR, and inappropriate code activation. Staff education and procedure rollout occurred from September 1, 2016 to September 30, 2016, and patient data from this period was excluded.

Results: IHCA events were designated as a pulseless electrical activity (PEA) code or non-PEA code. The pre-intervention non-PEA survival to discharge was 1/10 (10.0%) and the post-intervention non-PEA was 9/16 (56.2) (p=0.018). The pre-intervention non-PEA code survival was 7/10 (70.0%) and the post-intervention non-PEA code survival was 15/16 (93.8%), (p=0.10). The time to CPR, in seconds, was 180 versus 120 (p=0.58) for pre- and post-intervention non-PEA codes. There were 0 inappropriate code activations post-intervention.

Conclusions: Empowering telemetry technicians to activate code blue for general ward patients on centralized telemetry showed significantly improved survival to discharge and a trend in code survival benefit. Importantly, there were no inappropriate code activations by telemetry technicians, highlighting the safety of this intervention

Presentation #61

Title: Improving Documentation Rates of Non-Pharmacologic Therapies for Musculoskeletal Pain

Presenter: Megan Milne

Authors: Megan Milne, MD; Travis Welsh,MD; Una E. Makris, MD

Faculty Mentor(s): Una E. Makris

Abstract:

Background: Musculoskeletal pain is the leading cause of chronic disability in older adults. Non-pharmacologic interventions are key in guideline-based management, especially in elderly patients for whom pharmacologic agents may not be a safe option. A quality improvement project was conducted at the Dallas VAMC Rheumatology clinic to improve documentation of non-pharmacologic therapies offered to older veterans with musculoskeletal pain.

Methods: Fifty charts from a VA Rheumatology clinic were reviewed for documentation of non-pharmacologic musculoskeletal pain therapies (May 2018). Then, a new note template dedicated to musculoskeletal pain management was implemented. Next, Rheumatology Grand Rounds presentations were given on non-pharmacologic musculoskeletal therapies. A post-intervention chart review was conducted on 50 charts (November 2019).

Results: The majority of patients were men, aged 50 or older, with knee osteoarthritis. Therapies with the most improvement in documentation rates were: thermal therapies (2% to 58%), use of topical therapies (66% to 94%), weight loss (36% to 64%), physical therapy (60% to 86%), and exercise regimens (42% to 62%). Psychology-based therapies were among the least utilized interventions.

Conclusion: A dedicated musculoskeletal pain note template and departmental presentations on musculoskeletal pain improved rates of documenting non-pharmacologic therapies. Further improvement is needed as important modalities, specifically mental health interventions, remain under-utilized in this veteran population.

Presentation #62

Title: Self-Administration of Home Inotrope Therapy for Patients with End Stage Heart Failure

Presenter: Wally Omar

Authors: Wally Omar, MD; Chris Mathew, Pharm D; Kavita Bhavan, MD; Sandeep Das, MD; Jose Joglar, MD

Faculty Mentor(s): Jose Joglar

Abstract:

Background: Palliative use of continuous IV inotrope therapy has shown to improve quality of life and reduce hospital readmissions for patients with end-stage heart failure (HF) who are otherwise ineligible to receive advanced therapies. Administration of home inotrope therapy generally requires a hospice or home-health agency, placing this option out of reach for patients who lack funding. As such, underinsured patients are relegated to the difficult choice of either remaining in the hospital to receive IV inotropes, or going home without the therapy for as long as their symptoms allow. To address this issue at our large county safety-net hospital, we developed and implemented a patient self-administered home inotrope therapy program.

Methods: A multidisciplinary team of physicians, pharmacists, nurses, and social workers was assembled to pilot the program. Eligible patients were provided with a peripherally inserted central venous catheter (PICC) and a portable infusion pump. They were then instructed on proper use of the pump, medication administration, medication bag changes, and IV line care using a nursing teach-back technique. After proper understanding was demonstrated, patients were discharged home with weekly follow up in heart failure clinic for PICC-care and medication exchanges.

Results: During the initial 12 months of the program, 5 patients were deemed eligible for enrollment. Total hospitalized days for these patients was 277 (mean = 55.4 days) in the one year prior to enrollment and 19 (mean = 3.8 days) while enrolled for a cumulative period of 409 days (Figure 1). One patient was able to secure funding for advanced therapies, three patients died while enrolled, and one patient is currently enrolled and alive.

Discussion: A self-administered home IV inotrope therapy program is a feasible alternative for palliation in unfunded patients with end-stage HF who are otherwise not candidates for advanced therapies, allowing for more days at home in the end of life . Thus far, the cost impact of the program has been mitigated by the cost savings for inpatient hospitalizations. Studies to assess patient-centered outcomes are going and overall cost savings are ongoing.

Presentation #63

Title: Nephropleural fistula and urinothorax after percutaneous nephrolithotomy

Presenter: Carlos Cardenas

Authors: Carlos Cardenas, MD; Dylan Lovin, MD; Arthi Satyanarayan, MD; Traci Adams, MD

Faculty Mentor(s): Traci Adams

Abstract:

Case Report: A 54 year-old female with morbid obesity and bilateral staghorn calculi was admitted to the hospital for elective bilateral percutaneous nephrolithotomy (PCNL) for progressive renal dysfunction. A left sided PCNL was performed and a percutaneous nephrostomy (PCN) tube was left in place. Four days post procedure, the PCN tube was removed. Six days post procedure, the patient developed severe left-sided pleuritic chest pain, orthopnea, and dyspnea at rest. She required two liters of oxygen by nasal cannula to maintain her oxygen saturation above 90%. Exam was notable for super morbid obesity (BMI of 60), mild respiratory distress, and absent left sided breath sounds with dullness to percussion. Chest x-ray showed a large left pleural effusion. Urgent bedside thoracentesis was performed, and 1.8 liters of clear, pink-tinged fluid was removed. Pleural fluid analysis revealed a transudate by Light's criteria with a pH of 7.8, creatinine of 6.69 mg/dL, and a pleural fluid to serum creatinine ratio of 2.9. CT scan of her chest, abdomen, and pelvis revealed bilateral staghorn calculi, a large left pleural effusion, and a fistulous tract between the kidney and the posteroinferior pleural space. A chest tube was placed, and the patient underwent double J-stent placement within the urinary tract which relieved the obstruction and halted the accumulation of pleural fluid. The chest tube was removed, and the patient was discharged with plans to undergo right sided PCNL in the future.

Discussion: Urinothoraces can be caused by urinary tract obstruction or trauma. PCN tube placement above the 12th rib can lead to pleural transgression and injury, as in this case. Traumatic urinothoraces are typically symptomatic, unilateral, and large. In most cases, pleural fluid analysis shows an acidic transudate with a pleural fluid to serum creatinine ratio of greater than one. Diagnosis can be made on the basis of pleural fluid analysis or imaging with either CT or radionucleotide scans. Treatment with thoracentesis or chest tube drainage alone leads to unfavorable outcomes in nearly all cases; therefore, management should focus on correction of the uropathy which provides definitive treatment.

Presentation #64

Title: The Role of Hypertonic Continuous renal Replacement Therapy in the Treatment of Cerebral Edema

Presenter: Han-Cheng Chen

Authors: Han-Cheng Chen, DO; Tamim Hamdi, MD

Faculty Mentor(s): Tamim Hamdi

Abstract:

Background: Cerebral edema (CE) is a common complication of acute liver failure (ALF) and one of the main causes of death. Osmotherapy with hypertonic saline or mannitol is the mainstay of treatment of CE but might result in inconsistent fluctuations in serum osmolality especially if employed in a patient already receiving continuous renal replacement therapy (CRRT).

Methods: A 23-year-old previously healthy male presented with acute fulminant liver failure due to acute Hepatitis B virus infection and rapidly developed altered mental status concerning for cerebral edema. He was started on CRRT due to refractory hyperammonemia along with standard treatment for CE. The CRRT sodium concentration was raised by adding 23.4% saline to achieve high target serum sodium levels with frequent changes based on clinical evolution. This modality was exclusively used to deliver osmotherapy and proved highly reliable. Four weeks later, the patient's liver function was improving, and he was extubated. A repeat head CT showed normal brain structure.

Conclusions: CRRT prescription can be modified to safely and reliably deliver osmotherapy in patients with ALF and life-threatening CE.

Presentation #65

Title: A rare case of Paroxysmal Cold Hemoglobinuria (PCH) presenting with an underlying Lymphoma

Presenter: Nivan Chowattukunnel

Authors: Nivan Chowattukunnel, MD; Andrew Sumarsono, MD; Srikanth Nagalla, MD

Faculty Mentor(s): Srikanth Nagalla

Abstract:

Case Presentation: A 36 year-old male with no significant PMH presented with a few weeks of abdominal pain, intermittent nausea/vomiting, night sweats, and weight loss of 20-30lbs over the past year. He also noted recurrent episodes of fatigue and tea-colored urine only after drinking ice cold beverages and cold intolerance in his hands/feet. Exam revealed bilateral cervical and inguinal lymphadenopathy, and significant tenderness to palpation in the LUQ/LLQ with massive splenomegaly. Labs were significant for hgb 5.8, retic 5.91%, LDH 479, Tbili 2.3, haptoglobin <1. Fibrinogen and INR were normal. Peripheral smear showed RBC agglutination and nucleated RBCs. DAT was positive for C3 and negative for IgG, with antibody identification demonstrating the Danoth-Landsteiner antibody. He underwent a biopsy of a left inguinal LN which demonstrated CD5-/CD10-/CD20+ low-grade B-cell lymphoma. He received blood transfusions and was started on rituximab, Velcade/Dexamethasone with improvement in his symptoms.

Discussion: We present a rare case of paroxysmal cold hemoglobinuria (PCH) in the setting of marginal zone lymphoma. The exact incidence of PCH is unknown, but is estimated to be <1% of all autoimmune hemolytic anemias. PCH is more common in children, and usually presents transiently after a viral illness. Historically, PCH in adults was associated with infection, most commonly syphilis, but has become increasingly rare with the declining prevalence of syphilis. Detection of the Donath-Landsteiner antibody confirms the diagnosis. The Donath-Landsteiner antibody binds to the P antigen of RBCs and fixes complement at cold temperatures. After rewarming back to 37°C, the membrane attack complex activates and lyses the cell. Sensitivity of the test is low and should not be used to rule out PCH in someone with a compelling history and positive Coombs test for C3 complement. There are only a few case reports of B-cell lymphomas presenting with PCH, with most cases demonstrating clinical PCH remission with chemotherapy. General management includes avoidance of cold exposure. Patients may require transfusions for symptomatic anemia or intravenous hydration for AKI. Our patient's PCH responded well to chemotherapy for his underlying lymphoma. Although rare, it would be prudent to consider lymphoproliferative disorders for adults presenting with PCH.

Presentation #66

Title: Rapidly Progressing Interstitial Lung Disease in Suspected Clinically Amyopathic Dermatomyositis

Presenter: Aakash Deshpande

Authors: Aakash Deshpande, MD; Andrew Sumarsono, MD; Leah Cohen, MD

Faculty Mentor(s): Leah Cohen

Abstract:

Case Presentation: A 36-year-old man with vitiligo, autoimmune hepatitis, and newly diagnosed MSSA bacteremia presented to the hospital due to joint pain, weakness, and exertional dyspnea. His dyspnea began four months ago for which he received antibiotics with minimal improvement. He noted significant joint pains, rashes on his hands and eyelids, and dysphagia requiring esophageal dilation. He denied muscle weakness or pain. He had intermittently received steroids for his autoimmune hepatitis and worked as a welder. Vitals were T 97.2 F, BP 130/77, HR 86, RR 18, SpO2 95%. His exam was notable for oral and fingertip ulceration, violaceous rash of several MCP's and eyelids, and fine inspiratory crackles. Pertinent labs included WBC 16.58*10^9/L, AST 246 U/L, ALT 179 U/L, Alk Phos 591 u/L, ESR 33mm/h, CRP 44.9 mg/L, Ferritin 4592 ng/mL, Lactate 3.5 mmol/L. CK was normal. Aldolase sample was hemolyzed. SSA Ro52 was positive at 44.4 AU/mL and anti-smooth muscle antibody titer was elevated at 1:20; the remainder of his autoimmune serologies and extended myositis panel, including anti-MDA5, were negative. Blood cultures remained positive for MSSA and echocardiogram identified mitral valve endocarditis. Chest CT showed peripheral groundglass opacities and consolidations in a peri-bronchovascular distribution. Steroids were initially deferred due to active endocarditis. However, the patient's condition rapidly deteriorated and pulse dose steroids at 1mg/kg were initiated. Despite this, the patient soon required intubation and ICU admission for progression to ARDS. Repeat imaging identified worsening pulmonary opacities and diffuse alveolar damage. The patient's course was complicated by multi-system organ failure and the patient died on hospital day 16. Preliminary cause of death on autopsy was multifactorial due to underlying connective tissue disease, interstitial lung disease, and endocarditis.

Discussion: We present a case of rapidly progressive interstitial lung disease with clinical findings suggestive of clinically amyopathic dermatomyositis (CADM). CADM presents with cutaneous signs of dermatomyositis, but without evidence of myositis, and is commonly associated with anti-MDA5. Diagnosis of CADM requires at least six months of normal muscle strength, enzymes, and EMG. Treatment options include steroids, calcineurin inhibitors, cyclophosphamide, azathioprine, and mycophenolate.

Presentation #67

Title: Eosinophilia and Rash

Presenter: Lauren Franzblau

Authors: Lauren Franzblau, MD; Sandra Hofmann, MD, PhD

Faculty Mentor(s): Sandra Hoffman

Abstract:

Case Presentation: A 47-year-old African American man with history of hypertension, type 2 diabetes, and heart failure presented to the ED with a gluteal abscess and was noted to have a diffuse pruritic rash. The rash had been present for 2-3 years despite treatment with topical steroids. He denied fevers, chills, cough, bruising or bleeding, international travel, or animal exposure. His took furosemide and had no allergies. He worked as a truck driver and had no family history of autoimmune or hematologic disorders. Physical examination revealed diffuse hyperpigmented papules and plaques on his trunk and extremities. His labs were notable for absolute eosinophilia of 1.94x10^9/L. Chart review showed persistent eosinophilia up to 18.2x10^9/L for over 6 months. Skin punch biopsy showed lichen simplex chronicus. Infectious disease testing including HIV, T spot, blood cultures, strongyloides and toxocara serologies, and histoplasma urine antigen were negative. CT of his chest, abdomen, and pelvis demonstrated bilateral centrilobular nodules with surrounding ground glass and hepatosplenomegaly. Transthoracic echocardiogram showed normal LV function and mildly reduced RV systolic function. Further testing revealed markedly elevated IgE and a small atypical population of CD3-CD4+ lymphocytes on peripheral and bone marrow flow cytometry. Testing for JAK2, FIP1L1/PDGFRA, BCR-ABL, FGFR1/3, and PDGFRB were negative.

Discussion: Hypereosinophilia has a broad differential diagnosis including primary hypereosinophilic syndromes (HES) as well as allergic/atopic conditions, parasitic or fungal infections, autoimmune disease, malignancy, and drug reactions. In this middle-aged patient with chronic eosinophilia, rash, and hepatosplenomegaly we had high suspicion for primary HES although infectious etiologies had to be ruled out first. The atypical lymphocyte population is consistent with lymphocytic-variant HES, which is characterized by hypersecretion of IL-5, prominent skin findings, and elevated IgE as seen in this patient. Lymphocytic-variant HES is a risk factor for T cell lymphoma, although he had no evidence of this. Initial treatment consists of corticosteroids and is aimed at reducing end organ damage. The anti-IL5 antibody mepolizumab and pegylated interferon alpha-2 are used in refractory cases. Because of his concurrent abscess, he was continued on topical corticosteroids only and will be followed by hematology and immunology clinics.

Presentation #68

Title: Metastatic Neuroendocrine Tumor Presenting as Gastritis

Presenter: Surbhi Gupta

Authors: Surbhi Gupta, MD; Colin Hinkamp, MD; Neil Keshvani, MD

Faculty Mentor(s): Neil Keshvani

Abstract:

Case Presentation: A 74-year-old woman with type 2 diabetes presented to the hospital with abdominal pain and nausea. An EGD revealed H. pylori gastritis without peptic ulcer disease. Imaging demonstrated a large, cystic-appearing liver. She was seen in liver clinic for further workup, and presumed to have autosomal dominant polycystic kidney disease (ADPKD) without renal cysts. She presented to the hospital 5 additional times for similar complaints and diagnosed with candidal esophagitis and giardiasis. On one admission, a chromogranin A level was obtained for unknown reasons and found to be elevated to 13,060 ng/mL, but not followed-up further. She presented 12 months later with acute encephalopathy not oriented to year or place. Initial testing revealed new mild hyperammonemia to 52 mcmol/L without cirrhosis, portal hypertension, or abnormal liver function tests. Liver biopsy demonstrated well-differentiated grade 2 neuroendocrine tumor (NET), positive for chromogranin and synaptophysin. A PET gallium Ga-68 dotatate scan demonstrated uptake throughout the liver and a lesion in the T8 vertebral body. She started lanreotide injections with eventual resolution of her symptoms and encephalopathy.

Discussion: This patient had proven infectious reasons, such as H. pylori, to explain her symptoms. Her large, cystic liver remained a mystery for a year. This may have been due to poor imaging quality with motion artifact that precluded adequate evaluation of her liver, or poor sensitivity of CT for detecting NETs. Additionally, she did not have signs of a functionally active tumor such as peptic ulcer disease associated with Zollinger-Ellison syndrome, or flushing and diarrhea seen with carcinoid syndrome. Anchoring bias, despite an elevated chromogranin A level, to ADPKD may have also delayed her diagnosis. Neuroendocrine tumors typically originate from the pancreas and are rare, with an incidence of less than 1 case per 100,000 individuals a year. Hepatic neuroendocrine tumors are most presumed to be metastatic as primary hepatic tumors are exceedingly rare. In this case, it is unclear whether she had a primary hepatic neuroendocrine tumor, or another primary site not detected by dotatate scan. However, because her gallium Ga-68 dotatate scan suggested somatostatin-receptor expression, she was empirically treated with lanreotide with improvement.

Presentation #69

Title: Metastatic Breast cancer to the colon: A unique presentation with colon polyps and prominent drop in hemoglobin requiring blood transfusion

Presenter: Elizabeth Harris

Authors: Elizabeth Harris, MD; Moheb Boktor, MD; Suntrea Hammer, MD; Ezra Burstein, MD PhD

Faculty Mentor(s): Moheb Boktor

Abstract:

Case Presentation: A 59 year old female was diagnosed in 2006 with stage IIIC grade 1 estrogen receptor positive (ER+), progesterone receptor positive (PR+), and HER-2/neu mutation negative (Her2-) T2N3M0 invasive lobular breast carcinoma of left breast and treated with left modified radical mastectomy followed by 4 cycles of dose-dense adjuvant doxorubicin and cyclophosphamide, 12 weeks of Taxol, and radiation therapy to her left chest wall. She was in remission since 2007 and received maintenance hormonal therapy with anastrazole. She presented late 2018 with dyspnea and fatigue secondary to anemia. Of note, she had a roux-and-Y gastric bypass in 2008. Full hematologic workup including bone marrow biopsy showed no etiology. Her anemia worsened to the point that she required multiple transfusions and hospitalization in early 2019. She underwent esophagogastroduodenoscopy (EGD) and colonoscopy to determine if there was a gastrointestinal source of bleeding. EGD revealed LA grade A esophagitis and evidence of prior gastric bypass without evidence of bleeding. However, colonoscopy revealed polyps throughout her cecum, ascending, and transverse colon. The pathology on these polyps showed they were metastases of ER+, PR+, HER2- adenocarcinoma. She underwent re-staging with biopsy of a para-aortic lymph node and skeletal survey, both of which showed metastatic disease. After colonoscopy with polypectomy her anemia improved. She has subsequently started palliative chemotherapy with letrozole and palpociclib for recurrent lobular breast carcinoma with metastases.

Conclusions: This is a unique case of metastatic recurrent breast cancer presenting with severe anemia due to colonic metastases. To our knowledge, only a handful of case reports describe similar presentations of metastatic breast cancer presenting due to symptoms from gastrointestinal metastases. Breast cancer rarely metastasizes to the gastrointestinal tract and when it does most commonly spreads to the stomach with a presentation resembling linitis plastica. Metastases of breast cancer to the colon are less common, although there are case reports describing metastatic breast cancer being diagnosed based on a single colon polyp or colonic obstruction due to large metastatic masses. Given the propensity of lobular breast carcinoma to metastasize to the gastrointestinal tract, more frequent screening endoscopies may be beneficial to these patients.

Presentation #70

Title: Diffuse Ground Glass Opacities and an Elevated Fungitell - Weighed Down by Anchoring Bias

Presenter: Colin Hinkamp

Authors: Colin Hinkamp, MD; Surbhi Gupta, MD; Franck Hannallah, MD; Rosechelle Ruggiero, MD

Faculty Mentor(s): Rosechelle Ruggiero

Abstract:

Case Presentation: A 48-year-old man with sarcoidosis with moderate restrictive lung disease, pulmonary hypertension with RV dysfunction, and 2nd-degree atrioventricular block presented with acute hypoxemic respiratory failure. A Fungitell was negative, chest imaging was unchanged from baseline, and he had a new transaminitis and cytopenias. He improved with steroids and diuresis and was discharged on prednisone. Three weeks later he re-presented in respiratory failure with new bilateral opacities on his chest radiograph. A respiratory virus panel revealed coronavirus-HKU1, a repeat Fungitell was elevated, and pneumocystis jirovecii pneumonia (PJP) direct fluorescence antibody (DFA) was negative. He acutely decompensated despite empiric treatment for a sarcoidosis flare, hospital-acquired and PJP pneumonias, and decompensated RV failure. Chest CT-Angiogram revealed hilar and mediastinal lymphadenopathy with new diffuse ground-glass opacities (GGOs) and echocardiogram concerning for significantly worsening RV function. He was intubated with norepinephrine given his worsening PH, but shortly suffered from cardiac arrest several times before passing away. Autopsy revealed large, consolidated lungs with histoplasmosis, subsequently also found in his bone marrow and mediastinal lymph nodes.

Discussion: Histoplasmosis shares several features with sarcoidosis including non-caseating granulomas, erythema nodosum, and transaminitis. Histoplasmosis should be considered in patients with sarcoidosis as immunosuppression can worsen histoplasmosis and may present unusually in immunosuppressed patients. Pulmonary histoplasmosis classically presents as focal infiltrates with prominent adenopathy, whereas diffuse GGOs has only been described in a handful of reports.1 This patient's biopsy-confirmed sarcoidosis and recent negative Fungitell obscured suspicion for co-occurring histoplasmosis. His elevated repeat Fungitell was presumed to represent PJP, which more classically presents as diffuse GGOs, since the PJP DFA has poor sensitivity in non-HIV infected patients. Coronavirus-HKU1 superimposed on fibrotic pulmonary parenchyma offered a reasonable explanation for the new GGOs and clinical worsening, and his prominent lymphadenopathy was easily attributed to long-standing sarcoidosis, delaying further investigation of his declining oxygenation. Similarly, a PE could have explained his hypoxemia, worsening RV failure, and PEA-arrests. However, clinicians should be aware of anchoring bias in immunocompromised patients who are at heightened risk for multiple concurrent illnesses, especially as this patient's distorted lung architecture put him at greater risk of opportunistic infections.

Presentation #71

Title: Heart Failure, Fever, and a Diastolic Murmur: A Case of Left Atrial Myxoma

Presenter: Geoffrey Huntley

Authors: Geoffrey D. Huntley, MD; Katy Lonergan, MD

Faculty Mentor(s): Katy Lonergan

Abstract:

Case Presentation: A 52-year-old female without known past medical history presents to Parkland Hospital with 6 weeks of progressive shortness of breath which is worse with exertion, orthopnea, paroxysmal nocturnal dyspnea, leg swelling, and subjective fevers and chills. She reports taking no medications. She smokes cigarettes but does not use alcohol or other drugs. Her family history is not known. On presentation, she was afebrile, tachycardic, and normotensive. Her physical exam was notable for soft diastolic murmur best heard at the apex, jugular venous distension to 10cm, mild crackles at bilateral lung bases, and +1 pitting lower extremity edema. Initial lab work revealed microcytic anemia and an elevated NT-pro BNP of 2416. Electrocardiogram showed sinus tachycardia, and chest x-ray showed a small right pleural effusion. Heart failure was suspected, so a transthoracic echocardiogram was obtained. This demonstrated a large 2.9 x 5.9 cm mass attached to the left interatrial septum and prolapsing through the mitral valve causing left ventricle inflow stenosis. This was suspected to be an atrial myxoma, so resection at Clements University Hospital was planned. Pre-procedure transesophageal echocardiogram confirmed the intra-cardiac mass. This was resected via trans-septal approach, and pathology revealed a cartilaginous mass with myxoid changes consistent with an atrial myxoma. She did well post-operatively.

Discussion: This case is a classic presentation of a rare disease. The most common cardiac tumor is one of metastases, but of primary cardiac tumors, myxomas are the most common. The majority occur in the left atrium. Heart-failure like symptoms are the most common and occur due to tumor prolapse through the mitral valve causing left ventricle inflow stenosis or mitral regurgitation. Classically, a diastolic tumor plop is heard but this occurs in a minority of patients. One-third of patients have constitutional symptoms, such as fever and weight loss, as the myxoma cells originate from multipotent cells capable of neural differentiation. A feared complication is systemic embolization, which occurs in up to 30% of patients. Transthoracic and transesophageal echocardiogram confirm the diagnosis, and prompt resection is required. Postoperative recovery is rapid but can be complicated by atrial arrhythmias.

Presentation #72

Title: A Case of Chemotherapy-Induced Coronary Vasospasm in a Patient with Colorectal Cancer

Presenter: Ryan Kabir

Authors: Ryan Kabir, MD; Nestor Vasquez, MD; Neil Keshvani, MD; Wanpen Vongpatanasin, MD

Faculty Mentor(s): Wanpen Vongpatanasin

Abstract:

Case Presentation: A 59-year-old man with history of stage IV mucinous adenocarcinoma of the rectum on palliative chemotherapy presented to the emergency department with severe chest pain that radiated down his left arm. Two days prior to his presentation for chest pain, he completed his first full cycle of palliative chemotherapy with FOLFOX (5-flourouracil, leucovorin, oxaliplatin) and bevacizumab. Physical examination in the emergency department revealed a heart rate of 90 beats per minute and blood pressure of 155/84 mmHg. Cardiac examination revealed normal S1 and S2 with no extra heart sounds. His lungs were clear to auscultation bilaterally. He had no jugular venous distention or lower extremity edema. His ECG was significant for ST segment elevations and hyperacute T waves in the precordial and inferior limb leads. He was taken for left heart catheterization, where no coronary artery disease was found. His presentation was thus attributed to vasospasm induced by recent chemotherapy initiation. He was started on amlodipine, and his chemotherapy regimen was switched to capecitabine and oxaliplatin (XELOX). At cardiology follow-up 8 months later, he reported no further chest pain and his ST segment elevations on ECG had resolved.

Discussion: Cardiotoxicity is a well-known side effect of various chemotherapeutic agents. 5-flourouracil (5-FU) is a flouropyrimidine antimetabolite agent with potential cardiotoxicities that include cardiomyopathy, coronary thrombotic events, and coronary vasospasm. Studies have suggested that coronary vasospasm with 5-FU therapy is most likely to occur with the first cycle of treatment. Bevacizumab is a VEGF (vascular endothelial growth factor) inhibitor known to increase risk of cardiotoxicity when used with a regimen that also contains 5-FU. However, this increased risk is largely attributable to endothelial dysfunction resulting in arterial thrombotic events, and there are very few reports of bevacizumab-induced vasospasm. Our patient experienced vasospasm after being initiated on therapy with FOLFOX and bevacizumab, and vasospasm attributed to this combination of chemotherapy has never before been reported in the literature. Management for these cardiotoxicities may involve screening for modifiable cardiovascular risk factors and their optimization prior to initiating chemotherapy. Calcium channel blocking agents have also been effectively used in the treatment of vasospasm.

Presentation #73

Title: Unraveling Complications: A case of Migrating Embolization Coil Used to Treat Rasmussen's Aneurysm

Presenter: Tsuzumi Kanaoka

Authors: Tsuzumi Kanaoka, MD; Andrew Sumarsono, MD; Dylan Lovin, MD; Muhanned Abu-Hijleh, MD

Faculty Mentor(s): Muhanned Abu-Hijleh

Abstract:

Introduction: Rasmussen's aneurysm is a rare complication of pulmonary tuberculosis resulting in a pulmonary artery pseudoaneurysm. We report a case of a 75-year-old woman with pulmonary tuberculosis who presented with massive hemoptysis secondary to Rasmussen's aneurysm rupture and the subsequent endobronchial migration of the embolization coil.

Case Presentation: A 75-year-old woman with two months of non-productive cough presented to the ED with hemoptysis, dyspnea, and hypoxia. In the ED, the patient had massive hemoptysis and developed PEA arrest requiring emergent intubation. An emergent flexible bronchoscopy confirmed active hemorrhage from the left upper lobe, and CT angiography revealed a pulmonary artery pseudoaneurysm adjacent to a cavitary consolidation. Subsequent pulmonary angiogram identified the site of active extravasation, and a platinum embolization coil was placed in the superior segment branch of the lingula. M. tuberculosis PCR, sputum culture, and AFB smear all tested positive for tuberculosis. The patient was started on Rifampin, Isoniazid, Pyrazinamide and Ethambutol. Her chest radiograph on day 13 incidentally showed a string-like foreign body extending from the left upper bronchus, up towards the endotracheal tube tip, and ending in the right bronchus. Bronchoscopy visualized an unraveled portion of the embolization coil extending through the broncho-arterial fistula into the left main bronchus, crossing the midline by looping the Murphy eye of the ETT, and terminating into the right main bronchus. Interventional bronchoscopy was performed to cut and remove the unraveled portion of the coil. She underwent a repeat procedure six days later when the coil was found to be unraveling again. Her course was complicated by dependence on the mechanical ventilation due to significant neurological impairment secondary to severe anoxic brain injury. The patient received tracheostomy and a PEG tube, and was later discharged to a long-term acute care facility on day 36. Discussion/

Conclusion: Tuberculosis remains a major cause of infection and death worldwide. Recognizing life-threatening complications is essential. This case offers opportunities to discuss the diagnosis and management of hemoptysis related to Rasmussen's aneurysm and subsequent endobronchial migration of pulmonary artery embolization coil.

Presentation #74

Title: A Case Series of Patients with Unique Presentations of Proliferative Glomerulonephritis with Monoclonal Immune Deposits

Presenter: Deepa Koshti

Authors: Deepa Koshti, MD;. Ramesh Saxena, MD.

Faculty Mentor(s): Ramesh Saxena

Abstract:

Monoclonal gammopathy of renal significance (MGRS) comprises B-cell and plasma-cell clonal proliferative disorders that do not require immediate treatment for the clonal disease but produce nephrotoxic monoclonal immunoglobulins (mIg) that elicit a variety of kidney manifestations. One such presentation is proliferative glomerulonephritis associated with monoclonal immune deposits (PGNMID), typically presenting as membranoproliferative glomerulonephritis (MPGN) and non-organized glomerular mIg deposits. We herein describe 3 cases of PGNMID seen at our institution.

Case-1: A 16-year old female presented with abdominal pain, gross hematuria, nephrotic proteinuria, edema and normal kidney function. Serum and urine protein electrophoresis were negative, bone marrow (BM) biopsy showed no evidence of lymphoplasmacytoid malignancy. Kidney biopsy showed MPGN with monoclonal IgG-3 lambda deposits. She had inadequate response to B or plasma-cells-targeted therapies but responded very well to muti-targeted therapy (mycophenolate+tacrolimus) achieving complete response.

Case-2: A 39-year old woman with a history of antiphospholipid syndrome and 2 miscarriages had uncomplicated third pregnancy but developed persistent nephrotic proteinuria. Kidney biopsy showed membranous glomerulopathy with mesangial hypercellularity and monoclonal IgG3 lambda deposits. No T or B cell clone was identified on BM biopsy, and serum protein electrophoresis showed no M spike. She had partial response to rituximab. She is currently being treated with plasma-cell targeted therapy with good response so far.

Case-3: 28 year old male noted nephrotic range proteinuria on routine examination. Further evaluation showed unremarkable serologies. Serum protein immunofixation showed no definite M protein. BM biopsy was unremarkable. Kidney biopsy showed mesangial hypercellularity and monoclonal-IgG1 kappa deposits. He is currently being treated with rituximab. We describe 3 cases of PGNMID with diverse glomerular lesions associated with mIg deposits. Our patients were younger than those reported in literature and only one had MPGN pattern, the most common glomerular pattern described with PGMNID. None of our patient showed M spike on immunofixation studies and BM studies did not identify the source of the nephrotoxic mIg. The response to treatment was variable. Two patients showed no response to B-cell depleting therapy. One patient did not respond to plasma-cell directed therapy, but the other did. The third patient is currently receiving B-cell depleting therapy.

Presentation #75

Title: Abdominal Compartment Syndrome - A Morbid Complication of Pancreatitis

Presenter: Laurence Lindenmaier

Authors: Laurence B. Lindenmaier, MD; Andrew Sumarsono, MD; Rosechelle Ruggiero, MD

Faculty Mentor(s): Rosechelle Ruggiero

Abstract:

Case Presentation: A 39-year-old man with history of alcohol abuse presented with acute 9/10 mid-epigastric pain radiating to the back, nausea, and vomiting. He reported drinking 3- 4 24oz beers earlier that day. Initial exam revealed abdominal tenderness with guarding. Initial labs indicated lipase 2,405U/L and lactate 5.6mmol/L. RUQ ultrasound was negative for gallstones. A CT abdomen/pelvis showed acute interstitial edematous pancreatitis with necrotizing components. On hospital day 2, the triglyceride level was found elevated to 1,897mg/dL. After aggressive fluid resuscitation with 8L crystalloid, his abdominal exam worsened with increasing tenderness and rigidity. He developed shock necessitating vasopressors as well as increased work of breathing requiring intubation and paralytics. Bladder pressures were recorded as high as 30mmHg, supporting a diagnosis of abdominal compartment syndrome (ACS). The patient underwent decompressive laparotomy followed by open abdomen negative pressure therapy. The patient's metabolic acidosis and shock worsened, leading to multi-organ failure, and died on hospital day 4.

Discussion: Abdominal compartment syndrome, a lethal complication of acute pancreatitis, is known to occur in up to 38% of cases. By definition, normal abdominal pressures are <12mmHg, whereas ACS presents with pressures >20mmHg and new organ dysfunction. As intra-abdominal pressures (IAP) increases, end-organ perfusion is compromised, resulting in complications including bowel ischemia, acute renal failure, and decreased cardiac output. The most accurate method to measure IAP is bladder pressure via insertion of a Foley catheter connected to a pressure transducer. Importantly, for accurate pressure recordings the patient must be supine and abdominal muscles relaxed, the latter of which may require sedation, analgesia, or paralysis. Nonsurgical therapies may be attempted including: targeting abdominal perfusion pressure, defined as the difference between MAP and IAP, of >60mmHg, negative fluid balance, reverse Trendelenburg positioning, gastric decompression with nasogastric tube, bowel decompression with enemas and/or prokinetics, and paracentesis. Ultimately, surgical decompression and open abdomen are necessary if the above fail. ACS has only been recognized as a distinct entity for the last two decades, but given its high mortality rate (up to 49% in acute pancreatitis), it is an important clinical entity to consider and act on quickly if suspected.

Presentation #76

Title: Checkpoint Inhibitor and CMV Colitis in a Patient with Bloody Bowel Movements

Presenter: Patrick Marquardt

Authors: Patrick Marquardt, MD, MPH; Neha Patel, MD

Faculty Mentor(s): Neha Patel

Abstract:

Toxicity from immune checkpoint inhibitor medications is becoming increasingly common as they are utilized to treat a range of cancers. Toxicity may develop in any organ, but most frequently affects the skin and GI tract, specifically the colon. We present the case of a patient with Stage IV anaplastic thyroid cancer receiving pembrolizumab who developed multiple loose, bloody bowel movements. One week after his symptoms began, he visited an outside GI specialist who diagnosed him with checkpoint inhibitor colitis (CIC). He was prescribed high-dose prednisone and initially his condition improved, but after tapering the steroids, his symptoms recurred. He then presented to our hospital for further evaluation and underwent sigmoidoscopy. There was severe inflammation extending from the rectum to the splenic flexure with extensive ulceration. Biopsy of the area showed "severely active chronic colitis" and CMV virocytes were also noted. With these findings the patient was diagnosed with CIC and concurrent CMV colitis. For treatment of his CIC he received high-dose IV methylprednisolone and a single infusion of infliximab while inpatient and tapered prednisone over several months. To treat the CMV, he was given several weeks of IV ganciclovir which was eventually switched to PO valganciclovir for an extended course. His symptoms improved significantly with these interventions and he was discharged home after spending 8 days in the hospital with plans for another infliximab infusion once the CMV was treated. This case highlights several important points. First, CIC is a serious and potentially life-threatening condition. Based on the symptoms at presentation, CIC is graded from 1 (mild) to 4 (life-threatening). Our patient was classified as Grade 3. Classifying the severity of CIC is important because it drives treatment which ranges from asymptomatic measures to high-dose steroids and steroid-sparing agents. If there is a poor response or atypical presentation, endoscopy with biopsy is strongly recommended. CMV is a common culprit of infection in immunosuppressed patients and must be treated aggressively. With treatment our patient did well, but given the severity of his CIC, he is likely precluded from future checkpoint inhibitor use and providers should consider other cancer therapies moving forward.

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Presentation #78

Title: Neurotoxoplasmosis as Initial Presentation of HIV/AIDS

Presenter: Mridula Nadamuni

Authors: Mridula Nadamuni, MD; Catherine Chen, MD

Faculty Mentor(s): Catherine Chen

Abstract:

A 30-year old construction worker was brought in by concerned family members for several days of decreased alertness, associated with a four-day history of fecal and urinary incontinence. At presentation, he was febrile but otherwise hemodynamically stable. Physical examination was significant for agitation, nystagmus, and unintelligible speech. Computed tomography (CT) of the head demonstrated multifocal hypodensities in bilateral cerebral hemispheres with mass effect. Initial cerebral spinal fluid studies showed elevated protein and a lymphocytic predominance on cell count with plasma cells; opening pressure deferred during lumbar puncture due to patient agitation. Magnetic resonance imaging (MRI) was remarkable for innumerable foci of signal abnormality with peripheral restricted diffusion throughout the brain parenchyma. The patient was started on cefepime, metronidazole, vancomycin, ganciclovir and dexamethasone then high-dose sulfamethoxazole-trimethoprim (SMX-TMP) due to concern for neurotoxoplasmosis. On hospital day 7, Toxplasma gondii qualitative polymerase chain reaction (PCR) results returned as positive. Due to lack of clinical improvement, clindamycin, leucovorin, and pyrimethamine were initiated. Major ethical considerations arose around disclosure of HIV positive status to the patient's family. Repeat MRI of the brain demonstrated improvement in lesions but the patient remained nonverbal, inattentive, and without capacity. He was discharged to an inpatient rehabilitation facility on hospital day 33. Toxoplasmosis is the most common CNS infection in patients with AIDS not on prophylaxis. Exposure to cats is not necessary-reactivation in those who are toxoplasma seropositive with CD4 count <100 cells/µL is as high as 30%. Only half of patients are symptomatic. Brain MRI classically demonstrates multiple ring-enhancing lesions and edema. Presumptive diagnosis of neurotoxoplasmosis can be made in a patient with a CD4 count <100 cells/µL not on prophylaxis with high clinical suspicion, a positive T. gondii IgG antibody, and imaging findings. Sulfadiazine and pyrimethamine is preferred, with leucovorin administered to prevent pyrimethamine-induced toxicity. SMP-TMX is an alternative regimen that has been demonstrated to be equally effective. Corticosteroids should be restricted to patients with mass effect on imaging. Clinical improvement precedes radiographic with about three-quarters of patients improving by day 14. This case demonstrates the challenge and importance of recognizing CNS OIs in AIDS.

Presentation #79

Title: African Trypanosomasis in a Returning Traveler

Presenter: Benjamin Nelson

Authors: Benjamin Nelson, MD; Kruti Yagnik, DO; Alonso Pezo Salazar, MD; David Rosenbaum, MD; Megan McKenna, MD; Laila Castellino, MD

Faculty Mentor(s): Laila Castellino

Abstract:

A 51 year-old man of African descent with hypertension presented to Clements University Hospital in September 2019 with confusion, somnolence, lymphadenopathy and daily fevers. Beginning around May 2019, the patient began having daily fevers reaching up to 103□F, particularly at night. Around this time, he had also become increasingly confused and suffered from profound lethargy and weakness, such that he could not carry on with daily activities. He lost about 35 lb over this time as well. He had numerous recent travel exposures around the world as a traveling preacher, but notably had traveled to rural Ghana nine months earlier. During this trip, he had developed a large area of cellulitis on his thigh which seemed to respond to oral antibiotics. Initially he felt well after returning, but within one to two months began to have symptoms of fever and fatigue. These symptoms resolved within weeks, but eventually came to relapse on a near-monthly basis, each time seemingly worse than the last. He had been evaluated previously with no diagnosis, though malignancy was strongly suspected. The history and presentation were consistent with Human African Trypanosomiasis (HAT). Lab findings were largely non-specific but consistent with HAT, including anemia, elevated immunoglobulins, elevated ESR, elevated CRP and CSF pleocytosis. Bone marrow biopsy was pursued to rule out malignancy, but was also Giemsa-stained to identify potential protozoans. A paucity of Trypanosoma brucei, the causative organism of HAT, was eventually identified in the marrow aspirate. The patient was treated with eflornithine and nifurtimox and made a full recovery. This case is notable for its increasing rarity with fewer than 1,000 known cases worldwide in 2018, almost all diagnosed in sub-Saharan Africa. Notably as demonstrated by this case, tissue diagnosis can be very difficult and requires a high degree of clinical suspicion, especially during the convalescent periods when burden of organisms may be quite low. With early treatment prognosis is generally good, but it is invariably fatal without intervention.

Presentation #80

Title: Fixing the Blue Man, Treating Late Complications of Atrial Switch Procedures Through a Team Based Approach

Presenter: David Osula

Authors: David Osula, MD; Spencer Carter, MD; Beth Brickner, MD; Michael Luna, MD

Faculty Mentor(s): Michael Luna and Beth Brickner

Abstract:

Case Presentation: Mr. L is a 30 y/o male born with D-TGA who underwent a Mustard procedure in early infancy and had sinus node dysfunction requiring permanent pacemaker placement at age 8. He was admitted to an outside hospital with respiratory failure in the context of methamphetamine use, with a hospital course complicated by VT leading to cardiac arrest and multi-organ failure requiring ventilatory support, CRRT and inotropes. He was noted to "turn blue" every time he moved, prompting heavy sedation and continuous neuromuscular blockade. At our institution, bedside echocardiogram revealed a dilated and hypertrophied systemic RV with severe RV dysfunction and preserved venous ventricular function. Differential bubble studies showed findings consistent with shunting across the SVC limb of the baffle. Baffle angiography revealed severe stenosis at the distal aspect of the SVC baffle, and a dilated SVC proximally with contrast leaking into the morphologic right atrial appendage. Laser lead extraction of his pacemaker followed by balloon dilation and covered stent implantation was performed with no residual stenosis or shunting.. He was successfully extubated, weaned off inotropic support and has since regained renal function without further dialysis needs.

Discussion: D-TGA is a rare but severe congenital heart defect that leads to cyanosis and death if not addressed. Up to the late eighties, the atrial switch procedure was the standard of care. The Senning and Mustard procedures use synthetic material or pericardial tissue to baffle systemic venous blood across the resected interatrial septum to the mitral valve and into the morphologic left ventricle while pulmonary venous blood flows behind the baffle system into the morphologic right ventricle [1]. Late complications include failure of the systemic right ventricle, atrial and ventricular arrhythmias, and baffle leaks/stenosis requiring re-intervention in ~40% of patients.[2] These complications led to the development of the current standard of care, the arterial switch procedure. In our patient we see the full gamut of atrial switch complications as well as the benefit of a team-based approach in congenital heart disease.

Presentation #81

Title: Wilson disease: a diagnostic challenge in a patient with alcoholic liver disease

Presenter: Roshni Patel

Authors: Roshni Patel, MD

Faculty Mentor(s): Homer Herlong, MD

Abstract:

Case Presentation: A 32-year-old man previously hospitalized for alcoholic hepatitis presented with 2 weeks of abdominal pain and distension. During previous admission, viral and autoimmune workup was unremarkable; ceruloplasmin and level was normal. He reported 10 years of significant alcohol consumption, but denied medication or supplement use; thus he was diagnosed with alcoholic liver disease (ALD). At present, vital signs were normal; exam notable for jaundice with icteric sclera and protuberant abdomen with fluid wave. Labwork revealed white count 21.24x109/L, creatinine 6.7 mg/dL (0.5 mg/dL during prior admission), ALT 51 U/L, AST 113 U/L, ALP 153 U/L, total bilirubin 38.5 mg/dL. Infectious workup, including peritoneal studies, was negative. He became oliguric and developed acute anemia without obvious bleeding. Disease severity at his age, notwithstanding his alcoholism, and disproportionately mild ALP elevation relative to hyperbilirubinemia raised concern for Wilson disease (WD) despite previously normal ceruloplasmin. Ceruloplasmin was 17.6 mg/dL (reference >20 mg/d). Low ceruloplasmin, elevated urinary copper excretion, and Kayser-Fleischer rings led to a diagnosis of WD.

Discussion: Coexisting WD and ALD is rarely reported. Patients may exhibit features of both etiologies and workup may be misleading. Serum ceruloplasmin is normal in 20% of WD patients since it is an acute phase reactant. Elevated 24-hour-urine-copper and low ceruloplasmin may present in acute liver failure regardless of aetiology. Hyperbilirubinemia disproportionate to modest transaminase elevation suggests fulminant liver failure due to WD. One study suggests ALP-to-total-bilirubin ratio less than 4.0 is 94% sensitive and 96% specific, and an AST:ALT greater than 2.2 is 94% sensitive and 86% specific to diagnose WD. Sensitivity and specificity increased when ratios were combined. Renal failure and anemia are nonspecific in liver disease, but should prompt suspicion for WD when present in young patients. In WD, renal failure is associated with copper toxicity-related tubular dysfunction, and hemolytic anemia is presumably due to intravascular haemolysis from disruption of red cell membranes triggered by copper release from dying hepatocytes. Clinicians must maintain suspicion for WD in young patients even if workup suggests another etiology of disease, recognizing screening limitations. Liver transplantation is the definitive treatment, so accurate diagnosis is critical.

Presentation #82

Title: Congenital Thrombotic Thrombocytopenic Purpura Presenting in an 83 Year Old Man With Recurrent Cerebrovascular Events

Presenter: Viral Patel

Authors: Viral Patel, MD; Ibrahim Ibrahim, MD

Faculty Mentor(s): Ibrahim Ibrahim

Abstract:

Case Presentation: The patient is an 83 year old man with a history of multiple ischemic strokes and vascular dementia who initially presented to the emergency room with a one day history of difficulty speaking and following commands. MRI revealed an acute left paramedian parietal lobe and posterior cingulate gyrus infarct. Work-up revealed thrombocytopenia with 102 platelets/L, elevated LDH 422 U/L, and low haptoglobin <10 mg/dL. Coagulation and fibrinogen studies were within normal limits. Hemoglobin was unremarkable at 14.3 g/dL, as was creatinine at 0.9 mg/dL. No heparin/PF4 antibodies were detected. Review of the peripheral smear revealed schistocytosis. Due to the history of multiple ischemic strokes and thrombocytopenia, a workup for thrombotic thrombocytopenic purpura (TTP) was pursued. A Disintegrin And Metalloproteinase with a Thrombospondin type 1 Motif, member 13 (ADAMTS-13) activity and anti ADAMTS-13 antibodies were undetectable, confirming the diagnosis of TTP. He was managed with prednisone 60 mg for total six weeks with taper, rituximab 375 mg/m2 weekly for four weeks, and plasma exchange, requiring 7 sessions before normalization of platelet count. Subsequent levels after plasma exchange again revealed undetectable ADAMTS13 activity without inhibitor antibody detection, raising the suspicion for congential TTP. Molecular sequencing of the ADAMTS13 gene was performed. A heterozygous pathogenic variant on the ADAMTS13 gene, exon 6 (c.587 C>T) on chromosome 9 and a variant of uncertain significance (VUS) was detected on exon 28 (c.4006 C>T) of chromosome 9. Given the autosomal recessive inheritance of congenital TTP and the patient's markedly decreased baseline ADAMTS13 activity, these molecular findings suggest a compound heterozygous inheritance pattern with VUS playing a role.

Discussion: The pathogenesis of TTP involves a deficiency of ADAMTS-13, a protease that cleaves von willebrand factor (vWF). A deficiency in ADAMTS-13 results in large vWF multimers, creating a nidus for platelet aggregation and inducing a prothrombotic state. Congenital TTP is extremely rare, with the Hereditary TTP Registry estimating only 150 families worldwide. In one series of 43 patients, 18 (42%) were diagnosed after 15 years of age, with the oldest being 63 years old. To our knowledge, this patient represents the oldest case of congenital TTP.

Presentation #83

Title: Successful treatment of recalcitrant stuttering priapism with voxelotor

Presenter: Viral Patel

Authors: Viral Patel, MD; Ibrahim Ibrahim, MD

Faculty Mentor(s): Ibrahim Ibrahim

Abstract:

Case Presentation: The patient is a 24 year old male with homozygous hemoglobin S disease complicated by recurrent priapism. His sickle cell disease (SCD) has been managed with hydroxyurea 2000 mg daily (25 mg/kg) for the last 2 years. Baseline laboratory parameters include a hemoglobin 8.5 g/dL, reticulocyte index 4.9, total bilirubin 2.3 mg/dL, and LDH 954 U/L. The predominant manifestation of his disease is recurrent, stuttering priapism, occurring 1-2 episodes a week often requiring visits to the emergency room. He rarely experiences vaso-occlusive crises. He has undergone a number of urological interventions including pseudoephedrine, dutasteride, and multiple shunts without improvement. Given the severity of his symptoms, he has at times required red blood cell exchange for relief. Voxeletor 1500 mg daily was added to his current regimen with the aim of preventing further episodes of priapism and potentially sparing the patient red cell transfusion. Since starting the medication 2 months ago, he has not had any further episodes of priapism with no emergency room visits and has not required further red cell exchange.

Discussion: Priapism is well known for its association with sickle cell disease and other congenital hemolytic anemias and hemoglobinopathies. Voxelotor is a recently approved drug by the Food and Drug Administration for patients with sickle cell disease. It inhibits hemoglobin S polymerization and stabilizes sickle hemoglobin in an oxygenated state, reducing sickling of red cells. The stabilization of sickle hemoglobin in an oxygenated state may explain why our patient derived benefit from this medication. Nitric oxide scavenging is implicated in priapism associated with SCD, and has been observed to occur more rapidly in states of deoxygenated hemoglobin. The pivotal phase 3 HOPE (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS Polymerization) trial demonstrated an increase in hemoglobin levels (>1 g/dL) as well as a reduction in hemolysis markers but did not reveal significant clinical benefit given the study's small patient size. This case demonstrates the first known use of voxeletor in conjunction with hydroxyurea in the treatment of recurrent and refractory sickle cell associated priapism.

Presentation #84

Title: Bronchoscopic Management of a Primary Endobronchial Salivary Epithelial-Myoepithelial Carcinoma: A Case Report.

Presenter: Dalton Patterson

Authors: Dalton T. Patterson, MD; Quinn Halverson, MD; Sarah Williams, MD, Justin Bishop MD; Cristhiaan D. Ochoa, MD, and Kim Styrvoky, MD

Faculty Mentor(s): Cristhiaan D. Ochoa

Abstract:

Case Description: We present a 55 y/o African male who recently immigrated from Nigeria who presented Parkland Memorial Hospital with a productive intermittent cough with yellow sputum for the past year. The cough was associated with SOB and chest pain, but not associated with voice hoarseness, hemoptysis, melanoptysis, and wheezing. He had a a CT scan of the chest that showed a 1.9 cm mass in the right main stem bronchus with associated right lower lobe consolidation and bronchiectasis. Patient was seen by pulmonology who recommended bronchoscopy for diagnosis and possible intervention. Bronchoscopy showed a 90% obstructing mass in the proximal right mainstem bronchus and bronchus intermedius. The mass was large and circumferential, endobronchial, exophytic, and polypoid. The decision was made to undergo bronchoscpic tumor ablation using electrocautery snare, argon plasma coagulation(APC), suction, and forceps. The tumor was successful ablated. Microscopic examination of the tumor showed eosinophilic ducts, tightly coupled with a surrounding layer of clear cell myoepithelial cells and the diagnosis of EMC of the lung was made.

Conclusion: We conclude that EMC is a rare cause of an endobronchial mass and should be suspected in patients who present with chronic cough without other presenting symptoms and who are found to have an endobronchial lesion. Also, we conclude EMCs that are low to intermediate grade with no signs of lymph node involvement or distant metastasis can be successfully managed with endobronchial ablation. There is a risk of recurrence with EMCs and patients should have a follow-up for bronchoscopic and radiological evaluation within at least three months of the intervention and possibly need yearly imaging for monitoring

Presentation #85

Title: Thyrotoxicosis With Pre-Ventricular Complexes Resulting in Thyroid Storm and Cardiac Arrest.

Presenter: Nam Pham

Authors: Nam D. Pham, MD, PhD; Asra Kermani,MD; Iram Hussain, MD

Faculty Mentor(s): Iram Hussain Asra Kermani

Abstract:

Case Presentation: A 64 year old woman was diagnosed with thyrotoxicosis secondary to Graves' disease [TSH < 0.01 (0.40 - 4.5 mcIU/mL) and free T4 of 2.8 (0.8 - 1.8 ng/dL)] 1 year ago in the setting of a 6 month history of weight loss, palpitations, tremors, and a large goiter. She was started on methimazole and metoprolol XL and was intermittently compliant. During follow-up evaluation she complained of light headedness, developed agonal breathing, and became pulseless. Chest compressions were initiated. She regained spontaneous rhythm after receiving 1 shock with an Automated Electronic Defibrillator (AED). She was transferred to the Emergency Room (ER) and intubated for altered mental status. Emergent CT Angiography and bedside echocardiogram showed no pulmonary embolism and normal biventricular function. Troponin T high sensitivity assay was negative and electrolytes were normal. Repeat thyroid function tests showed TSH <0.01, Free T4 of 5.6 and free T3 of 14.5 (2.0 - 4.4 pg/mL). She was started on propylthiouracil, glucocorticoids, potassium iodide and treated for thyroid storm. EKG in the ER showed sinus tachycardia with no ischemic ST changes but PVCs and fusion complexes were noted. These were also present on EKG at the time of her initial diagnosis of hyperthyroidism. EKGs prior to the diagnosis of hyperthyroidism showed normal sinus rhythm. Cardiac arrest was attributed to thyrotoxicosis as there was no infectious nidus and no evidence of structural cardiac disease. The AED rhythm strips could not be obtained but she was presumed to have an appropriately shockable ventricular tachyarrhythmia such as ventricular tachycardia (VT) or ventricular fibrillation (VF). Her thyroid hormone levels declined appropriately over the course of the hospitalization and PVCs were no longer noted on telemetry and daily EKGs. Her Grave's disease has been definitely treated with radioactive iodine ablation (RAIA) as outpatient.

Discussion: Failure to achieve rapid euthyroidism in thyrotoxicosis is associated with increased cardiovascular morbidity and mortality. Most arrythmias associated with thyrotoxicosis are supraventricular and ventricular arrythmias are a rare sequela. This is one of the few cases reported of antecedent PVCs being noted on EKG. The PVCs resolved with anti-thyroid medications.

Presentation #86

Title: It's Not A Bad Trip with This Acid: Sodium Thiosulfate Use in Refractory Metabolic Alkalosis

Presenter: Melby Philip

Authors: Melby Philip, MD; Kamalanathan Sambandam MD

Faculty Mentor(s): Kamalanathan Sambandam

Abstract:

Case Presentation: We present two patients, a 63 year old female and an 81 year old gentleman, both admitted with shortness of breath and found to be in acute on chronic hypercapnic, hypoxemic respiratory failure. The hospital course in each case was notable for oligoanuria and significant volume overload, the former in the setting of heart failure exacerbation and the latter in the setting of acute tubular necrosis. This prompted the use of sequential nephron blockade with loop diuretics, thiazide diuretics, metolazone, and potassium sparing diuretics. Both patients responded to aggressive diuresis with robust urine output and improvement of respiratory status, however, the rising serum bicarbonate (HCO3) concentration increased to 38mmol/L and 39mmol/L respectively, thereby limiting our ability to correct the hypervolemia. Serum HCO3 continued to rise despite holding diuretics and the use of acetazolamide. This was expected as acetazolamide has limited efficacy with low effective circulating volume and renal insufficiency. Given the known side effect of sodium thiosulfate (STS) to cause metabolic acidosis, STS was administered, resulting in a decrease in the serum HCO3 level and an ability to resume diuresis.

Discussion: Several mechanisms were at play in the generation of severe metabolic alkalosis in these cases: a diuretic-induced increase in sodium and fluid delivery to the distal nephron which accelerates proton (H+) and potassium (K+) secretion; volume contraction that further augments tubular H+ and K+ secretion via stimulation of renin and aldosterone ; and potassium depletion which augments urinary acid excretion as well as transcellular shift of protons into cells. When continued diuresis is necessary and the correction of metabolic alkalosis cannot be facilitated by volume resuscitation due to persistent hypervolemia, potassium repletion and carbonic anhydrase inhibitors are the common tools that are employed. When this does not work, refractory alkalosis can be corrected by hydrochloric acid and ammonium chloride administration; however, these medications are not always accessible. By utilizing STS and its known ability to generate an acid load during metabolism, the clinician has another safe and effective tool to treat refractory alkalosis when other therapies have failed.

5th Annual Donald W. Seldin, M.D. Research Symposium

Presentation #87

Title: Cardiac implantable device infection with Phialemonium obovatum

Presenter: Hala Saad

Authors: Hala Saad, MD; James Cutrell, MD; Reuben Arasaratnam, MD; Andrew Clark, MD

Faculty Mentor(s): James Cutrell

Abstract:

Case Presentation: 50 year old Hispanic male with congenital heart disease and congestive heart failure (CHF) status post Cardiac Resynchronization Therapy-Defibrillator (CRT-D) admitted with dyspnea and CRT-D "vibrations" for two weeks. He has not taken any CHF medications for 4 years. His CRT-D was found to require exchange. Social history is notable for work remodeling old homes. On exam, he was noted to have a holosystolic murmur without stigmata of endocarditis. Transthoracic echocardiography (TTE) showed a large mobile echo-density on one of the ventricular leads. Chest computed tomography (CT) showed a right upper lobe spiculated mass-like opacity surrounding multiple dilated airways. Laboratory data was significant for B-Natriuretic Peptide (BNP) : 3,350, Blood cultures x2: negative, ESR: 80, CRP 12.4, RF < 10. Infectious work-up included negative Aspergillus galactomannan antigen and serologies for Histoplasma and Blastomyces; 1,3-Beta-D-glucan: 210; Serum coccidioides Antibody reactive but Serum coccidiodes Antibody complement fixation & immunodiffusion negative; and positive Quantiferon gold. Sputum stain for acid fast bacilli smear x3 negative, and Mycobacterium tuberculosis (MTB) PCR negative. The CRT-D was removed, with bacterial cultures showing light growth Cutibacterium (Propionibacterium) acnes, and fungal cultures showing "mold". The mold grew on Sabouraud dextrose agar with yellow white colonies, provisionally identified as Acremonium spp. The isolate was ultimately identified as Phialemonium obovatum by Mass- Assisted Laser Desorption/Ionization (MALDI) by reference laboratory. Patient was initially treated with liposomal Amphotericin B and voriconazole empirically, but this regimen was transitioned to voriconazole alone for a planned duration of 6 weeks along with doxycycline for the C. acnes. Patient was lost to follow-up with Parkland ID clinic.

Discussion: Phialemonium obovatum is a dematiaceous fungus that principally causes infections in immunocompromised patients. First identified in 1983, it is ubiquitous in the environment and often regarded as an environmental contaminant. Its capacity to grow at or above body temperature is a key pathogenic determinant. No susceptibility data currently exists to guide treatment decisions. This pathogen has been reported to cause various systemic infections, including endocarditis, but this case represents the first report of its involvement in a cardiac implantable device infection.

Presentation #88

Title: The use of cabozantinib at 80 mg daily for metastatic clear-cell renal cell carcinoma.

Presenter: Akanksha Sharma

Authors: Akanksha Sharma, MD; Roy Elias, MD; James Brugarolas, MD PhD

Faculty Mentor(s): James Brugarolas

Abstract:

Case Presentation: Mr. T, a 65-year-old male, was diagnosed with clear-cell renal cell carcinoma (ccRCC) and underwent radical nephrectomy and regional lymphadenectomy. He subsequently had disease progression with development of pulmonary nodules as well as worsening abdominal disease burden. Several treatments including pazopanib, nivolumab, and lenvatinib plus everolimus were trialed. Cabozantinib was then initiated at the FDA approved maximum dose of 60 mg daily providing 8 months of disease control, the longest thus far. After 8 months, given increasing mesenteric lymphadenopathy and worsening abdominal implants, cabozantinib was increased to 80 mg daily. This allowed Mr. T 12 months of controlled disease and improved quality of life. Mr. G is a 46-year-old male who was diagnosed with metastatic ccRCC and underwent radical nephrectomy and lymph node dissection. He subsequently demonstrated refractory disease to multiple treatment modalities including pazopanib, nivolumab plus ipilimumab and interleukin -2 with worsening biopsy proven skin and brain metastases and increasing disease burden in the liver. He also demonstrated mediastinal and pulmonary disease requiring radiation therapy in addition to chemotherapy. Cabozantinib was initiated and subsequently increased to 80 mg daily allowing 9 months of improved disease control.

Discussion: Kidney cancers are prevalent in the United States and represent around 70,000 cases this past year. There has been exciting research emerging regarding the genetics of renal cell carcinoma and the most common clear-cell histologic subtype. We present cases of progressive ccRCC with specific emphasis on the use of cabozantinib. Treatment options for advanced ccRCC have undergone changes over the past years, and depends on prognostic risk factors. Patients categorized in the intermediate-/poor-risk groups per the International Metastatic RCC Database consortium (IMDC), as opposed to the favorable-risk group have limited treatment options. These include immunotherapy with ipilimumab plus nivolumab, axitinib plus pembrolizumab, and cabozantinib. The above cases represent two examples of disease progression on limited treatment options. The increased dose of cabozantinib above the FDA approved dose of 60 mg daily allowed disease control and improvement in symptoms and quality of life for these cases. This opens the door for further studies with prospective trials on higher doses of cabozantinib.

Presentation #89

Title: Vaping is Not Cool: A Case of Vaping Related Lung Injury

Presenter: Shruti Singh

Authors: Shruti Singh, MD; Nainesh Shah, MD

Faculty Mentor(s): Nainesh Shah

Abstract:

Case Presentation: A 21 year-old-man with no medical history presented with 2 weeks of fevers, non-productive cough, nausea, and diarrhea. He reported occasional use of e-cigarettes with most recent use 3-4 weeks prior to admission. His workup revealed leukocytosis and CT chest showed scattered pulmonary nodules with apical predominance and centrilobular ground glass opacities suggesting bronchopneumonia, as well as mediastinal lymphadenopathy. He was started on treatment for community acquired pneumonia with Ceftriaxone and Azithromycin, but his symptoms persisted. Rheumatologic workup including ENA panel, ANCA studies, and RF was negative. Due to persistence of fever, he underwent bronchoscopy with BAL and transbronchial biopsy. He was started on an empiric course of steroids for suspected vaping related lung injury. His symptoms started to resolve within a day of starting steroids, and he was discharged on a steroid taper. Biopsy results revealed diffuse interstitial mononuclear pneumonitis with patchy organizing pneumonia, with cytology showing abundant lipid-laden alveolar macrophages and extracellular lipid droplets.

Discussion: In July-September 2019, there was a sharp rise in cases of acute lung injury associated with vaping, which was later termed by CDC as e-cigarette, or vaping, product use-associated lung injury (EVALI). Most patients (83%) with EVALI reported use of THC products, with just 17% of patients reporting use of only nicotine containing products. Here we present a case where the patient reported vaping with only nicotine containing products. A consistent pathological finding in all patients, including our patient, was lipid-laden pulmonary alveolar macrophages, representing a chemical pneumonitis. The causative agent of this pneumonitis was thought to be Vitamin E acetate, a chemical which was isolated in BAL fluids from patients with EVALI. There has been a decline in EVALI cases since September 2019, due to increased public awareness of this epidemic and FDA mandated removal of Vitamin E acetate from e-cigarette products. This case presentation allows for discussion of diagnostic approach and treatment of a new disease without any available guidelines in the midst of an epidemic through evaluation of one of the first known cases of EVALI at Parkland hospital.

Presentation #90

Title: Post-infarct VSD: silent or deadly?

Presenter: Shruti Singh

Authors: Shruti Singh, MD; Andrew Sun, MD; Thomas Koshy, MD

Faculty Mentor(s): Thomas Koshy

Abstract:

Case Presentation: A 69-year-old man with a history of hypertension presented to an outside hospital with chest pressure and fatigue. He was found to have an NSTEMI, in the setting of elevated troponin I (1.744 ng/ml) and non-specific ST segment changes on ECG. Left heart catheterization revealed a 70% stenosis of the LAD and otherwise non-obstructive disease. Ventriculogram during the catheterization revealed left to right shunting across the interventricular septum. The patient was transferred to CUH for futher workup. The finding of an incidental VSD led to the question of its origin. It would be unusual for a hemodynamically significant congenital VSD to present at this age. However, post-infarct VSD has a very high fatality rate and is rarely silent. Right heart catheterization revealed hemodynamically significant left to right shunting across the defect. Cardiac MRI was performed and revealed findings consistent with a post-infarct VSD. On further questioning, the patient reported feeling of severe fatigue one year prior to this presentation, which was thought to be the inciting event. He was discharged with plans for transcatheter device closure for the VSD.

Discussion: VSD is an increasingly rare complication of an acute myocardial infarction in the era of early reperfusion (1). However, it is still associated with a high in-hospital mortality of above 90% with medical management alone (1). Most cases present with cardiogenic shock or signs of RV overload, and require immediate attention and intervention. Per 2013 ACC guidelines, early surgical repair of postinfarct VSD is recommended even in clinically stable patients (2). However there is controversy associated with timing and method of repair. A systematic review reported reduced mortality with transcatheter closure when compared with surgical intervention, with early surgery having the worst outcomes (3). Our patient was hemodyamically stable yet he had significant shunting which warrented repair of his VSD. After a multidisciplinary discussion with interventional cardiology and cardiothoracic surgery, a transcatheter device closure was planned. This case represents a rare case of remote asymptomatic postinfarct VSD, and serves as a platform for discussion of the treatment options and the decision making process with limited evidence.

Presentation #91

Title: Bronchiecstatic: The case of a 17-year-old female with recurrent pneumonia

Presenter: Edward Stephens

Authors: Eddie Stephens, MD; Katarina Yaros, MD; Leah Cohen, MD

Faculty Mentor(s): Leah Cohen, MD

Abstract:

A 17-year-old female with 5 months of recurrent pneumonia presented to the Emergency Department with persistent fever and productive cough. She had been healthy and doing well until about 5 months prior to presentation when she developed cough, fever, and chills and was treated by her primary care doctor for presumed pneumonia. She had since had at least 6 additional visits at different hospitals for similar symptoms, each time receiving a course of antibiotics with transient or minimal improvement. Over the 2-3 months prior to presentation, she lost approximately 20 pounds due to anorexia. Starting a few weeks prior to presentation, she began feeling short of breath and experienced palpitations with minimal exertion. She also noted being intermittently dyspneic at rest, especially when laying on her left side. The severity of her symptoms had caused her to miss numerous school days and was at risk of having to repeat the school year. She had not traveled outside Texas. Exam revealed a thin young female who was tachycardic with significant anterior cervical lymphadenopathy. Initial chest x-ray revealed left upper lobe opacities with cavitary change and bronchiectasis as well as a right midlung opacity. Subsequent chest CT without contrast demonstrated findings suggestive of multifocal infection, varicose bronchiectasis, and mediastinal and hilar lymphadenopathy. Given the patient's age, chronicity of her problems, and appearance on CT, the initial concern was for underlying structural lung disease, possibly Cystic Fibrosis (CF) or Non-CF bronchiectasis. Upon further questioning, the patient's mother revealed that the patient had been exposed to mycobacterium tuberculosis (TB) as a two-year old via a maternal uncle who frequently babysat her and later passed away from complications of AIDS. Final active pulmonary TB diagnosis was confirmed by positive sputum MTB PCR. Sputum culture sent for acid fast bacilli returned positive and the culture eventually grew M tuberculosis. Although patient's age, life in developed country, and lack of travel can be more concerning for a genetic disorder predisposing to a structural lung disease, this case describes the importance of taking a thorough personal and family history to help arrive at correct diagnosis.

Presentation #92

Title: A Striking Case of Propafenone Toxicity

Presenter: Belal Suleiman

Authors: Belal Suleiman, MD; Karen Rosario Flores, MD; Sonia Shah, MD; Jose Joglar, MD

Faculty Mentor(s): Jose Joglar

Abstract:

Case Presentation: We present a case of propafenone toxicity causing a poorly tolerated striking arrhythmia. A 50-year-old female with recently diagnosed breast cancer presented for right internal jugular port placement. During placement, she developed acute dyspnea and palpitations. Initial electrocardiogram (EKG) showed atrial fibrillation with rapid ventricular response (RVR). Initial rate control with IV metoprolol slowed the heart rate (HR) but symptomatic atrial fibrillation with RVR persisted. After rule-out of pulmonary embolism, electrolyte abnormalities, renal or hepatic dysfunction, medication interactions, and pericardial effusion, electrophysiology was consulted. A rhythm control strategy was pursued with 600 mg propafenone as the patient was known to have a structurally normal heart. Shortly after administration, the patient began complaining of worsening palpitations and lightheadedness and became hypotensive to 70-60/50-40 mmHg with HR 120's bpm. Her cardiovascular exam revealed an irregular tachycardia with frequent pauses. Her extremities were cool to the touch with no edema. EKG showed sinus rhythm with 1st degree atrioventricular (AV) block, widening of the QRS, and interpolated premature ventricular contractions with runs of nonsustained ventricular tachycardia. Due to these findings, the patient was thought to have propafenone toxicity leading to hemodynamic compromise. For presumed propafenone toxicity, she was treated with an ampule of sodium bicarbonate which decreased her PVC burden. Following an additional ampule of sodium bicarbonate, her EKG showed sinus rhythm with 1st degree AV block and cessation of ectopic ventricular beats. Her blood pressure recovered to baseline in the subsequent hours.

Discussion: Propafenone is a Class IC antiarrhythmic that decreases the rate of cardiac depolarization and increases ventricular refractoriness. An off-label use of propafenone is for pharmacologic cardioversion of paroxysmal atrial fibrillation. Adverse effects of propafenone include increased ventricular ectopy and worsening of ventricular tachycardias. Sodium bicarbonate is thought to displace propafenone from its binding sites on the sodium channel and decrease the affinity of propafenone for the sodium channel by increasing the pH. This report highlights a poorly tolerated NSVT after a single dose of propafenone for pharmacologic cardioversion of atrial fibrillation. In a study on a pill in a pocket approach, <1 % of patients developed an adverse cardiac tachyarrhythmia.

Presentation #93

Title: Severe murine typhus presenting with acute acalculous cholecystitis

Presenter: Lauren Ward

Authors: Lauren Ward, MD ; Lauren Franzblau, MD

Faculty Mentor(s): Susana Lazarte, MD

Abstract:

Case Presentation: A 33-year-old six-week post-partum female with history of recurrent urinary tract infections (UTIs) presented with fever, hypotension, and abdominal pain and was initially treated for septic shock, thought secondary to urinary source. The patient developed clinical and ultrasonographic signs of acalculous cholecystitis, and she received appropriate source control with a cholecystostomy tube and broad spectrum antibiotics but continued to have fevers. She developed a rash on her extremities later during her hospital stay, which raised suspicion of Rickettsial disease. Serologies were sent and the patient was treated empirically with doxycycline with rapid clinical improvement. Diagnosis of murine typhus was confirmed by serology results after patient was discharged home. She had her cholecystostomy tube removed 5 months after placement and has remained well.

Discussion: This case highlights a unique presentation of R. typhi infection resulting in acalculous cholecystitis. Though the patient did well overall, treatment was delayed due to the nonspecific symptoms she presented with, as well as anchoring on a presumed UTI due to patient's history and reported symptoms. Her case illustrates the challenge of early diagnosis in murine typhus and suggests that clinical suspicion for this disease should be heightened in endemic areas. Treatment with doxycycline should not be delayed while awaiting serologic results. Additionally, murine typhus associated with acalculous cholecystitis is a rare presentation that can make diagnosis difficult. The pathophysiology of acalculous cholecystitis from Rickettsial disease is unclear, but is suspected to be from Rickettsia species attacking endothelial cells lining blood vessels in the gallbladder. This then leads to local vasculitis and eventually gallbladder ischemia and necrosis, causing acalculous cholecystitis. However, acalculous cholecystitis is most often seen in critically ill patients as they are predisposed to prolonged fever and hypoperfusion, causing gallbladder ischemia and stasis. Our patient did not have a cholecystectomy so it is unknown whether her acalculous cholecystitis resulted from direct pathogen injury or was a sequela of septic shock.

Presentation #94

Title: Diagnosis and Management of a Patient with Limited Stage Small Cell Lung Cancer Detected by Low Dose Computed Tomography Screening

Presenter: Sarah Williams

Authors: Sarah Williams, MD; Dalton Patterson, MD; Paul Lederer MD; David Gerber, MD; Jose Torrealba MD; Jayati Mallick MD; Kim Styrvoky, MD; Cristhiaan D. Ochoa, MD

Faculty Mentor(s): Cristhiaan Ochoa

Abstract:

Low dose computed tomography (LDCT) detects both small cell (SCLC) and non-small cell lung cancer (NSCLC); however, its utility as a screening modality is limited to NSCLC, as SCLC is most often detected at advanced stages. Here we present the diagnosis and management of a very limited stage SCLC detected by LDCT. A 65-year-old woman with severe peripheral vascular disease, type two diabetes, COPD, and a 40 pack-year smoking history presented to the Smoking Cessation Clinic for medication renewal. She had no acute complaints but noted chronic, stable weakness and dyspnea on exertion attributed to generalized deconditioning. A review of systems was negative for cough or weight loss. She had a normal oxygen saturation on room air, and physical exam revealed a well-developed woman with a normal exam of the lungs. Given her age and smoking history, a lung cancer screening CT was ordered. This revealed a 1.9 cm solid, noncalcified nodule in the right lower lobe as well as several suspicious mediastinal, axillary, and pre-carinal lymph nodes. Transbronchial biopsy of the nodule revealed a high-grade neuroendocrine carcinoma. Further, despite lymphadenopathy on CT, PET/CT scan and mediastinoscopy confirmed a T1N0M0 stage. The case was presented at the multidisciplinary tumor board, which recommended surgical biopsy and right lower lobectomy due to the favorable stage. Unfortunately, she was ultimately deemed a poor surgical candidate. Therefore, she was scheduled for stereotactic radiation of the lung followed by four cycles of carboplatin and etoposide, as extrapolated from the postoperative chemotherapy regimen for SCLC. The patient is currently doing well seven months after her LDCT. Detection of SCLC by screening is rare; only 13% of lung cancer detected by LDCT is small cell in origin, and 4% of these SCLC diagnosed by screening are stage I. Due to SCLC's typically advanced stage at presentation, screening interventions are thought to play no role in extending survival at present. While this patient's poor functional status limits generalizability, the case suggests that detection of early limited stage SCLC may lead to interventions that could prevent disease progression and decrease SCLC-related mortality.

Presentation #95

Title: Cardiac Chest Pain in a Young Female

Presenter: Averi Wilson

Authors: Averi Wilson, MD

Faculty Mentor(s): Carrie Herbert, MD

Abstract:

Case Presentation: An 18-year-old female with a history of ALCAPA status-post non-traditional repair by patch closure of the ostium of the LCA presents with exertional, "squeezing" chest pain associated with nausea, light headedness, shortness of breath, and a tingling sensation. The patient was initially evaluated by EMS on the scene. EKG was reportedly normal and she was released to her parents, but later that evening presented to an emergency room for further evaluation after having persistent pain. Serial EKGs, CXR, and troponins were reportedly normal and the patient was discharged home. At follow-up with her cardiologist, the patient described several episodes of chest pain lasting 1-2 minutes. The patient underwent cardiac MRI stress test, revealing an inducible perfusion defect in the LAD and LCx coronary artery distribution and apical hypokinesis of the left ventricle. Cardiac CT demonstrated small collaterals from the dominant RCA supplying the left coronary artery system. The patient underwent cardiac catheterization which revealed a significant reduction in the number and caliber of RCA collaterals supplying the left coronary system in comparison to the time of her initial diagnosis. Angiography also showed a collateral system from the left coronary cusp that supplied the left anterior descending and left circumflex and was not present on previous angiography. Following catheterization, the patient was scheduled for CABG which was completed four weeks later.

Discussion: Notably, this patient was diagnosed with ALCAPA incidentally at 13 years of age. Due to patient anatomy and sufficiency of collateralization from the right coronary artery and Vieussen's ring, the left coronary artery ostium at the MPA was patch closed rather than translocating the coronary artery as is traditionally done in ALCAPA repair. This case highlights the importance of continued flow through collateral systems to maintain perfusion to poorly vascularized territories. Additionally, this case highlights the importance of having a high index of suspicion for cardiac ischemia in cases of typical chest pain, regardless of age, gender, or known risk factors. In this case, it was vital that the patient and her family had a good understanding of her underlying disease process and sought cardiology follow-up for further evaluation.

Presentation #96

Title: Check Your Skin: Disseminated Cryptococcal Infection in a Solid Organ Transplant Patient Diagnosed by Skin Lesions

Presenter: Kruti Yagnik

Authors: Kruti Yagnik, DO

Faculty Mentor(s): Jeffrey Tessier, MD

Abstract:

Cryptococcosis is an invasive fungal infection caused by *Cryptococcus neoformans* or *Cryptococcus gattii. C. neoformans* lives in the environment and can cause several types of infections including meningitis, pulmonary, cutaneous, and disseminated disease. It is an important pathogen in immunocompromised patients and is the third most common invasive fungal infection in SOT recipients. This infection is especially important in transplant patients because discontinuation of immunosuppressive therapy along with administration of antifungal therapy can lead to IRIS.

A 66-year-old Hispanic woman with history of DDKT in 2018 presented to the ED with bilateral ear pain. Imaging was done which showed concern for bilateral mastoid effusion and after ENT evaluated the patient, she was discharged with decongestants. She presented to transplant nephrology clinic for ER follow-up, where it was noted that she had an ulcerated lesion of her right ear, along with other small lesions on her left cheek, temple, and palm. She was sent to dermatology clinic for an urgent appointment, where multiple skin biopsies were taken. Skin biopsies showed *C. neoformans*, so patient was told to present to the hospital for admission. Admission labs showed positive cryptococcal serum antigen with very high titer 1:4096. CT chest was done which showed innumerable bilateral pulmonary nodules/masses. A lumbar puncture was performed which showed yeast on gram stain and *C. neoformans* on CSF culture. Transplant ID was consulted, and patient was started on liposomal amphotericin B along with flucytosine for disseminated infection. Repeat lumbar puncture continued to show *C. neoformans* on CSF culture. Patient symptomatically improved and completed 4 weeks of induction therapy with IV liposomal amphotericin B with flucytosine, followed by oral fluconazole for consolidation and maintenance therapy.

This was an interesting case because patient did not have any significant symptoms of disseminated infection apart from her skin lesions. Despite this, she had high burden of disease as evidenced by her high serum antigen titer, innumerable pulmonary nodules, and CNS involvement. This highlights the importance of a thorough physical and skin exam for all patients, but especially for those who are immunocompromised.