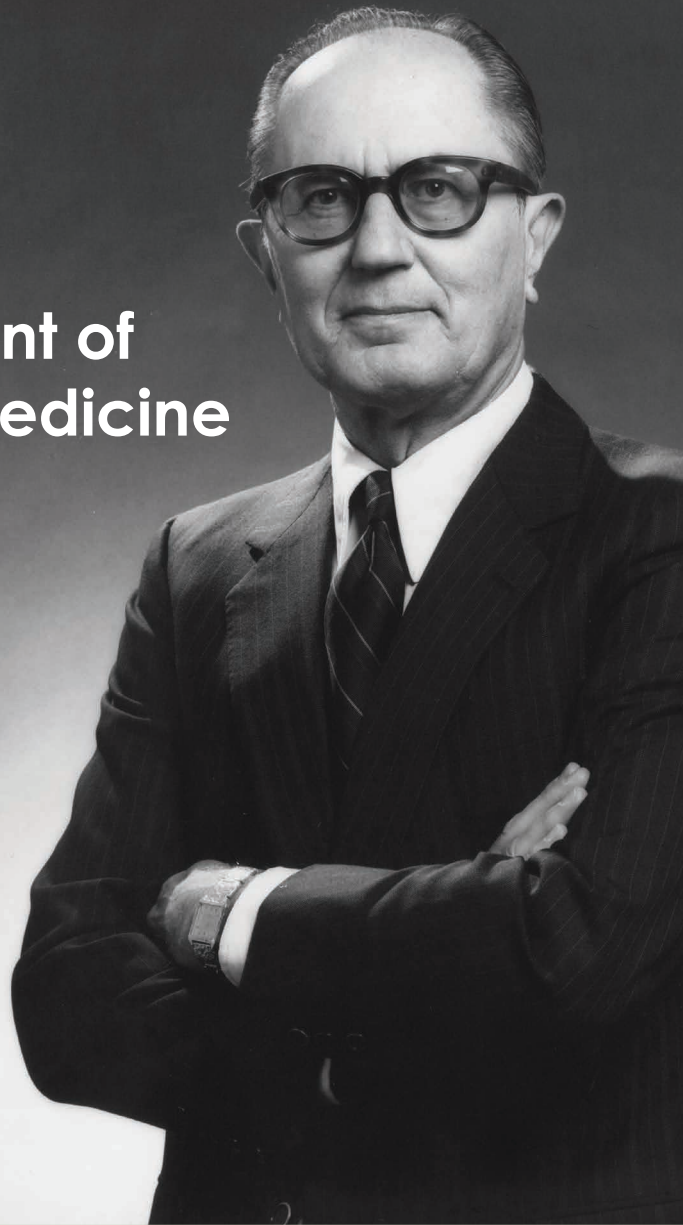The

Department of Internal Medicine

Presents

UT Southwestern
Medical Center

The 3rd Annual

Donald W. Seldin, M.D.
Research Symposium
May 3-4, 2018

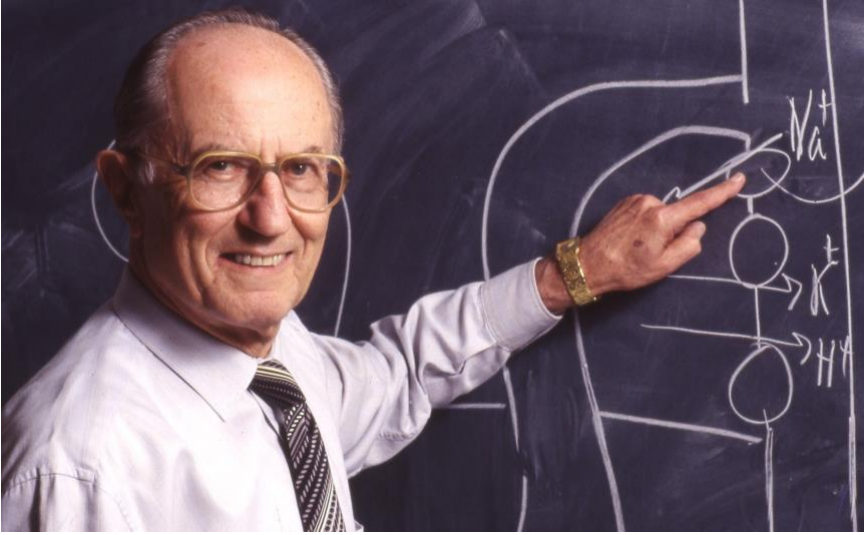**A Message from the Chairman**
David Johnson, M.D., MACP
Donald W. Seldin Distinguished Chair in Internal Medicine

When the chief residents and I first conceived of the Donald W. Seldin Research Symposium, we believed that the Internal Medicine Department's strengths in research, education, and patient care represented a unique opportunity to highlight and emphasize the interaction of those three missions through a celebration of our trainees' mentored research accomplishments. Highlighting those achievements every year not only allows us to appreciate our trainees and their mentors for their hard work, but also gives us an opportunity to open the eyes of faculty across our entire department and campus to the enthusiasm and dedication of our residents and fellows to research.

This year, our talented trainees will be presenting an incredible 132 posters, an increase of 53 percent from our 2017 Symposium. Presentations this year span the entire range of research, from case reports to clinical research, from quality improvement to fundamental pathobiology. This bountiful variety of research wouldn't be possible without the uniquely fertile grounds enjoyed by our residents, with a multi-decade institutional pedigree in basic research, and the enormous opportunities offered by our three major hospitals: Clements University Hospital, the Dallas VA Medical Center, and Parkland Memorial Hospital. Together, in partnership with Internal Medicine and UTSW faculty, our trainees have access to one of the most uniquely broad and varied opportunities for research in all fields and interests.

As we gather this year for the third time to celebrate the incredible research collaborations between our trainees and faculty across campus, I am excited not only by how far we have come, but also the vast potential still ready to be unlocked in our faculty-trainee relationships, highlighting both the sheer enthusiasm for research among our trainees, but also the wealth of opportunities for impactful and insightful research among our faculty. Looking forward, the Seldin Research Symposium will continue to serve as our springboard for new initiatives to increase resident interest and participation in research, foster new collaborations between our faculty and trainees to contribute towards our fund of knowledge, and train our residents and fellows for the future of medicine, today.

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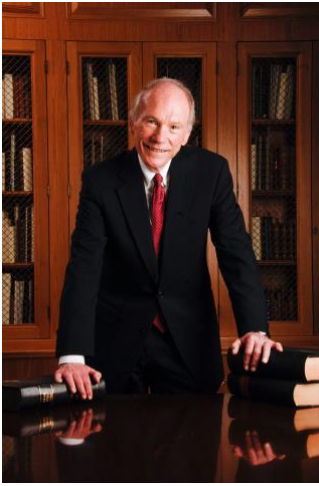
The list of honors achieved by Dr. Seldin during and after his chairmanship is as varied as it is long. Seven societies can lay claim to him as past president: the American Society of Nephrology, The Association of Professors of Medicine, the Association of American Physicians, the International Society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

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

"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.

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.

Michael S. Brown, M.D.

Dr. Michael S. Brown is The W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research, Regental Professor, and the Paul J. Thomas Chair in Medicine at UT Southwestern Medical Center. He began his career at the University of Pennsylvania as an undergraduate in Chemistry. After earning his M.D. from the University of Pennsylvania School of Medicine in 1966, Dr. Brown pursued his residency in Internal Medicine at Massachusetts General Hospital – where he developed a friendship with fellow intern and colleague, Dr. Joseph L. Goldstein. Following residency, he undertook four years of research training at the National Institutes of Health with Dr. Earl Stadtman, studying the enzymology of *E. coli* glutamine synthetase.

In part, due to his friendship with Dr. Goldstein, Dr. Brown joined the Department of Internal Medicine at UT Southwestern, where he fell into the orbit of the legendary Chairman Dr. Donald W. Seldin. At Dr. Seldin's urging, Drs. Brown and Goldstein forged a joint research collaboration studying the pathobiology of familial hypercholesterolemia. Their seminal discovery of the low-density lipoprotein receptor and the mutations that cause familial hypercholesterolemia represents a paradigm for academic internal medicine – a shining example of what patient-oriented biomedical research can achieve to improve human health and healthcare.   Their seminal research contributions have been widely recognized, including the Nobel Prize for Medicine or Physiology, awarded in 1985, and the National Medal of Science, awarded in 1988. His current research emphasizes a family of transcription factors called sterol regulatory element-binding proteins that control cholesterol and fatty acid biosynthesis. Today, Dr. Brown currently serves as director of the Jonsson Center for Molecular Genetics, and serves as a highly valued mentor to the next generation of physician-scientists at UT Southwestern and across our nation.

Thursday, May 3rd

      12:00-3:00pm: Trainee Poster Presentations, Eugene McDermott Hall
      3:30-5:30pm: Seldin Symposium Reception, A.W. Harris Faculty Club

Friday, May 4th

      Internal Medicine Grand Rounds
      Michael S. Brown, M.D.
      The W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and
      Arteriosclerosis research
      Regental Professor
      Paul J. Thomas Professor of Molecular Genetics
      Director, Jonsson Center for Molecular Genetics
      Recipient of the Nobel Prize in Physiology or Medicine 1985
      "Controlling Cholesterol"
      Eugene McDermott Plaza, D1.502

Friday, May 11th

      Internal Medicine Grand Rounds
      Oral Abstract Presentations by Foster Fellow Finalists
      Audience vote selection of Seldin Scholar
      Eugene McDermott Plaza, D1.502

Presentation #1

Title: Repeat FIT and FOBT and Failures-- a meta analysis

Presenter: Ahana Sen

Authors: Ahana Sen, MD; Bianca M. Sigel; Amit Singal, MD, MS; Helen Mayo, MLS; Caitlin Murphy, PhD, MPH

Faculty Mentor: Amit Singal

Abstract

Background: Efficacy of annual FOBT with high rates of adherence reduces mortality in equivalent rates to colonoscopy every 10 years. We conducted a meta-analysis to address (1) if FIT/FOBT are occurring in accordance with recommended guidelines (2) extent of adherence, and (3) the correlates of adherence in these patients.

Methods: We searched Medline, PubMed, Embase, and the Cochrane Library for studies that reported repeat CRC screening and follow-up from 1997 through 2017. Search terms included mass screening, screening program, and guideline adherence. Studies were considered eligible for review if they: (1) were written in English; (2) reported data from a primary study; (3) measured repeat FIT, FOBT. Two investigators independently screened the titles and abstracts of all potentially eligible articles to determine eligibility. Abstracts were coded as 'no' or 'maybe' for further inclusion.

Results: Literature search yielded 6,257 unique articles. 37 studies were specifically eligible for our assessment for repeat FIT/FOBT. Looking at the proportion of individuals who completed 2 rounds of FIT/FOBT, the pooled proportion was 67%, ranging from 25-89%. We found that in safety net and opportunistic programs, total pooled proportion of adherence was 35%. This was notably lower than studies based in large integrated systems of 81%. Finally, in studies based in population outreach, pooled proportion of adherence was 71%. When looking at country of origin, the lowest pooled cohort for adherence occurred in Australia with adherence of 37% and the highest in Canada, 86%. Among participants who completed three rounds of FIT or FOBT, the pooled estimate of participation was 62% ranging from 43-86%. Finally using a five-point quality assessment score we noted most studies consistently used the proper patient population, used reproducible methodology, and used EMR over patient report in their studies. Studies varied in how many rounds of FIT/FOBT they reported, with most reporting <3 rounds.

Conclusion: There is great heterogeneity at multiple levels in studies assessing the use of FIT/FOBT. Adherence declines with multiple years of repeat testing and thus more studies should assess feasibility of more than 2 consecutive rounds as efficacy of FIT/FOBT is based on consistent use over multiple years.

Presentation #2

Title: Promoting High Value Care by De-adopting The Neutropenic Diet

Presenter: Ahana Sen

Authors: Ahana Sen, MD; Arjun Gupta, MD; Deepak Agrawal, MD; Hsiao Ching Li, MD; David H. Johnson, MD; Navid Sadeghi, MD

Faculty Mentor: Deepak Agrawal

Abstract

Background: Patients with cancer-associated neutropenia are commonly prescribed 'neutropenic diets' despite multiple randomized controlled trials demonstrating that restrictive 'neutropenic diets' do not reduce infection rates compared to more liberal diets. Neutropenic diets are associated with lower quality-of-life and malnutrition. This study aimed to demonstrate the de-adoption of the neutropenic diet at our institution.

Methods: We studied the inpatient utilization of neutropenic diets at Parkland Health & Hospital System, Dallas, Texas from September 2016- September 2017. We analyzed the contents and duration of the neutropenic diet, and its prescription patterns. We used the Culture, Oversight, Systems Change, Training (COST) framework to guide the delivery of high value care by ultimately abandoning the use of the neutropenic diet.

Results: In the 1-year study period, there were 4,781 admissions in which patients were neutropenic (absolute neutrophil count, < 1,000 /μL) at any given time during the admission. Of these, 163 unique patients with 229 admissions (4.7%) had a neutropenic diet ordered. In 20/ 229 admission (8.7%), the patient was not neutropenic. The most common ordering providers were internal medicine (53%), and oncology (29%). Internal medicine and oncology physicians were educated regarding the lack of efficacy of a neutropenic diet (Training) and ordering patterns were monitored (Oversight) using the information technology department. Involved trainees recruited multi-departmental leaders, from the administration, infection control, nutrition services, oncology, and internal medicine to champion this initiative (Culture). The neutropenic diet order was then removed from the system through an electronic medical record modification (Systems change).

Conclusions: Inpatients with neutropenia at our institution received the neutropenic diet inconsistently, and with inconsistent contents. Guided by a standardized value framework, we abandoned the use of a low-value practice, neutropenic diet, at our institution, resulting in high-value care change with minimal resource utilization. Other institutions should encourage the de-adoption of the neutropenic diet.

Presentation #3

Title: The Use of Classification Systems in the Diagnosis of Chronic Pancreatitis

Presenter: Deepika Satish

Authors: Deepika Satish, MD; Deepak Agrawal, MD

Faculty Mentor: Deepak Agrawal

Abstract

Background: Chronic pancreatitis is a continuum of structural and functional changes in the pancreas. However, making the diagnosis, especially in early stages, can be difficult. Diagnostic criteria based on symptoms, laboratory tests, and imaging have been proposed. M-ANNHEIM and Mayo are amongst the more widely used classifications. Not using these criteria or relying on only a few clinical and imaging features can result in the incorrect diagnosis of chronic pancreatitis, leading to unnecessary treatment with pancreatic enzyme replacement therapy (PERT). The goal of this study is to determine how many patients prescribed PERT met the diagnostic criteria of chronic pancreatitis based on M-ANNHEIM and Mayo classification.

Methods: A retrospective, cross sectional study of all patients with PERT prescriptions at an 862 bed urban public hospital with a chart diagnosis of chronic pancreatitis from 2008 to 2016 was conducted. Medical records were reviewed to determine how many of these patients met the M-ANNHEIM and the Mayo diagnostic criteria of chronic pancreatitis.

Results: Seventy-four patients with an active prescription of pancreatic enzymes had a chart diagnosis of chronic pancreatitis. 27 (36%) patients did not meet the M-ANNHEIM criteria and 23 (31%) patients did not meet the Mayo criteria of chronic pancreatitis. The prescription of pancreatic enzymes to those without chronic pancreatitis led to a total of 1023 months and $365,000 of unnecessary PERT use, without benefit to patients.

Conclusion: About one third of patients are inappropriately diagnosed with chronic pancreatitis. The incorrect diagnosis leads to unnecessary prescriptions of PERT, a practice that increases cost and medication burden on patients.

Presentation #4

Title: Lipoprotein(a) and Family History of Myocardial Infarction: Insights from the Dallas Heart Study

Presenter: Anurag Mehta

Authors: Anurag Mehta, MD; Anand Rohatgi, MD; Colby Ayers, MS; Jarett Berry, MD; Parag Joshi, MD; Amit Khera, MD

Faculty Mentor: Amit Khera

<u>**Abstract**</u>

Background: Circulating lipoprotein(a) [Lp(a)] levels and family history of myocardial infarction (FHMI) are independent predictors of major adverse cardiovascular events (MACE). Lp(a) is genetically determined and is frequently tested in those with FHMI. Whether the relationship of Lp(a) with MACE is consistent with and without FHMI is unclear.

Methods: Dallas Heart Study participants who were free of CVD and had Lp(a) measured using an apolipoprotein(a) isoform size independent assay were followed for clinical events. The association of race-specific Lp(a) quartiles with MACE (CV death, non-fatal MI, non-fatal stroke, coronary/carotid/peripheral artery revascularization) among those with and without FHMI was assessed using Cox proportional hazards models adjusted for ACC/AHA pooled cohort equation (PCE) risk factors and statin use, with interaction testing performed between Lp(a) and FHMI. The models were further adjusted for high sensitivity C-reactive protein (hsCRP) and coronary artery calcium (CAC).

Results: Among 2,756 participants included, the mean age was 44 years, 57% were female, 50% were black, and 31% had FHMI. The median Lp(a) level among participants with and without FHMI was 58.6 and 46.4 nmol/L, respectively (p<0.001). After a median follow-up of 10 years, 251 MACE were observed and 47% occurred in those with FHMI. High race-specific Lp(a) levels (quartile 4 versus quartile 1) were associated with MACE in models adjusted for PCE risk factors and statin use among participants with FHMI (hazard ratio 1.99, 95% CI 1.15-3.43), but not among those without FHMI (hazard ratio 1.24, 95% CI 0.76-2.03). However, there was no significant interaction between Lp(a) and FHMI (p=0.30). The association between Lp(a) and MACE among those with FHMI was not attenuated after further adjustment for hsCRP and CAC (hazard ratio 1.99, 95% CI 1.09-3.63).

Conclusion: In this young, multiethnic, population-based cohort of individuals free of CVD, we observed an independent association of Lp(a) with MACE in those with FHMI but no statistical association in those without. Further studies with a larger sample size are needed to determine if the association of Lp(a) with MACE is enhanced in those with FHMI.

Presentation #5

Title: Validation of the ACC/AHA Pooled Cohort Equations for Cardiovascular Risk Assessment: A Meta-Analysis

Presenter: Anurag Mehta

Authors: Anurag Mehta, MD; Rohan Khera ,MD; Parag Joshi, MD; Khurram Nasir, MD; Amit Khera, MD; Ambarish Pandey, MD

Faculty Mentor: Ambarish Pandey

Abstract

Background: Validation studies assessing performance of ACC/AHA pooled cohort equations (PCE) to predict ASCVD risk have revealed conflicting results. A quantitative synthesis of these studies, particularly in sub-groups of sex and race/ethnicity, is critical given the important clinical decisions predicated on PCE predicted risk thresholds.

Methods: Through a critical review of MEDLINE, EMBASE, and Cochrane Central databases from January-2011 to June-2017, we identified all studies assessing discrimination and/or calibration of PCE in adults without clinical ASCVD. We abstracted data for overall as well as sex and race/ethnicity-specific model characteristics - concordance statistic (or c-statistic; model discrimination) and the expected-to-observed (E/O) events (model calibration). Study quality was assessed on the CHARMS checklist using the PICOTS criteria.

Results: Eighteen validation cohorts with 728,682 participants (mean age 53.7 years, 56% women, 44% White, 4% Black, and 49% Asian), 21,368 ASCVD events, and 5,833,031 person-years of follow-up were included. Most studies were of moderate-to-good quality. Given the substantial heterogeneity across studies, study-level estimates were pooled in a random effects meta-analysis. In pooled analyses, the PCE showed modest discrimination across all studies with an overall pooled c-statistic of 0.73 (95% CI 0.71, 0.75). Similar discrimination was observed in sub-groups stratified by sex and race/ethnicity. In assessing model calibration, there was a 55% overestimation of risk (pooled E/O ratio 1.55 [1.21-1.98]) across all studies. Miscalibration was similar among men (E/O ratio 1.67 [1.37-2.04]). PCE was better calibrated among women, with a smaller and non-significant overestimation of risk (E/O ratio 1.35 [0.97, 1.89]). Further, there was a significant interaction by race/ethnicity among women (P <0.05), with a 57% overestimation of risk in studies of predominantly white women compared with 10% non-significant underestimation of risk among studies of predominantly Asian women. PCE are well calibrated when predicted 10-year risk is less than 5% and risk overestimation occurs with increasing predicted ten-year risk.

Conclusion: While the ACC/AHA PCE shows modest discrimination across demographic groups, there is a consistent, nearly 50% overestimation of ASCVD risk among white women and among all men. Risk overestimation becomes worse with increasing predicted ten-year risk. These findings may have significant implications for clinical decision-making.

Presentation #6

Title: New onset asthma associated with Toxocara infection

Presenter: Alexander Monroe

Authors: Alexander Monroe, MD; Okeefe Simmons, MD

Faculty Mentor: Chad Newton

Abstract

Case Presentation: Mr. M is a 25 year old man with no prior medial history who presented to the Parkland ER with dyspnea, wheezing, and cough that started 3 weeks after immigrating from Kenya Over the span of 4 months, he had 6 admissions to the hospital for similar symptoms, including several ICU stays and one intubation. Initial lab workup also revealed eosinophilia (up to 2,170 x10^6) and elevated IgE. The patient improved rapidly with IV steroids and inhaled bronchodilators. His symptoms remained controlled as an outpatient as long as his oral steroids and short-acting bronchodilators lasted, but they worsened significantly when each of these treatments stopped. CT angiography, performed twice, was unremarkable. The peripheral eosinophilia and recent immigration prompted a parasitic workup (including Strongyloides and Ascaris) which was negative. He was later found to have Toxocara IgG in his blood. He was treated with 2 courses of albendazole with marked improvement of his symptoms, though he has required systemic steroids a few times since treatment.

Discussion: Toxocariasis, infection by roundworms in the genus Toxocara, is one of the most common zoonotic parasitic diseases in the world. The most common method of transmission to humans is though ingestion of food or water contaminated with animal feces containing parasite eggs. Most commonly, infection causes visceral or ocular larval migrans. Associated symptoms include wheezing and asthma-like airway hyperreactivity due to presumed influx of helper T cells into the pulmonary system2. Studies have shown an association between infection with Toxocara and development of asthma as presumed in this patient. In a mouse model, Toxocara antigen may persist up to 8 months after treatment, which may explain why this patient continues to have asthma symptoms.. Currently, there is no data on the long-term progression of respiratory symptoms in these patients. Treatment includes usual treatment for asthma, including short- and long-acting bronchodilators, inhaled steroids, and other medications as indicated for severity. Anti-IL5 treatments don't appear to have significant effect in animal models.

Presentation #7

Title: 'Are you sure it's my liver and not my back?': a peculiar presentation masking a rare diagnosis

Presenter: Allexa Allyn Hammond

Authors: Allexa Hammond, MD; Gary Reed, MD

Faculty Mentor: Gary Reed

Abstract

Case Presentation: A 42 year old male with congestive heart failure, chronic kidney disease and hypertension recently started on hydralazine presented with a one day history of bilateral flank pain. The patient denied fevers, chills, genitourinary or gastrointestinal symptoms. The flank pain resolved without treatment soon after presentation. Vital signs and physical examination were normal. Labs incidentally showed an AST of 1718 U/L and ALT of 1491 U/L with elevated total bilirubin. Further work-up ruled out viral hepatitis or acetaminophen toxicity. Gamma globulin level was elevated (IgG 2780 mg/dl; reference range 767 -1590 mg/dl) with positive ANA (1:320) and Sjogren's antibody (>8.0 U); liver biopsy showed hepatitis with autoimmune features. The patient was emergently started on prednisone and azathioprine; hydralazine was discontinued given suspicions for drug-induced autoimmune hepatitis (DI-AIH). Upon follow-up in clinic, the patient remained asymptomatic with near resolution of liver injury.

Discussion: Few conditions induce liver injury with transaminase levels above 1000 U/L. Such conditions include viral hepatitis, acetaminophen toxicity, drug induced liver injury (DILI) and autoimmune hepatitis (AIH). Although DILI and AIH are distinct clinical entities, there are occasions when one may encounter a patient with clinical, laboratory and histologic findings to suggest a diagnostic overlap. In the literature, 'drug-induced autoimmune hepatitis' (DI-AIH) is rare. Differentiating AIH from DI-AIH is extremely difficult, as the clinical symptoms vary widely in both conditions (from asymptomatic to decompensated acute liver failure) with almost identical laboratory and histological findings, including significantly elevated transaminases, positive autoantibodies, elevated gamma globulin levels, and lymphoplasmacytic and eosinophilic infiltration. Medications that are common culprits of DI-AIH include hydralazine, minocycline and nitrofurantoin. In addition to removing the offending agent, treatment of DI-AIH includes glucocorticoid therapy with the possible addition of azathioprine. Whereas those with DI-AIH are likely to be cured following completion of treatment, those with autoimmune hepatitis often relapse once off tailored therapy and require long-term immunosuppressants. Thus, although these conditions may share nearly identical features, the long term management is likely to differ depending on the diagnosis; the clinician should have a low threshold to consider DI-AIH in the appropriate clinical context for this reason.

Presentation #8

Title: Blood pressure outcomes in patients with primary aldosteronism after adrenalectomy versus medical management in relation to the new 2017 ACC/AHA blood pressure guidelines

Presenter: Allexa Allyn Hammond

Authors: Allexa Hammond, MD; Bryan Wu, MD; Hamza Lodhi, MD; Jeomi Maduka, MD; Danielle Tientcheu, MD; Angela Price, MD; Wanpen Vongpatanasin, MD

Faculty Mentor: Wanpen Vongpatanasin

<u>**Abstract**</u>

Background: Primary aldosteronism (PA) is a common cause of secondary hypertension, which may lead to cardiovascular and renal complications, if left untreated. Surgical and medical interventions are effective in reducing blood pressure (BP) in PA patients. However, previous studies have not investigated BP outcomes following adrenalectomy or medical therapy in the context of the lower BP target goal and threshold proposed by the 2017 ACC/AHA blood pressure guidelines.

Methods: We conducted a retrospective study in patients with confirmed diagnosis of PA who were referred to Hypertension clinic at the University of Texas Southwestern between March 2006 and August 2017. Patients were categorized into adrenalectomy or medical therapy groups. The average BP and number of antihypertensive medications were recorded at each clinic visit. Hypertension cure rate of PA patients undergoing adrenalectomy was compared using the JNC8 threshold BP of 140/90 mmHg versus the 2017 ACC/AHA threshold BP of 130/80 mmHg.

Results: 58 were confirmed to have PA by salt loading test. Adrenal vein sampling demonstrated evidence of unilateral PA in 27 patients and bilateral PA in 31 patients. Among the unilateral PA group, 26 patients underwent adrenalectomy while 31 patients in the bilateral PA group were medically managed with mineralocorticoid receptor antagonists. The adrenalectomy subgroup required fewer numbers of anti-hypertensive drugs at the last follow-up visit (p=0.0012) when compared to medically treated group. Systolic BP reduced similarly from the baseline visit to the last visit in both adrenalectomy group when compared to medical therapy group (from 146.7 +/- 4.7 to 130.7 +/- 3.7 mmHg vs. 144.2 +/- 4.4 to 132.5 +/- 3.7 mmHg, p < 0.01 for visit and p=0.9 for group). 22.2% of adrenalectomy patients achieved cure based on the previous JNC 8 guidelines, whereas only 11.1% achieved cure based on the current guidelines.

Conclusion: Adrenalectomy is more efficacious than medical management regarding reducing the number and dose of anti-hypertensive medications needed for BP control and achieving cure. Although some patients who underwent adrenalectomy were subsequently cured from hypertension, the percentage achieving cure decreased substantially when defined by the new ACC/AHA guidelines.

Presentation #9

Title: Utilization of Palliative Care Services in End-Stage Liver Disease Patients Admitted to a Safety-Net Intensive Care Unit

Presenter: Andrew Sumarsono

Authors: Andrew Sumarsono, MD; Giuliana Cerro Chiang, MD; Thomas Tielleman, MD, Padmaja Reddy, MD; Catherine Chen, MD; Matthew Leveno, MD

Faculty Mentor: Matthew Leveno

Abstract

Background: Patients with cirrhosis admitted to the intensive care unit (ICU) in non-transplant centers have mortality ranging between 31% and 47%. Yet palliative care is rarely integrated into the active management of these patients despite being able to assist with symptom management, emotional support, and family discussions. A national study reported that among all end-stage liver disease (ESLD) patients who died in the hospital, regardless of transplant candidacy, only 30.3% incorporated palliative care in their treatment plan. To date, no studies have evaluated the role of palliative care in cirrhotic patients admitted to safety-net ICUs.

Methods: We conducted a retrospective cohort study of patients with cirrhosis admitted to an ICU in a large, safety-net hospital system between dates March 2015 to March 2017. A diagnosis of cirrhosis confirmed by imaging and lab findings was required for inclusion into the cohort. Patients demographics, illness severity scores, mechanical ventilation, vasopressors, renal replacement therapy, and the utilization of palliative care were recorded.

Results: 389 patients with cirrhosis admitted to the ICU were included in this study. The overall in-hospital mortality was 23.4% (91/389). The initiation of renal replacement therapy, administration of vasopressors, or requirement of intubation conferred in-hospital mortality risks of 82.6%, 61.6%, and 46.8%, respectively. In-hospital palliative care consult was obtained for 14.6% (57/389) of the cohort. Of the 91 patients who died in the hospital, 27.3% received a palliative care consult. Only 5% (20/389) of the patients had been seen in an outpatient palliative care clinic prior to admission.

Conclusions: Patients with cirrhosis admitted to the ICU represent a population with high in-hospital mortality yet palliative care continues to be underutilized in the management of these patients. Most of the studies regarding palliative care in ESLD patients are performed in centers where transplant remains a possibility. In this study, we describe how palliative care is utilized in a critically ill patient population with extremely limited transplantation options. These data suggest that a better understanding of the role of palliative care in critically ill ESLD patients is warranted.

<div align="center">**Presentation #10**</div>

Title: Early Encapsulated Peritoneal Sclerosis in a Patient on Peritoneal Dialysis

Presenter: Andrew Sumarsono

Authors: Andrew Sumarsono, MD; Kamalanathan Sambandam, MD

Faculty Mentor: Kamalanathan Sambandam

Abstract

Case Presentation: A 62 year old man with a history of diabetes, hypertension, and end-stage renal disease on peritoneal dialysis presented the ER with abdominal pain, shortness of breath, and subjective low-grade fevers. Seven months ago, he was started on peritoneal dialysis. Last month, he had an episode of abdominal pain for which he received antibiotics, but denied any dialysis-associated infection. His dialysis prescription recently changed from 2L to 1.5L every 6 hours due to pain at the end of the exchange. He denies prolonged fill times or drain times, or bloody or cloudy dialysate. On admission, the patient was hypertensive (173/74 mmHg), tachypneic (30 breaths per minute), and saturating at 93%. Exam revealed a chronically ill-appearing male in no acute distress. Bibasilar rales were present. His abdomen was diffusely tender, but without peritoneal signs. His right peritoneal dialysis catheter exit site was clean and intact. Labs revealed potassium 5.6 and creatinine 13.79. CT abdomen identified a large fluid collection with well-defined walls and early tethering of the small bowel loops with mild proximal dilatation of a few loops consistent with encapsulated peritoneal sclerosis. The peritoneal fluid identified 390 nucleated cells; cultures grew coagulase negative staph. The patient was transitioned to hemodialysis and treated with two weeks of IV vancomycin.

Discussion: Encapsulating peritoneal sclerosis (EPS) is a rare but serious complication of peritoneal dialysis with significant mortality. The reported incidence is between 0.7 and 13.6 per 1000-person years and risk increases with time on PD. In one cohort study, the incidence of EPS was 0 within 1 year of PD initiation. The most common presenting symptoms include abdominal pain, vomiting, and abdominal distention. CT may show peritoneal thickening or calcification, or bowel tethering. Management includes tamoxifen and either temporary or permanent switch to hemodialysis. Acute obstruction due to adhesions is a serious complication that requires surgical intervention. The overall prognosis for EPS is poor; one study identified a one-year and two-year survival of 67% and 52%. Our patient represents an interesting case in which EPS developed within one year of the initiation of his PD.

Presentation #11

Title: Impact of Gain or Loss of Individual Fat Depots on Cardiac Structure and Function: The Dallas Heart Study

Presenter: Bryan Wilner

Authors: Bryan Wilner, MD; Ambarish Pandey, MD; Colby Ayers, MS; Gloria Vega, PhD; Scott Grundy, MD, PhD; Sonia Garg, MD; Susan Matulevicius, MD; Ron Peshock, MD; Mark Drazner, MD; Ian Neeland, MD

Faculty Mentor: Ian Neeland

<u>**Abstract**</u>

Background: Body fat depots are differentially related to cardiac structural phenotypes in cross-sectional studies. The impact of changes in visceral adipose tissue (VAT), subcutaneous abdominal adipose tissue (SAT), and lower body fat (LBF) on the left ventricle (LV) over time are unknown.

Methods: Participants without baseline cardiovascular disease or LV dysfunction in the Dallas Heart Study underwent assessment of fat distribution by dual-energy X-ray absorptiometry (DXA) and cardiac structure/function by MRI between 2000-2002 and repeated ~7 years later. Associations between changes in VAT, SAT, and LBF with alterations in LV structure and function were assessed.

Results: The study cohort (n=1303) was mean age 44 years with 57% (747/1303) male, 43% (558/1303) black, and 36% (470/1303) obese. Those with >5% VAT gain were younger and more likely to have lower BMI, triglycerides, LDL-C, and hs-CRP, at baseline and had greater increases in blood pressure, glucose, cholesterol, and hs-CRP over follow up. The relationship between VAT change and change in LV concentricity (mass/volume) was linear (Fig. A), indicating worsening concentric remodeling with VAT gain and improvement with VAT loss. In multivariable linear regression models, gain in all fat depots was significantly associated with increases in LV mass, LV wall thickness, concentricity, cardiac output, and decreased systemic vascular resistance (Fig. B). After additional adjustment for BMI change, only VAT gain remained significantly associated with concentric remodeling; other associations were attenuated. Fat depot changes were not associated with changes in LV end-diastolic volume or ejection fraction. Conclusion Expansion of fat depots over time is associated with adverse cardiac remodeling. In the case of VAT, this association is independent of changes in BMI. These data suggest that reduction in VAT is a potential target to prevent adverse concentric LV remodeling, itself an important intermediate phenotype in the progression to heart failure.

Presentation #12

Title: MPGN and mixed cryoglobulinemia diagnosed after HCV treatment: a case report

Presenter: An Lu

Authors: An Lu, MD; Benjamin Hewitt, MD; Bryan Wu, MD; Jenna Wiles, Jeanney Lew, MD

Faculty Mentor: Jeanney Lew

<u>**Abstract**</u>

Mr. B is a 55-year-old male veteran who presented with a 2-week history of fatigue, nausea, vomiting, decreased oral intake and urine output. Past medical history was notable for schizophrenia, T2DM, hypertension, and chronic HCV treated with ledipasvir/sofosbuvir with SVR. On exam, he was hypertensive at 157/97, but his other vitals were unremarkable. Physical exam was notable for dry mucus membranes and diminished skin turgor. Laboratory results showed WBC 19.5K, Na 120, BUN 105, Cr 3.73 (baseline normal), and serum osmolarity 283. Urinalysis had greater than 500 protein with 11-20 RBCs along with RBC casts on microscopy. 24-hours urine collection yielded 7.6g of protein. He had positive cryoglobulins and RF (1105), but his ANA, ANCAs, M-component, complement levels, and repeat HCV RNA level were unremarkable. His Na normalized with isotonic crystalloid resuscitation but elevation in creatinine persisted, prompting percutaneous kidney biopsy. Pathology showed MPGN pattern with necrotizing arteriolitis and cryoglobulins. Prednisone 60mg was initiated, resulting in improvement in renal function. He was discharged on prednisone 40mg, and had negative serum cryoglobulins and decrease in RF (141) at outpatient nephrology follow up 2 weeks later. Chronic HCV infection is commonly associated with extrahepatic manifestations, such as mixed cryoglobulinemia (MC) and membranoproliferative glomerulonephritis (MPGN) (1). Successful treatment of HCV infection with SVR can result in resolution of cryoglobulinemia and vasculitis (2). Rarely, MC and vasculitis can persist despite eradication of HCV with modern antiviral therapy. Here we present a rare case where a patient was successfully treated for HCV, yet still developed MC and MPGN. Upon further chart review, the patient has significant proteinuria with normal creatinine level as far as 2 years prior to his initial diagnosis of MPGN. It is plausible that he may have developed indolent MC associated with HCV prior to receiving treatment. Although cryoglobulins are found in 25%-30% of patients with HCV, only 10%-15% of them develop clinically significant disease, with different ranges of symptoms (3). This interesting case challenges us to keep in mind the potential complications associated with HCV even upon achieving viral eradication.

Presentation #13

Title: Assessing the Role of ASCVD Score in Primary Thrombosis Prophylaxis Strategy Among Asymptomatic Antiphospholipid Antibody Carriers.

Presenter: Akrithi Udupa (Aki)

Authors: Yu Zuo, MD; Akrithi Udupa, MD; Jennifer Fan, MD; Una Makris, MD; David Karp, MD; Yu-Min Shen, MD

Faculty Mentor: Yu Zuo

Abstract

Background: Primary thrombosis prophylaxis among asymptomatic antiphospholipid antibody (aPL) carriers is challenging. The presence of aPL does not always lead to thromboembolic events. Additional factors are needed to potentiate thrombus formation. A risk stratification tool to guide primary thrombosis prophylaxis among aPL positive carriers does not yet exist. Aims: To evaluate the role of ASCVD score in primary thrombosis prophylaxis among asymptomatic aPL carriers.

Methods: This study included a convenience cohort of 198 persistent aPL positive patients who attended clinic at University of Texas Southwestern Medical Center. All patients had persistent high titer (≥99 percentiles) aPL. The aPL testing was performed using FDA approved commercial kits. LA was tested by dilute Russell's viper venom time, partial thromboplastin time-LA and silica clotting time, with appropriate cut-offs established in the laboratory. ASCVD is calculated based on patients' age, total cholesterol, HDL, most recently documented systolic blood pressure, diabetes status, and smoking status. Pearson Chi-squared analysis was used to determine the association between increased ASCVD>10 and various thromboembolic events. Non-parametric comparison of ASCVD as a continuous variable was performed among different groups.

Results: Of the 198 aPL positive patients, 31 (15.7%) patients had arterial thrombosis, 72 (36.4%) patients had venous thrombosis, and 95 (48%) patients were asymptomatic. When comparing thrombotic APS patients to asymptomatic aPL positive carriers, ASCVD >10 (OR= 2.281, 95% CI 1.034 - 5.247, P=0.045) was significantly associated with arterial thrombosis (Fig 1) but not venous thrombosis or any thrombosis. Significantly higher ASCVD scores are seen among aPL patients with arterial thrombosis compared to asymptomatic carriers (P=0.029). There are no significant ASCVD score differences observed between aPL patients with venous thrombosis/or any thrombosis and asymptomatic carriers.

Conclusion: Increased 10 year cardiovascular disease risk determined by ASCVD among aPL positive patients is significantly associated with arterial thrombosis but not venous thrombosis. Since the protective effect of aspirin against incident thrombosis in all aPL carriers is not supported by randomized controlled data, our result suggests that ASCVD may be useful in identifying a subgroup of aPL carriers who benefit from aspirin.

Presentation #14

Title: Efficacy of alpha adrenergic receptor blockers in the treatment of VEGF inhibitor-induced Hypertension

Presenter: Bryan Boyuan Wu

Authors: Bryan Wu, MD; Hamza Lodhi, MD; Debbie Arbique, MD; Angela Price, MD; James Brugarolas, MD; Wanpen Vongpatanasin, MD

Faculty Mentor: Wanpen Vongpatanasin

Abstract

Background: Hypertension is one of the most common side effects of Vascular Endothelial Growth Factor (VEGF) Inhibitor, which may limit its use at the maximal effective dosage for anticancer treatment. The National Cancer Institute has endorsed the use of thiazide diuretics, beta blockers (BBs), calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors, and angiotensin receptor antagonists in the treatment of VEGF inhibitor-induced hypertension. Alpha adrenergic receptor blockers (AR) is known to be effective when used as fourth-line therapy in essential hypertension. However, its efficacy has not been evaluated in this setting. Method: We conducted a retrospective analysis to determine association between alpha-adrenergic receptor blocker drug use and BP outcome in patients with VEGF inhibitor-induced hypertension.

Results: From 8/2012 to 7/2017, 519 patients were referred to the UT Southwestern Hypertension Clinic, and 17 patients met our inclusion criteria and had a median follow-up of 455 days. Most (94%) patients had metastatic renal cell carcinoma. None of the patients were treated with alpha-blocker during the first hypertension clinic visit. Doxazosin was initiated and titrated during subsequent visits in a subset of patients whom BP remained elevated despite uptitration of antihypertensive drug at the maximal dosage. At the final visit, percentage of patients treated with doxazosin increased significantly to 35% ($p < 0.05$). We found that initiation of alpha blockers in combination with uptitration of central sympatholytics, CCBs and BBs was associated with improvement in BP from: $144\pm21/85\pm9$, $131\pm20/79\pm9$, $135\pm23/77\pm9$ during the first, second, and last visits, respectively (P=0.2 for systolic BP, P=0.03 for diastolic BP). At the beginning of therapy anti-VEGF therapy was held or reduced in 7/17 (41%) due to elevated BP, whereas only one patient had such interval interruption prior to last visit (P=0.04). Patients' renal function remained stable during period of follow-up despite re-initiation of anti-VEGF therapy during follow up (serum creatinine, 1.51 ± 0.87, 1.46 ± 0.77, 1.50 ± 1.05 for first, second, and last visits, respectively, p =0.982).

Conclusions: Alpha adrenergic receptor blockers should be considered as an add-on treatment for patients with anti-VEGF-induced hypertension, whose BP remain uncontrolled despite guideline-directed medical therapy.

Presentation #15

Title: Rates of gastrointestinal bleeding in cirrhotics treated with warfarin

Presenter: Jaehyun Kim

Authors: Tiffany Lee, MD; Jaehyun Kim, MD; Rick Weideman, PharmD; Linda A. Feagins, MD

Faculty Mentor: Linda A. Feagins

Abstract

Background: While the risk for bleeding from varices is well accepted, the risk of bleeding from coagulopathy in patients with cirrhosis has been debated. There is little data on the risk of gastrointestinal bleeding (GIB) in patients with cirrhosis who are treated with anticoagulants like warfarin.

Methods: Retrospective review comparing patients at our local VA who were prescribed warfarin between 2009-2016 and had cirrhosis (cases) or did not have cirrhosis (controls). Patients were enrolled into the study at the timepoint where anticoagulation was begun or when cirrhosis was diagnosed if already on anticoagulation and anticoagulation was continued. Controls were required to have a fib-4 score of < 1.45. Calculation of MELD and Childs-Pugh scores were not performed for patients without baseline INR prior to starting anticoagulation.

Results: We identified 82 cases and 62 controls who were taking warfarin. Etiology of cirrhosis for the cases included 49% with hepatitis C, 39% using alcohol, 22% with non-alcoholic steatohepatitis, 2% hepatitis B, and 17% other. Average MELD was 12, Childs-Pugh 6.6 and 14 (17%) had a history of esophageal varices. More than 80% of cases and controls were on warfarin for atrial fibrillation, deep vein thrombosis, or pulmonary embolus. Charlson comorbidity index and HAS-BLED score were significantly higher in the cases as compared to controls (7.1 vs 2.6, $p<0.0001$ and 2.7 vs 1.0, $p<0.0001$, respectively). There were no differences in use of concomitant antiplatelet agents or antisecretory agents. Cases were treated more often with beta-blockers (71% vs 37%, $p<0.0001$) versus controls. At least 60% of both cases and controls who experienced GIB presented with supratherapeutic INRs. Cumulative rates of GIB trended towards occurring significantly more often for cases; 2 (2.4%) vs 0 (0%) at 30 days ($p=0.51$), 7 (8.5%) vs 0 (0%) at 90 days ($p=0.02$), 9 (11%) vs 2 (3.2%) at 1 year ($p=0.12$) and 10 (12.2%) vs 2 (3.2%) at 2 years ($p=0.07$), cases versus controls, respectively.

Conclusions: Cirrhotics treated with warfarin have high rates of GIB with over 10% of patients experiencing GIB after 1 year of therapy. 75% of cirrhotics on warfarin bled from non-portal hypertensive sources.

Presentation #16

Title: Utility of Fecal Leukocyte Testing for Inpatients with Diarrhea

Presenter: Jessy Barnes

Authors: Jessica A. Barnes, MD; Kadam Patel; Paul Southern, MD; Neha Patel, MD; Deepak Agrawal, MD

Faculty Mentor: Deepak Agrawal

Abstract

Background: Fecal leukocyte (FL) testing is frequently ordered along with ova and parasites (O&P) and stool cultures for workup of patients with diarrhea. FL are ordered with the notion that a positive test suggests bacterial diarrhea, clostridium difficile (C Diff), or inflammatory bowel disease. However, studies have questioned the clinical and diagnostic utility of FL. The aim of this study was to determine the diagnostic utility of FL for inpatients and correlation of FL with positive stool cultures, O&P and Clostridium Difficile.

Methods: Retrospective analysis of all stool studies performed on patients in the emergency room and inpatients at a county hospital from December 2011 to February 2017. The sensitivity, specificity, positive predictive value (PPV), and likelihood ratio (LR) of FL testing was calculated for positive stool cultures, C Diff, and O&P. The results were also analyzed depending on FL test performed less or greater than 72 hours after admission.

Results: FL testing was performed 8,966 times and was positive in 327 (3.7%) cases. FL were ordered at the same time as stool cultures in 72% of patients and O&P in 60% of patients, suggesting reflex ordering of these tests. The sensitivity, specificity, PPV and positive likelihood ratio of FL testing in relation to stool cultures, C Diff and O&P, performed less than or greater than 72 hours since admission, are provided in Table 1. FL testing had a 10.3% PPV for positive stool cultures, which declined after 72 hours of admission (0% PPV). For O&P, FL had a 1.1% PPV, which adjusted to 0% PPV after 72 hours of admission. Finally for C Diff, FL had a 19.3% PPV, which adjusted to 21.3% PPV after 72 of admission. When FL testing was positive and other stool studies negative, the results were largely ignored suggesting clinical futility of the test.

Conclusion: Fecal leukocyte testing has low diagnostic and clinical utility as illustrated by its low diagnostic yield and poor correlation with other stool studies. The use of this test should be questioned for evaluation of diarrhea in patients admitted to the hospital.

Presentation #17

Title: Diagnostic Utility of Ova and Parasite Testing in Hospitalized Patients

Presenter: Jessy Barnes

Authors: Jessica A. Barnes, MD; Kadam Patel; Paul Southern, MD; Neha Patel, MD; Deepak Agrawal, MD

Faculty Mentor: Deepak Agrawal

<u>**Abstract**</u>

Background: Patients presenting to emergency room or admitted to the hospital with loose bowel movements are usually evaluated with multiple tests, including ova and parasite (O&P) stool testing. Prior studies have shown low yield for O&P, especially when checked greater than 3 days after admission. The aim of this study was to evaluate the diagnostic utility of stool O&P testing, at a large county hospital, and determine the most cost-effective utilization of the test.

Methods: Retrospective analysis of O&P stool studies performed on patients in the emergency room or as inpatients at a county hospital from December 2011 to February 2017. The frequency of positive results was evaluated. Subgroup analysis was performed based on timing of testing, greater or less than 72 hours since admission. Detailed chart review was performed for patients with positive O&P results to determine duration and severity of diarrhea, immunosuppressed state (HIV, malignancy, end stage renal disease, immunosuppressive disorders), co-infection with C-difficile and treatment.

Results: Stool O&P was positive in 112 out of 7,478 patients, giving an overall yield of 1.5%. For studies ordered 72 hours after admission, the yield decreased to 0.8%. Of the patients with positive results within 72 hours, 102 (89%) had predisposing factors of diarrhea related to parasites including immunocompromised status, diarrhea for >7 days, or travel history (table). Excluding these patients, the diagnostic yield for remaining 10 patients was 0.1%. In 5 of these patients, positive O&P did not change management (2 with self limiting diarrhea and 3 treated for concurrent C Diff). The other patients included 1 with uncontrolled diabetes, 1 with Entamoeba Histolytica liver abscess, 1 elderly nursing home resident, 1 with cirrhosis on lactulose, and 1 pregnant patient. The most common pathogens found (>25%) were Giardia, Cryptosporidia, and Strongyloides.

Conclusion: Stool O&P is an overused test for patients in the emergency room and hospital with very low yield. Based on these results, the most cost-effective way of ordering stool O&P would be restricting the test to patients with a high clinical probability of positive O&P (immunocompromised status, diarrhea for > 7 days, or travel to endemic areas).

Presentation #18

Title: Yield of Stool Cultures and Prevalence of Pathogens at a Safety Net Hospital

Presenter: Jessy Barnes

Authors: Jessica A. Barnes, MD; Kadam Patel; Paul Southern, MD; Neha Patel, MD; Deepak Agrawal, MD

Faculty Mentor: Deepak Agrawal

<u>**Abstract**</u>

Background: Diarrheal illness remains an extremely common and resource intensive complaint. Reflex ordering of stool studies including stool cultures and ova and parasites are commonly performed in the emergency department and hospital setting, with variable reported yields. Prior studies have shown the diagnostic yield of this test is maximized in the outpatient setting and within 72 hours of hospital admission. The aim of this study was to evaluate the diagnostic yield of stool cultures and examine the prevalence of pathogens at a large, safety-net, county hospital.

Methods: Retrospective analysis of stool cultures performed on patients in the emergency room or as inpatients at a county hospital from December 2011 to February 2017. The frequency of positive results was evaluated. Subgroup analysis was performed based on timing of testing (greater or less than 72 hours since admission). The prevalence of specific pathogens was calculated among all positive samples. Cost data for stool cultures was estimated to be $40 per sample based on Medicare reimbursement rates.

Results: The overall yield of stool cultures was 3.6% (312 out of 8,625 studies performed). 7,670 samples were sent within 72 hours of admission and 955 were sent after 72 hours. The yield of stool cultures after 72 hours of admission decreased to 0.6% (6 positive samples). Of these 6 patients - 2 patients were HIV positive, 2 had salmonella bacteremia, and 2 had positive findings which were ignored and not treated. The prevalence of pathogens found are provided in Table 1. Stool cultures were estimated to cost $69,000 annually, which equates to $221 per positive sample. Limiting samples to within 72 hours of admission could save an estimated $7,640 annually.

Conclusion: The yield of routine testing of stool cultures at a large county hospital is very low especially after 72 hours of admission. Restricting checking stool cultures only to patients within 72 hours, except specific cases, is the most cost-effective approach.

Presentation #19

Title: Rhabdomyolysis After Conducted Electrical Weapon Exposure

Presenter: Gary Parizher

Authors: Gary Parizher, MD; Blake Barker, MD

Faculty Mentor: Blake Barker

Abstract

A 22-year-old man was brought to the emergency department by police for 'sleepiness.' He was apprehended after a confrontation a few hours prior, during which a TASER device was deployed twice. On arrival he was only oriented to self. Vital signs were within normal limits, and physical exam was only notable for a superficial abrasion to his right cheek. Due to agitation, he required soft restraints. Blood chemistries were significant for Cr 1.54, lactate 4.7, AST 536, ALT 190, ethanol 190mg/dL, and CPK 42,838units/L; urine toxicology was positive only for cannabinoids. ECG, CT head, and CXR were normal. Following volume resuscitation with crystalloids, his lactic acidosis resolved and his mental status improved. He was admitted for continuous IV fluids titrated to a urine output of 200cc/hr. The patient later endorsed consuming at least six alcoholic beverages the previous night. He denied the use of substances other than occasional marijuana and alcohol. He reported no medical history or medication use and no prior police encounters. He did not exhibit any signs of withdrawal or psychiatric illness. He fully recovered and was discharged into police custody.

Discussion: TASER deployment transiently raises both lactate and CPK to non-critical levels in healthy volunteers. Real-world use of the TASER carries a <1% risk of developing rhabdomyolysis. In prior experience, all TASER victims who developed rhabdomyolysis tested positive for stimulants by urine or serum toxicology. Our patient tested positive for cannabinoids but not for stimulants. He exhibited no manifestations of chronic substance abuse or mental illness. However, dehydration and alcohol use likely contributed to his presentation. Indeed, alcoholic rhabdomyolysis has been described. However, prolonged immobilization is a key component of the pathophysiology of acute alcoholic rhabdomyolysis, and our patient lacked a history of immobilization. Overall it seems that the use of the TASER device was the most significant contributor to his muscular injury. While TASERs are safer than firearms, they are not without risks. This case highlights the need for evaluation of all patients exposed to TASERs during apprehension by police. CPK should be routinely tested in these patients regardless of whether they have a history of illicit substance abuse.

Presentation #20

Title: Sacral bone cyst treatment resulting in paraplegia

Presenter: Corbin Eule

Authors: Corbin Eule, MD; Neil Keshvani, MD; Arjun Gupta, MD; Navid Sadeghi, MD

Faculty Mentor: Navid Sadeghi

Abstract

Case Presentation: A 50-year-old man with a stage 1 solitary right sacral plasmacytoma presented with sharp, burning lower back pain that radiates into his right lower extremity and is worsened by movement. He had undergone localized radiation therapy and seven cycles of VRD (dexamethasone, lenalidomide and bortezomib) chemotherapy, but an 18-fluorodeoxyglucose-positron emission tomography/CT scan showed a new area of uptake in the right sacral ala near the initial plasmacytoma. The lesion was believed to be a residual cyst with inflammatory changes from radiotherapy. Examination revealed no neurological deficits. After failing medical pain management, he was referred to orthopedics for cyst aspiration and bone grafting. Under fluoroscopy, the cyst was aspirated then injected with calcium sulfate-calcium phosphate composite bone graft (PRO-DENSE, Wright Medical Technology, Arlington, Tennessee, USA). Two hours later, the patient developed severe back pain, lower extremity weakness, and bladder and bowel incontinence. A CT scan demonstrated intraspinal and intradural extension of a bone substitute material occupying the entirety of the spinal canal through L1. On physical exam, he had near-complete sensory loss below the umbilicus and complete loss of motor function in his lower extremities. Neurosurgery was consulted, but they believed that the patient would not regain meaningful neurological function with emergent laminectomy. The patient declined operative intervention. Presently, he has complete paraplegia with no sensation below L1 on the right and L2 on the left side. Cyst aspirate pathology was negative for malignant cells.

Discussion: Bone graft substitutes promote bone defect repair by providing a scaffold for bone growth on their surface. The injected substitute is eventually resorbed by the body, with newly deposited bone remaining in place. They are used to treat open bone voids and gaps secondary to cysts, tumors and trauma-related osseous defects. Previously published studies have reported superficial and deep infections and postoperative fractures as adverse effects from their use. However, more serious adverse effects such as intraspinal bone leakage have been observed with polymethyl methacrylate bone cement. This case presents a rare, debilitating adverse effect of complete paraplegia after intraspinal extension of injected bone graft intended for symptomatic relief.

Presentation #21

Title: Cardiac Point of Care Ultrasound in Parkland CCU: An ACGME Back to Bedside Initiative and Randomized Controlled Trial

Presenter: Kershaw Patel

Authors: Kershaw Patel, MD; Ambarish Pandey, MD; Arjun Gupta, MD; Nitin Kondamudi, MD; Susan Matulevicius, MD

Faculty Mentor: Susan Matulevicius

Abstract

Background: Compared to working adults in the United States, physicians experience more burnout. Physicians who spend their time performing meaningful work have lower rates of burnout. The goal of the ACGME Back to Bedside Initiative is to increase time trainees spend at the bedside, enhance the doctor-patient relationship, improve trainee satisfaction, and reduce burnout. Cardiac point of care ultrasound (C-POCUS) is a readily learned bedside skill that can augment bedside cardiac diagnostic accuracy and increase patient satisfaction. We plan to examine whether a C-POCUS strategy can improve Internal Medicine resident satisfaction in the Parkland CCU.

Methods: In this prospective, randomized, controlled, cross-over, non-blinded, pilot trial, Internal Medicine residents on Parkland CCU will be randomized to usual care or usual care plus a C-POCUS strategy (including access to C-POCUS, CCU fellow encouragement to use C-POCUS, and feedback). Two buddy teams (ex: A/C teams) will receive the C-POCUS strategy for two weeks and then cross-over to usual care, while the other two buddy teams (ex: B/D teams) will receive usual care for two weeks and then cross-over to the C-POCUS strategy. The primary outcome will be change in satisfaction with the Parkland CCU rotation over two weeks. Secondary outcomes will include resident reported duty hours, C-POCUS utilization, and time performing C-POCUS examination. Expected

Results: We expect the following results: (1) Change in satisfaction with the Parkland CCU rotation over two weeks will be higher in the C-POCUS strategy group compared to the usual care group; (2) Resident reported duty hours will be similar in the C-POCUS strategy group and control group; (3) C-POCUS utilization will increase throughout the study period. Conclusions / Future Directions: To the best of our knowledge, this is the first study to examine the utility of a C-POCUS strategy in improving Internal Medicine resident satisfaction on an inpatient cardiology rotation. This study will investigate the amount of time used to perform a C-POCUS examination allowing for calculation of the time spent at the bedside, an important patient centered outcome.

Presentation #22

Title: The Hidden Curriculum Uncovered

Presenter: Christina Mosher

Authors: Christina Mosher, MD; Sarah Collins, PhD, MBA; Jerzy Lysikowski, PhD; Reeni Abraham, MD

Faculty Mentor: Reeni Abraham

Abstract

Background: Empathy in physicians is associated with improved patient outcomes such as reaching target HgbA1C and LDL levels, but out current system does not adequately foster empathy. In fact, it has been shown that medical students in their pre-clinical years report increased empathy, but once they enter their clerkships, empathy scores decline. Furthermore, empathy continues to fall as depression and anger increase during residency, ultimately leading to burnout. Many have proposed explanations for these trends. There is extensive literature on themes extracted from students' reflections on their clerkship experiences. These topics revealed a 'hidden curriculum' of lessons never explicitly stated but implicitly taught through pervasive attitudes in the medical community that ultimately shape values and behaviors for medical trainees.

Methods: Medical educators have the opportunity and obligation to mitigate negative impacts of the hidden curriculum during medical training. To that end, this project conducts a prospective non-randomized controlled study to examine the hidden curriculum as experienced by medical students when they reflect on their experiences during the Internal Medicine Clerkship. A quantitative analysis will be performed on pre and post reflection survey data as well as qualitative analysis on narratives describing challenging or distressing situations. Results and

Conclusions: Data collection and analysis is ongoing. By identifying those issues with which students grapple as they encounter their first real patients, project personnel will design a formal curriculum that ameliorates distress and equips students to better deal with difficult situations, maintain resilience, and be emotionally attuned to their patients.

Presentation #23

Title: The effect of statin use on thyroid diseases.

Presenter: Laurette Prisca Femnou Mbuntum

Authors: Laurette Femnou Mbuntum, MD; Ishak Mansi, MD

Faculty Mentor: Ishak Mansi

<u>**Abstract**</u>

Background: Despite their widespread use, few studies examined the effects of statin on the thyroid gland. The objective of this study was to determine any association between statin use and incidence of thyroid disease, specifically thyroiditis, thyrotoxicosis, goiter and thyroid cancer.

Methods: We performed a retrospective cohort study analyzing data from the San Antonio military health care system from October 2003 through March 2012. Statin users were propensity score matched to non-users using several characteristics including demographics, baseline comorbidities, medication use and hospital utilization. Study outcome were prevalence and incidence of thyroiditis, thyrotoxicosis, goiter and thyroid cancer. Result: Of the general cohort, 6,342 statin users and 6,342 non-users were matched using propensity scoring. There was no significant difference in the baseline characteristics between the two groups. There was a slight statistical significance in thyroid cancer in this study with OR 0.62 CI 0.39-0.996 P 0.048. This did not remain statistically significant when excluding participants with previous diagnosis of thyroid cancer. However, there was decreased incidence of thyrotoxicosis in statin users OR 0.71 CI 0.51-0.99 P 0.04.

Conclusion: Long-term statin use may be associated with decrease in thyroid cancer owing it to its antiproliferative properties previously describes. Statins may also be associated with decreased incidence of thyrotoxicosis.

Presentation #24

Title: Prevalence and usage patterns of opiates in lung, breast, and head and neck cancer patients

Presenter: Kyle Westbrook

Authors: Kyle Westbrook, MD; Ang Gao, Jingyuan Gu, Alejandra Madrigales, MS, CTR; Pamela Kurian MS; Chul Ahn, PhD; Saad Khan, MD

Faculty Mentor: Saad Khan

Abstract

Background: Prescription opiate abuse is a declared public health emergency that was involved in 17,536 deaths in 2015. We don't know how many cancer patients died from prescription opiates and there is little published data about their prescribing patterns.

Methods: Using the UTSW tumor registry, we analyzed all prescriptions for 6424 lung/breast/head and neck cancer patients undergoing therapy including radiation from 2009-2016. We analyzed patient demographics, cancer information, treatment modality, concurrent medicines, substance abuse history and survival. Chi-square tests were used to investigate if higher rates of opiate use were seen in those who receive chemotherapy, actively smoke or use alcohol, have head and neck cancer.

Results: Opiate use was highly prevalent in cancer patients with 2902/4307 (67%) of women and 1597/2112 (76%) of men requiring opiates. Hydrocodone was the most common opiate at (out of 6424 total) 67%, followed by morphine 12%, fentanyl 9%, oxycodone 7% and hydromorphone 6%. Patients diagnosed at University were prescribed opiates 2086/3501 (60%) compared to Parkland 369/857 (43%), other hospitals 954/2066 (46%). Gabapentin was prescribed to 18.7% women and 15.9% men; 494/6424 (8%) patients had 3 or more different opiates prescribed; those who were given gabapentin had a higher rate of 3 or more opiates 249/1241 (20%). Those with current alcohol use required opiates 2001/2643 (76%) compared to those with no alcohol use 2101/3145 (67%) ($p<0.0001$); while active smokers used opiates 1033/1366 (76%) compared to never smokers 1859/2815 (66%) ($p<0.0001$). Head and neck patients at 1529/1982 (77%) had higher opiate use than those with breast 1913/2932 (65%) or lung cancer 1061/1510 (70%) ($p<0.0001$). Patients receiving chemotherapy with their radiation required opiates 696/850 (82%) compared to those who got no chemotherapy 3807/5574 (68%) ($p<0.0001$). In patients with a radiation course lasting >4 weeks, 8.8% received opiates 12 months after completion of their therapy.

Conclusions: More than 70% of cancer patients use opiates after radiation; significantly higher rates of opiate use are seen in those who receive chemotherapy, actively smoke, use alcohol, or have head and neck cancer. Patients treated with radiation for >4weeks have high rates of opiate use a year after treatment completion.

Presentation #25

Title: Validation of the pooled cohort equations in Hispanics: insights from Multi-Ethnic Study of Atherosclerosis and Dallas Heart Study

Presenter: Karen Flores Rosario

Authors: Karen Flores Rosario, MD; Anurag Mehta, MD; Pedro Engel Gonzalez, MD; Rohan Khera, MD; Carlos Rodriguez, MD; Michael Blaha, MD; Khurram Nasir, MD; Roger Blumenthal, MD; Amit Khera, MD; Colby Ayers, MS; Ambarish Pandey, MD; Robert Kaplan, PhD; Parag Joshi, MD

Faculty Mentor: Parag Joshi

Abstract

Background: Atherosclerotic cardiovascular disease (ASCVD) is the most common cause of death among Hispanics in the US. Hispanics have a higher prevalence of several ASCVD risk factors than other ethnicities, but there is no Hispanic-specific ASCVD risk assessment tool. The aim of this study is to evaluate the performance of the 2013 ACC/AHA pooled cohort equations (PCE) for ASCVD risk assessment among Hispanic participants from two contemporary, US population-based, multiethnic cardiovascular cohorts.

Methods: Participants from the Dallas Heart Study (DHS) and the Multi Ethnic Study of Atherosclerosis (MESA), aged 40-75 years were stratified by self-reported race into Non-Hispanic Whites, Non-Hispanic Blacks, and Hispanics. The predicted number of events was calculated based on the mean predicted ASCVD incidence by the PCE and was compared with the observed number of ASCVD events at 10 years. Risk calibration was examined by comparing predicted to observed ratios of 10-year ASCVD risk with Chi-square analysis and risk discrimination was assessed via the c-statistics. PCE performance analyses were performed for the three racial groups.

Results: There were 4,914 participants including 2163 NH-Whites (mean 55.5 years; 53% F), 1681 NH-Blacks (56.5 years; 58% F), and 1070 Hispanics (56.6 years; 53% F). During a 10-year period there were 295 observed ASCVD events in the three groups. The predicted to observed ratio (P/O ratio) of 10-year ASCVD was 1.43 in NH-whites, 1.44 in NH-Blacks, 1.41 in Hispanics using NH-White equation, and 1.49 in Hispanics using NH-Black equation. Chi-square was greater than 20 and $p<0.05$ in all groups, indicating poor risk calibration. The c-statistic of the NH-White PCE applied to Hispanics was 0.74 (CI 0.68-0.80) and 0.75 (CI 0.71-0.79) when applied to Whites. The c-statistic of the NH-Black PCE applied to Hispanics was 0.75 (CI 0.70-0.80) and 0.69 (CI 0.65-0.74) when applied to NH-Blacks. Both NH-White and NH-Black PCE equations over-predict ASCVD risk across all levels of predicted risk among Hispanics.

Conclusion: Both the Black and White PCEs systematically and similarly over-predict ASCVD risk in Hispanic participants of DHS and MESA. A Hispanic-specific ASCVD risk equation will be needed to accurately estimate cardiovascular risk in this racial group.

Presentation #26

Title: Concurrent diagnoses of West Nile encephalitis and Cryptococcal neoformans meningitis in an immunocompromised patient.

Presenter: Brandon Robert Jakubowski

Authors: Brandon Jakubowski, MD

Faculty Mentor: Rosechelle Ruggiero

Abstract

Case Presentation: A 57 year-old man with poorly-controlled AIDS (CD4 of 20, non-adherent to HAART) presented with a subacute progressively worsening headache. On initial presentation, he was without nuchal rigidity and soon thereafter underwent a lumbar puncture that demonstrated a lymphocytic pleocytosis as well as an opening pressure of 14 cm H2O. Cryptococcal antigen sent from the cerebrospinal fluid was positive with a titer of 1:256 and he was started on Amphotericin B and Flucytosine. Ten days after starting treatment for cryptococcal meningitis, he became subacutely confused. Exam at that time was notable for akathisia and an inability to follow simple commands. He underwent a repeat lumbar puncture with an opening pressure of 15 cm H2O. MRA of the brain showed development of 3 foci of acute infarction in the left superior frontal gyrus as well as two involving the midbrain. At this time, a West Nile IgM serology sent from the cerebrospinal fluid had returned positive; IgG antibodies sent from the same sample were negative.

Discussion: The clinical presentation of neuroinvasive West Nile (WNV) can be extremely varied, from the typical presentation of meningitis to flaccid paralysis or even Parkinsonian-like features. Given the non-specific clinical findings associated with WNV, imaging and laboratory testing is key in establishing a diagnosis. MRI imaging can demonstrate signal abnormalities on diffusion weighted imaging and hyperintensities on T2 imaging of the basal ganglia, thalami, caudate nuclei, brainstem and spinal cord. A positive IgM antibody to WNV from the CSF is considered a probable case of WNV encephalitis per the current CDC guidelines. Confirmatory testing can be performed by obtaining virus-specific antibody titers using plaque reduction neutralization testing or polymerase chain reduction testing specific to WNV, though ultimately confirmation of disease does not change a patient's treatment course. Here we present a patient with poorly-controlled AIDS admitted for primary treatment of cryptococcal meningitis who was later found to have markers of acute infection with the WNV, a case that emphasizes that clinical suspicion for atypical infections should be heightened when an immunocompromised host is involved.

Presentation #27

Title: Severe Symptomatic Hypocalcemia Following a Single Injection of Denosumab in a Patient with Chronic Kidney Disease

Presenter: Jake Cameron Hutto

Authors: Jake Cameron Hutto, MD

Faculty Mentor: Biff Palmer

Abstract

Case Presentation: A 42-year-old man with past medical history of chronic tophaceous gout, secondary adrenal insufficiency from chronic steroid use, osteoporosis, and chronic kidney disease who presented to the emergency department with two weeks of bilateral leg spasticity, generalized weakness, and a two-day history of peri-oral tingling. He had never experienced these symptoms before and denied any recent changes in diet or medications. On further evaluation and chart review, it was discovered he received denosumab 60mg (a RANK-ligand inhibitor) for osteoporosis twenty days prior to presentation. On presentation, he was afebrile and noted to be in sinus tachycardia with a heart rate of 130 bpm. Physical exam was notable for non-tender tophi of the hands and feet, involuntary leg jerking bilaterally, and a positive Chvostek's sign. Labs were significant for a Cr of 1.61 (baseline), total calcium level of 5.5, ionized calcium of 4.2 (with normal calcium levels noted two months prior to presentation), and albumin of 4.3. Further studies revealed intact PTH was elevated to 676.4 (previously 193.2 two months prior), 25-OH Vit D was 19.4 (grossly unchanged from prior values). Given his multiple risk factors for hypocalcemia, his acute symptomatic hypocalcemia was believed to be secondary to his recent denosumab injection. Calcium was repleted heavily with IV and oral calcium, and he was started on twice daily calcitriol (1,25-OH vitamin D). Within one day, his symptoms completely resolved.

Discussion: Denosumab is a monoclonal antibody used for treatment of osteoporosis and bone metastases in solid tumors and myeloma by binding to and preventing RANK-ligand from activating osteoclasts. There is a risk of severe, symptomatic hypocalcemia associated with the first administration of denosumab with multiple case reports noted in the literature, particularly in patients with impaired renal function already at risk of hypocalcemia. Labs typically show elevated PTH, low total and ionized calcium, and variable phosphorus levels. It is crucial to review any medication changes, check levels of vitamin D and calcium prior to treatment, and to supplement vitamin D and calcium during treatment to lessen this risk. Calcitriol is recommended for treatment if hypocalcemia does occur.

Presentation #28

Title: Reducing Inappropriate Rasburicase Use to Promote Cost-effective Care

Presenter: Komal Patel

Authors: Komal Patel, MD; Arjun Gupta, MD; Eileen Marley, PharmD, BCOP; Hsiao Li, MD; Navid Sadeghi, MD

Faculty Mentor: Dr. Navid Sadeghi

<u>**Abstract**</u>

Background: Rasburicase is the preferred treatment of hyperuricemia in patients (pts) with tumor lysis syndrome (TLS) and those at high-risk for TLS. However, its overuse commonly leads to increased cost of care.

Methods: We reviewed the process of ordering rasburicase and its prescription patterns at our safety net hospital between October 2015-September 2017. We reviewed pertinent labs and clinical documentation to determine appropriate vs. inappropriate use based on internally approved indications (laboratory TLS, intermediate- or high-risk for TLS, acute kidney injury and hyperuricemia). Quality improvement interventions were implemented to improve ordering patterns.

Results: Sixty-five pts received ≥1 rasburicase dose during the study period. Rasburicase was deemed inappropriate in 21 patients (32.3%). Ordering providers included oncologists (23 pts, 35%), hospitalists (16 pts, 25%), intensivists (11 pts, 17%), emergency medicine (8 pts, 12%), and other (7 pts, 11%). A high percentage of hospitalists and emergency medicine orders were inappropriate, at 50% and 25% respectively. Ordering process review identified several pitfalls. Providers were not required to review the approved indications listed in the electronic order. Any provider could order rasburicase and a secondary review by pharmacy was not required prior to administration. Thus, we proposed a best practice advisory alert requiring providers to select an indication from the approved list in the electronic order and limited ordering to oncologists. Other providers required approval from oncology. A mandatory secondary review by pharmacy prior to dispensing the medication was implemented.

Conclusions: All providers are responsible for cost of care reduction, and critical appraisal of medical interventions can lead to significant cost saving nationally. A third of rasburicase orders were inappropriate at our hospital, leading to unnecessary costs. Simple electronic medical record interventions have been implemented to improve ordering patterns. The impact of these interventions will be assessed periodically to improve rasburicase utilization.

Presentation #29

Title: Performance of a genetic risk score for coronary artery disease in a multi-ethnic cohort

Presenter: Ezimamaka Ajufo

Authors: Ezimamaka Ajufo, BM BCh; Colby Ayers, MS; Julia Kozlitina, PhD; Amit Khera, MD, MSc

Faculty Mentor: Amit Khera

Abstract

Background: The addition of polygenic risk scores (GRS) to conventional risk factor models has been shown to improve coronary artery disease (CAD) risk prediction. However, variants used in these scores come from studies of predominantly Caucasian cohorts. There is conflicting data on the utility of GRS in multi-ethnic cohorts. We sought to examine the utility of a contemporary GRS for CAD risk prediction in a US multi-ethnic cohort.

Methods: We identified eligible subjects in the Dallas Heart Study I (DHS-I) population followed from 2000 to 2012. Our GRS comprised 52 genetic variants associated with CAD at genome-wide significance level Participant scores were calculated by adding the number of risk alleles carried at each locus multiplied by published effect sizes. The study primary outcome measure was a composite of non-fatal myocardial infarction, CAD death, coronary artery bypass grafting and percutaneous coronary intervention. Cox proportional hazards regression models adjusted for conventional cardiovascular risk factors were used to test the association between GRS and the primary outcome.

Results: The study cohort comprised 3030 DHS I participants including 973 Caucasians (EA, 32%),1587 African Americans (AA, 52%) and 470 Hispanics (HA, 16%). Mean GRS was lower in AA compared to EA and HP (AA vs EA, 3.30 vs 3.61, $p<0.0001$; AA vs HP, 3.30 vs 3.65; $p<0.0001$). However, there were more CAD events amongst AA compared to EA and HP (AA vs EA, 10% vs 4.6%, $p<0.0001$; AA vs HP, 10% vs 3.4%, $p<0.0001$) over a median follow-up of 11.3 years. In the overall cohort, GRS was not associated with CAD (adjusted HR 1.13, 95% CI 0.97-1.33; $p=0.1$). However, in subgroup analyses, there was a positive association with CAD amongst EA (adjusted HR 1.42, 95% CI 1.07-1.89, $p=0.0149$) but not AA (adjusted HR 1.04, 95% CI 0.89-1.22; $p=0.2$) or HP (adjusted HR 0.92, 95% CI 0.57-1.483; $p=0.7$).

Conclusions: We show that a contemporary GRS was not associated with CAD in a multi-ethnic US cohort. Importantly, the score showed a positive correlation with CAD amongst Caucasians in this population, but not African American or Hispanics. Further studies are needed to refine GRS for race/ethnic specific groups.

Presentation #30

Title: Practice Patterns and Impact of Post-chemotherapy Retroperitoneal Lymph Node Dissection (PC-RPLND) on Testicular Cancer Outcomes

Presenter: Joseph Moore

Authors: Solomon L. Woldu, MD; Joseph A. Moore, MD; Bo Ci, Yuval Freifeld, MD; Timothy N. Clinton, MD; Ahmet A. Murat, MD; Nirmish Singla, MD; Laura-Maria Krabbe, MD; Ryan C. Hutchinson, MD; James F Amatruda, MD, PhD; Arthur Sagalowsky, MD; Yair Lotan, MD; Yull Arriaga, MD; Vitaly Margulis, MD; Yang Xie, PhD; Aditya Bagrodia, MD

Faculty Mentor: Aditya Bagrodia

<u>**Abstract**</u>

Background: There is wide practice pattern variation due to surgical complexity and controversy surrounding indications for post-chemotherapy retroperitoneal lymph node dissection (PC-RPLND). We utilize the National Cancer Database (NCDB) to identify factors associated with omission of PC-RPLND and the impact on survival outcomes in patients with advanced nonseminomatous germ cell tumors (NSGCT).

Methods: We queried the NCDB for men with Stage II/III NSGCT from 2004-2014 (n=5,062). Patients were compared based on receipt or omission of PC-RPLND, with primary outcome of interest being impact on overall survival (OS). Kaplan-Meier analysis, log-rank testing, logistic regression, Cox regression, and propensity-score matching (PSM) were conducted.

Results: Patients who underwent PC-RPLND were more likely to be younger, white, privately insured, and come from more highly educated/wealthier regions (p<0.001). Patient insurance status was independently predictive of receipt of PC-RPLND; compared to patients with private insurance, those without insurance (OR 0.49, p<0.001) were significantly less likely to receive PC-RPLND. After multivariate adjustment, age, comorbidity status, non-private insurance, distance from hospital, clinical stage, and IGCCCG risk grouping were independent predictors of all-cause mortality. Additionally, the omission of PC-RPLND remained a significant predictor of all-cause mortality (HR 1.98, p<0.001). After PSM, median 5-year OS was significantly lower in those who did not undergo PC-RPLND (72% vs. 77%, p=0.007).

Conclusions: PC-RPLND represents a critical part of the multidisciplinary management of advanced NSGCT. Our results suggest poorer outcomes for those patients who do not undergo PC-RPLND. Further studies to identify and modify these underlying factors may benefit patients with testicular cancer.

Presentation #31

Title: Radiation Recall Dermatitis in a Metastatic Renal Cell Carcinoma Patient Treated with Nivolumab with Xenograft PD-L1 Expression Correlates

Presenter: Joseph Vento

Authors: Joseph Vento, MD; Isaac Bowman, MD; Payal Kapur, MD; Raquibul Hannan, MD, PhD; Xiankai Sun, PhD; James Brugarolas, MD, PhD

Faculty Mentor: Isaac Bowman

Abstract

Case Report: A 49 year old man presented with chest wall pain and weight loss, leading to the diagnosis of metastatic renal cell carcinoma (mRCC) with disease in the right kidney, left ribs, liver, and bilateral lungs. Following radical nephrectomy, partial hepatectomy, and stereotactic ablative radiotherapy (SABR) to his rib and lung metastases, he began systemic therapy. Unfortunately, his disease progressed after two courses of high dose interleukin-2 (HD-IL2) and again after targeted therapy with pazopanib for three months, and thus he began treatment with the immunologic checkpoint inhibitor nivolumab. Two weeks after his first nivolumab infusion, he developed a severe cutaneous reaction at sites of prior radiation, primarily his rib, requiring hospital admission. Synthesizing his treatment history and laboratory data, he was diagnosed with radiation recall dermatitis and managed with careful observation and pain control with gradual improvement of his reaction sites. After resolution, he resumed nivolumab without recurrence of reaction and with a remarkably favorable tumor response.

Discussion: As the use of immune checkpoint inhibitors continues to expand, management of complex immune related adverse reactions (iRAEs) and prediction of tumor response remain important challenges. Here we present a metastatic renal cell carcinoma (mRCC) patient treated with nivolumab, an antibody to the immune checkpoint protein programmed death 1 (PD-1) as third-line systemic therapy. Not only did he develop the rare reaction of radiation recall dermatitis but also responded remarkably well to checkpoint inhibitor therapy. His inclusion in a murine patient derived xenograft (PDX) model in the Kidney Cancer Program laboratory permits presentation and discussion of his tumor's programmed death ligand 1 (PD-L1) expression by immunohistochemistry as well as an investigational 89Zr-DFO-atezolizumab (anti-PD-L1) immuno-PET scan. We use this case to characterize radiation recall dermatitis in the setting of immune checkpoint blockade and speculate correlations of our investigational PD-L1 expression modalities to his treatment course.

Presentation #32

Title: Role of MLF1 in Cardiomyocyte Cell Cycle Regulation

Presenter: Jainy Savla

Authors: Jainy Savla, MD; Feng Xiao, PhD; Alisson Campos Cardoso, PhD; Ana Macedo Pereira, PhD; Shalini Muralidhar, PhD; Diana Conseco, PhD; Hesham Sadek, MD, PhD

Faculty Mentor: Hesham Sadek

<u>**Abstract**</u>

Background: The neonatal mammalian heart is capable of significant regeneration after cardiac injury. However, that ability is lost in the early postnatal period, coinciding with the development of cardiomyocyte cell cycle arrest. Myeloid leukemia factor 1 (MLF1) is a protein expressed in hematopoietic cells, skeletal muscle and cardiac muscle. In hematopoietic cells, MLF1 may act as a negative cell cycle regulator, but its role in the cardiovascular system is not well understood. Here, we investigate the role of MLF1 in cardiomyocyte cell cycle regulation.

Methods: Using wild-type C57BL/6 mice, we examined the expression of MLF1 in hearts from postnatal day 1 (P1) and postnatal day 7 (P7). Using siRNA knockdown of MLF1 in neonatal rat ventricular cardiomyocytes (NRVMs), we determined the effect of MLF1 deletion by immunostaining for a mitosis marker. We generated a cardiac-specific inducible knockout mouse model of MLF1 and assessed for the prolongation of the proliferative window by echocardiography, cell size analysis, and immunostaining for cell cycle markers. We evaluated for evidence of cell cycle reentry using similar methods in a mouse model with cardiac-specific temporally controlled deletion of MLF1. Finally, to evaluate the mechanism of action of MLF1, we performed co-immunoprecipitation of MLF1 in a wild-type C57BL/6 heart at P7.

Results: In wildtype C57BL/6 mice, MLF1 expression increases from P1 to P7 and is prominent in the nucleus at P7. In vitro siRNA knockdown of MLF1 in NRVMs results in increased cell cycle entry. In the cardiac-specific inducible knockout model of MLF1, deletion of MLF1 from birth results in increased cell cycle entry as demonstrated by immunostaining for a mitosis marker and a cytokinesis maker in adult mice. Tamoxifen-induced, cardiac-specific deletion of MLF1 in the adult mouse also results in increased evidence of cell cycle reentry. Through co-immunoprecipitation, we determined that MLF1 interacts with 3 critical members of the Skp1-Rbx1-Cul1-F box (SCF) protein complex E3 ubiquitin ligase. The SCF complex has high specificity for ubiquitination of substrates involved in cell cycle regulation.

Conclusions: MLF1 is a negative cell cycle regulator of cardiomyocyte proliferation and may act as a component of the SCF E3 ubiquitin ligase complex.

Presentation #33

Title: Systematic Review of Patient Decision Aids for Chronic Musculoskeletal Pain

Presenter: Emily Bowen

Authors: Emily Bowen, MD; Rabih Nayfe, MD; Nathaniel Milburn, MD; Helen Mayo, MLS; Ethan Halm, MD; Una Makris, MD

Faculty Mentor: Una Makris

<u>**Abstract**</u>

Background: Chronic musculoskeletal pain is a prevalent, disabling, and costly condition. Most treatment decisions for chronic musculoskeletal pain are preference-sensitive, as there are multiple reasonable and evidence-based approaches to treatment. Patient decision aids are tools designed to help patients participate in their healthcare decisions and have been shown to improve decision quality. We performed a systematic review evaluating the use of patient decision aids for adults making treatment decisions for chronic musculoskeletal pain.

Methods: We searched Ovid MEDLINE, Ovid MEDLINE In-Process and EPub Ahead of Print, Ovid Embase, Ovid PsycINFO, EBSCO CINAHL, the Cochrane CENTRAL database, clinicaltrials.gov, and the International Clinical Trials Registry Platform from inception through March 2017 for randomized controlled trials of adults using patient decision aids to make treatment decisions for chronic musculoskeletal pain in the outpatient setting.

Results: Out of 342 records screened, twelve studies met the inclusion criteria. Musculoskeletal conditions evaluated were osteoarthritis of the hip or knee and back pain. Eleven of the twelve studies evaluated the use of a video patient decision aid for patients deciding between surgical and non-surgical management. One study evaluated a paper decision aid to help patients choose among physiotherapy treatments for chronic lower back pain. Six of seven studies found an improvement in patient knowledge with use of a patient decision aid. Two of five studies found a decrease in decisional conflict with use of a patient decision aid. Seven of eight studies found no difference in surgery rates with use of a patient decision aid. Only one study looked at pain and function outcomes and did not find an improvement with use of a patient decision aid.

Conclusions: Patient decision aids may improve the decision making process and decision quality for patients deciding between surgical and medical management of hip or knee osteoarthritis and chronic back pain. Additional research is needed to evaluate the effect of patient decision aids on pain and function. Especially for older adults with multimorbidity and polypharmacy, who are often not surgical candidates, further research should develop patient decision aids for non-surgical treatment of chronic musculoskeletal pain.

Presentation #34

Title: Solid Organ Transplantation and Data Mining: Risk Factors for Invasive Fungal Disease in Heart Transplant Recipients

Presenter: Nicolas Barros Baertl

Authors: Nicolas Barros, D Xie, Christina Yek, MD; T Liu, X Li, B Adams-Huet, MS; J J Martinez, Sonia Garg, MD; Justin L. Grodin, MD; R Morelend, Alpesh Amin, MD; F Aras, J Thibodeau, Pradeep Mammen, MD; Matthias Peltz, MD; Mark H. Drazner, MD; W S Ring, Robert W. Haley, MD; Ricardo M La Hoz, MD

Faculty Mentor: Ricardo La Hoz

<u>Abstract</u>

Background: We created a database of solid organ transplant (SOT) recipients using innovative data mining tools. This study describing the epidemiology of invasive fungal disease (IFD) in heart transplant (HT) recipients serves as a proof of concept of such techniques in clinical research.

Methods: This is a retrospective single center cohort study. Data mining tools were used to extract data from the electronic medical record and merged it with information from the scientific registry of transplant recipients (SRTR). Recipients of their first HT from 2010-2016 were included. Medical records of subjects with positive cultures, fungal serologies, histopathology and autopsies were manually adjudicated using MSG/EOCRT criteria. The source of the infection was adjudicated using CDC/NHSN and MSG/EORTC Criteria. The 1-year cumulative incidence was calculated using the Kaplan-Meier method. Cox proportional hazards models were used to identify risk factors for IFD and 1-year mortality. CMV was defined using the CMV Drug Development Forum definition, acute cellular and antibody mediated rejection and primary graft dysfunction were defined using ISHLT criteria, while delayed chest closure and re-operation were defined using STS criteria. IFD was analyzed as a time-dependent covariate in the mortality model.

Results: 204 HT recipients met inclusion criteria, 19 developed an IFD. The cumulative incidence was 9.5% at 1 year, and median time to onset 52 days (7-344). The most common pathogens were: Aspergillus sp. (31.6%), Candida sp. (31.6%), H. capsulatum (10.6%), Mucormycosis (10.6%). The most common sources of IFD were: lower respiratory tract infection (36.8%), surgical site infection (21.1%), disseminated disease (15.8%), and central line associated bloodstream infection (10.5%). In multivariable analysis, the risk of 1-year mortality was associated with post-transplant ECMO (HR: 11.9 [2.0-71.6]), and post-transplant RRT (HR: 13.6 [2.3-80.4]). The 12-week mortality was 37% (7/19) and 64% (7/11) after the first IFD and invasive mold infection, respectively. In multivariable analysis, the risk of 1-year mortality was associated with IFD (p=0.0003, HR: 9.0).

Conclusions: Post-transplant ECMO, and RRT were associated with an increased risk of acquisition of an IFD in HT. Furthermore, this study illustrates the potential of data mining tools to study infectious complications in solid organ transplant recipients.

Presentation #35

Title: Supporting Overcoming Booze by Enhancing Recovery with Medications (SOBERMax) - A resident-led initiative to increase naltrexone-assisted treatment for alcohol use disorders

Presenter: Kaivalya Deshpande

Authors: Nimish N. Shah, MD; Stephanie Chiao, MD; Neil Keshvani, MD; Kaivalya Deshpande, MD; Rohini Downs, PharmD; Anil Makam, MD;

Faculty Mentor: Anil Makam

Abstract

Background: Alcohol use disorder (AUD) is highly prevalent among hospitalized adults, especially among low-income minority populations, and causes significant morbidity and mortality. However, fewer than 10% receive treatment despite the availability of safe and effective pharmacotherapy. We are conducting a multifaceted quality improvement (QI) project aiming to increase the use of naltrexone, an evidence-based, medication-assisted treatment (MAT) of AUD, among inpatient medicine teaching services at Parkland Hospital.

Methods: We developed our intervention with a series of plan-do-study-act (PDSA) cycles. Initially, we (1) estimated the prevalence of AUD by reviewing the medical records of 95 consecutively hospitalized adults; (2) surveyed resident physicians' attitudes and practice patterns for treating AUD (n=203; response rate 28%); and (3) conducted stakeholder engagement with social workers, pharmacists, and peer recovery navigators. Guided by these findings, our intervention thus far includes: (1) resident physician education consisting of one 10-minute interactive didactic session, a 1-hour journal club on the effectiveness of naltrexone, and brief updates to on-service residents via visual aids and e-mail reminders; (2) development of an algorithm to evaluate patients for naltrexone, prescribe naltrexone, and establish appropriate psychotherapeutic and medical follow-up post-discharge; and (3) a redesigned patient information sheet for community AUD treatment programs and support groups. We preliminarily evaluated our intervention at the population level using a before-and-after design to assess whether the number of naltrexone prescriptions increased during each resident service time block between November 2017 and March 2018.

Results: The prevalence of AUD was 15%. Prior to the intervention, residents expressed low confidence in treating AUD (mean score 2.09 on 5-point Likert scale), a lack of experience with AUD pharmacotherapies (77%), and uncertainty about arranging follow-up. The average number of naltrexone prescriptions increased from 5.2 prescriptions per 30 days to 11 prescriptions per 30 days, a 111% increase from pre- to post-intervention. Conclusion Implementing a multifaceted intervention increased naltrexone prescriptions among internal medicine residents while revealing new opportunities for supportive stakeholder roles. Next steps include EHR orderset development, further evaluating naltrexone prescribing using process improvement methodology, and continuing iterative improvement to AUD MAT using PDSA cycles.

Presentation #36

Title: Determinants of a Safe Insulin Dose at the Time of Hospital Discharge

Presenter: Mehwish Ismaily

Authors: David Carruthers, MD; Mehwish Ismaily, MD; Anna Vanderheiden, MD; Mariana Yates, MD; Amy DeGueme, MD; Beverley Adams-Huet, MS; Samata Basani, MD; Marconi Abreu, MD; Ildiko Lingvay, MD

Faculty Mentor: Ildiko Lingvay

Abstract

Background: Focus should be placed on the hospital discharge period as discharge insulin regimens can influence hospital re-admissions and outpatient complications. Method: Using a retrospective cross-sectional analysis, 797 electronic medical records were reviewed of patients discharged with insulin from Parkland between January 1st, 2010 and December 31st, 2012. Baseline patient characteristics were collected including demographics, diabetes type and duration, admission hemoglobin A1c, and discharge insulin type and dose. Insulin total daily dose (TDD), hemoglobin A1c, and interim emergency room visits were collected at the follow-up visit.

Results: The median time to post-discharge follow up was 33 days. Patients were grouped by changes in TDD from discharge to follow-up with a clinically meaningful change as more than 5%. Data analysis showed 60% of the patients required an insulin dose adjustment with 47% of the patients requiring a dose decrease. Admission TDD ($p=1.0$), hemoglobin A1c ($p=0.31$), and principal diagnosis ($p=0.33$) were not statistically different. Admission BMI was statistically higher in patients requiring a follow-up dose decrease ($p=0.003$). The group requiring an insulin dose decrease had the most patients with ketosis-prone diabetes, and was more likely to be prescribed metformin at the time of discharge ($p=0.003$). Diabetes-related emergency room visits or readmissions were similar between groups with 110 (13.8%) patients with events in the total cohort. We also divided the cohort by whether diabetes was newly diagnosed on admission, previously diagnosed but insulin-naïve, and previously diagnosed and treated with insulin. The largest decrease in hemoglobin A1c between admission and follow-up was noted in the newly diagnosed group, with a decrease from 12.6% to 7.03%. Patients with prior insulin use had the longest duration of diabetes, were less likely to need a dose adjustment post-discharge, but were the most likely to have a diabetes-related ER visit or readmission (22.8%). The linear regression model showed the most significant predictors of a decrease insulin requirement post hospital discharge are: newly diagnosed diabetes, ketosis-prone diabetes, metformin prescription, and hemoglobin A1c<10%.

Conclusion: At the time of discharge, there should be consideration of an insulin dose reduction particularly for patients with newly diagnosed diabetes and ketosis-prone diabetes.

Presentation #37

Title: Assessment of American College of Rheumatology Endorsed Quality Indicators in Rheumatoid Arthritis Patients Seen in an Academic Setting.

Presenter: Luigino Bernabela

Authors: Luigino Bernabela MD; Lucas Bernal-Pineda MD; Pheba Sunny

Faculty Mentor: Puneet Bajaj

<u>**Abstract**</u>

Introduction: The American College of Rheumatology (ACR) has endorsed a set of meaningful quality measures for use in rheumatoid arthritis (RA). We focused on two validated RA assessment instruments; Routine Assessment of Patient Index Data (RAPID3) and Clinical Disease Activity Index (CDAI). ACR national registry encourages providers to document either of these in at least 50% of patient visits in a 12-month period. Rapid3 and CDAI flowsheets, introduced in our Electronic Medical Records system (EMR) in 2014, are rarely utilized with low compliance rate (~10%). We aim to improve compliance rates to 30% with a stretch goal of 50%.

Methods: A retrospective chart review was performed using the RA ICD-9 diagnosis grouper from December 2016 to January 2018. RA patients seen by fellows, resident, or physician assistant were included. Patients without definite diagnosis of RA were excluded. Charts were further reviewed to determine whether these instruments were completed for at least 50% of the visits in a 12-month period. The team is utilizing Plan-Do-Study-Act (PDSA) cycle for process improvement, clinic work flow standardization, and better EMR documentation practices. One of those interventions included collaborating with the rheumatology clinic nursing manager in November of 2017 to re-enforce completion of RAPID3 on all RA patients.

Results: 2637 patient charts were included in the project. The average RAPID3/CDAI compliance was about 10 and 9% respectively. Fellows completed ~71% of RAPID3/CDAI. Of about 1/3 of patients who didn't have either RAPID3/CDAI completed in at least 50% of visits within 12 months, 82% of them were on the resident or nurse practitioner panels. Our intervention to the nursing staff has resulted in a trend towards improvement of RAPID3 completion and documentation.

Conclusion: These findings confirm the underutilization of functional assessment and disease activity score tools in our academic rheumatology practice. Residents and the nurse practitioner rarely use any of these instruments. These quality indicators were more often utilized by rheumatology fellows but even in this group there's great room for improvement. Future interventions will aim at educating and motivating providers to compete CDAI. This will require a collaborative effort by the clinic staff and providers.

Presentation #38

Title: Promoting High-Value Change By Addressing the Structure of Order Sets: Lessons from the Cardiac Catherization Lab

Presenter: Nagendra Pokala

Authors: Nagendra Pokala, MD; Arjun Gupta, MD; Julia Tran, Ambarish Pandey, MD; Sandeep Das, MD

Faculty Mentor: Sandeep Das

Abstract

Background: Order sets in electronic medical records can promote efficiency and reduce variability in patient care, but can also influence ordering practices. At our institution, a single order set was used for both right (RHC) and left heart catheterization (LHC). It included opt-out prescriptions for IV normal saline, intended to reduce risk of contrast-induced nephropathy (CIN), as well as oral opioids (hydrocodone) for procedure-related pain. Recent data suggest that prophylactic hydration in LHC does not prevent CIN, while prophylactic hydration is always unnecessary and may be harmful in RHC. Additionally, procedure-related pain is usually mild. We hypothesized that the presence of 'opt out' saline and opioid orders would lead to overuse. Methods and

Results: This quality improvement study aimed to minimize unintentional harm and waste - use of unnecessary IV fluids and opioids - for patients undergoing RHC and LHC. Medical records of patients undergoing RHC and LHC at our institution were reviewed from October- December 2017. Of 58 and 221 patients undergoing RHC and LHC respectively, 6.9% received IVF with RHC and 35.6% received IVF with LHC. Hydrocodone was prescribed to 1.7% of patients undergoing RHC, and 1.0% of patients undergoing LHC. Based on these results, we removed IVF and opioids completely from the order set in January 2018. End users were involved in making changes, and changes were communicated to all staff who used the order set.

Conclusions: Over a 3-month period at our hospital, 1 in 3 patients undergoing LHC and 1 in 14 patients undergoing RHC received unnecessary IVF. Opioid prescription rates were low but still present. We will evaluate the changes in IVF/ opioid prescription patterns in the next few months post the order set changes.

Presentation #39

Title: The Great Imitator

Presenter: Nagendra Pokala

Authors: Nagendra Pokala, MD; Melanie Holtrop,MD; Madison Argo, Shan Luong, MD

Faculty Mentor: Shan Luong

<u>**Abstract**</u>

Case Presentation: A 58 year-old woman presented with four months of nightly fevers and worsening back pain. The 'stabbing' lower back pain was constant, but worse with bending down. It was not associated with bowel or bladder incontinence, numbness or tingling, or focal weakness. The patient was visiting Mexico when the symptoms started. In Mexico, she ate local cheese products and drank unpasteurized milk. Since her trip, she had noticed an unintentional twenty-five pound weight loss. She denied any family history of malignancy. She did not use intravenous drugs. She was febrile to 38oC. She was tender to palpation in the lumbosacral region with negative straight leg raise. There was no palpable lymphadenopathy. C-reactive protein was elevated at 10.9 and erythrocyte sedimentation rate was elevated at 33. T-spot was negative. There were abnormally enhancing lesions in the T4-T5 region on MRI spine. The T4 region was biopsied and there were no malignant cells on pathology. Brucella antibody titer was 1:160 and Brucella melitensis grew on two sets of blood cultures.

Discussion: Brucellosis, although rare in the United States, is one of the most common zoonotic infections worldwide, including Mexico, South and Central America. It is usually contracted via consumption of unpasteurized milk and cheese. Symptoms of brucellosis can vary widely, including fevers, weight loss, arthralgias and myalgias, osteoarticular involvement, as well as cardiac involvement. Osteoarticular involvement is the most common complication and occurs in 40% of cases. Brucella osteomyelitis requires a prolonged oral antibiotic course, usually of doxycycline plus rifampin or streptomycin, for 3 months. The differential diagnosis for our patient with progressively worsening back pain, fevers, and weight loss varied widely, including multiple myeloma, metastases, primary bone tumor, tuberculosis, other bacterial osteomyelitis. Obtaining a detailed history was crucial in the diagnosis of brucellosis. Per IDSA guidelines, in a patient found with osteomyelitis and with appropriate risk factors such as pertinent travel history and ingestion of unpasteurized dairy products, blood cultures and serologies to evaluate for Brucella infection should be obtained.

Presentation #40

Title: Usefulness of Blood Pressure Variability markers derived from Ambulatory Blood Pressure Monitoring in detecting Autonomic Failure.

Presenter: Kevin Schesing

Authors: Hamza Lodhi, MD; Poghni Peri-Okonny, MD; Kevin Schesing, MD; Kamal Phelps, Christian Ngo, MD; Hillary Evans, MD; Debbie Arbique, DNP; Angela Price, MD; Steven Vernino, MD; Lauren Phillips MD; Pravin Khemani MD; Yuichiro Yano, MD, PhD; Sandeep R. Das, MD; Tao Wang, PhD; Wanpen Vongpatanasin, MD

Faculty Mentor: Wanpen Vongpatanasin

Abstract

Background: Increased BP lability is a hallmark of autonomic dysfunction, which may be captured by 24-hour ambulatory BP monitoring (ABPM). However, usefulness of different measures of BP variability (BPV) in detecting autonomic failure (AF) has not been determined.

Methods: We assessed BPV in 273 patients undergoing ABPM at UT Southwestern Medical Center between 2010-2017. Standard deviation (SD), Coefficient of variance (CV), average real variability (ARV), and variation independent of mean (VIM) were determined in 201 patients in the discovery cohort and 72 patients in the validation cohort. The presence of AF was determined during the Valsalva maneuver and head-up tilt.

Results: In the discovery set, 24-hour and nighttime SD, CV, ARV, and VIM did not differ significantly between AF (n=25) and controls (n = 176, all p > 0.05). However, SD, CV and VIM of daytime systolic BP (SBP) were all significantly higher in patients with AF than in controls (p < 0.01) while ARV remained non-significant for daytime SBP. No diastolic BPV markers were different between the 2 groups. In the validation cohort, SD, CV and VIM of the daytime SBP of AF (n =22) were significantly higher than controls (n = 50, p < 0.001). Nocturnal dipping was more blunted in the AF patients than the controls in both cohorts (both p < 0.01). The AUROC of SD, CV and VIM of daytime SBP were superior to nocturnal dipping in predicting AF, with SD being the best. When combined together SD and nocturnal dipping had superior AUROC compared to any other BPV index alone.

Conclusion: Our study shows that SD of daytime SBP is superior to conventional markers such as abnormal nocturnal BP dipping in detecting autonomic failure in patients with labile blood pressure. This simple tool has a strong potential for utilization in clinical practice.

Presentation #41

Title: Plasmablastic Lymphoma: A Single Center Experience

Presenter: Nivedita Arora

Authors: Nivedita Arora, MD; Arjun Gupta, MD; Navid Sadeghi, MD

Faculty Mentor: Navid Sadeghi

Abstract

Introduction: Plasmablastic lymphoma (PBL) is a rare aggressive form of non-Hodgkin lymphoma occurring most commonly in patients with HIV. Given its rarity, optimal therapy is not clearly defined and outcomes are generally poor. We describe the epidemiology, management and outcomes of PBL at a single institution. Materials and Methods We performed a retrospective analysis PBL cases at Parkland Hospital and Clements University Hospital between 2007 to 2017. Adult patients in whom the diagnosis of PBL was confirmed by hematopathology were included in the study. Baseline characteristics, treatment and follow up data were extracted from the electronic medical records.

Results: Twenty-nine patients were identified who met diagnostic criteria for PBL during the study period. Patients were predominantly male. 48% of patients were over 50 years of age, 41% between 30-50 years and 10% below 30 years. The median age at presentation was 50 years. 34% of patients were Caucasian, 21% African American and 45% Hispanic. 90% of patients were HIV positive. 69% had advanced stage (III-IV) at presentation. Median CD4 count at diagnosis for the HIV positive patients was 42 cells/μL. Of the HIV positive patients, 27% were diagnosed with HIV at the same time as the diagnosis of PBL. EBV was detected in 93% of cases. MYC rearrangements were detected in 75% of cases where it was tested. The most common extranodal site of disease was gastrointestinal (12 patients) followed by oral/maxillofacial (9 patients). The most commonly used regimen was EPOCH (69% of patients). Complete remission was achieved in 44% of patients. 17 patients (58%) died during the follow up period. Their median overall survival was 9.86 months. 11 patients were alive after a median follow up of 45 months. Median overall survival of the group was 15.86 months.

Conclusion: PBL is a rare AIDS-related lymphoma, but can occur in other immunocompromised states as well as in immunocompetent patients. Gastrointestinal, oral/maxillofacial and nodal involvement is common. Patients commonly present with advanced stage disease. EPOCH based regimens are commonly used but the outcome remains poor.

Presentation #42

Title: Dissemination of Information on Neutropenic Diet (ND) by Top US Cancer Centers: In line with Evidence?

Presenter: Nivedita Arora

Authors: Nivedita Arora, MD; Arjun Gupta, MD

Faculty Mentor: Arjun Gupta

<u>**Abstract**</u>

Introduction: Neutropenic Diet (ND) is commonly recommended and widely practiced for cancer patients with neutropenia with the goal of reducing infections. However, multiple randomized trials suggest that the overall risks of infection and mortality with ND are equivalent to less restricted diets. Moreover, ND affects the quality of life of patients significantly and contributes to malnutrition and reduced patient satisfaction. Therefore, we aimed to ascertain if top cancer centers recommended for or against the use of ND on their official websites, a common source of information for patients. We also evaluated if these recommendations are supported by literature.

Methods: Websites of the top 20 hospitals in the 2017 US News Best Hospitals for Cancer © were reviewed independently by two authors, and recommendations on ND were ascertained (i.e. for, against, equivocal, or not addressed) based on provided information. Further, it was determined if the recommendation provided was backed by evidence. Inter-rater agreement was 90%. The discordance in two instances was due to mention of a 'low microbial diet' which was resolved by including it with ND. Non-parametric statistics were used.

Results: 7 out of 20 websites (35%) made recommendations for ND, 4 (20%) against and 9 (45%) did not address ND at all. Only 5 out of 20 (25%) backed any of their recommendations with evidence, including 2 (10%) links to abstracts, whereas 7 mentioned the FDA safe food handling guidelines (non-exclusive). Type of recommendation made (for or against) did not depend on US news rank (top vs bottom 10; p=n.s.). 7 (35%) websites mentioned date of last content update and the median age of the posts was 1075.5 days (range 32-5886 days). Age of website content did not impact recommendation for or against ND.

Conclusion: ND continues to be recommended or not addressed on the majority (80%) websites of top US cancer centers, despite strong evidence against their use. The website content of major US cancer centers pertaining to ND should be updated sooner to better guide patients.

Presentation #43

Title: Use of Platelet and Erythroid Growth Factors during Induction Chemotherapy for Acute Lymphoblastic Leukemia in a Jehovah's Witness

Presenter: Nivedita Arora

Authors: Nivedita Arora, MD; Arjun Gupta, MD; Navid Sadeghi, MD

Faculty Mentor: Navid Sadeghi

<u>**Abstract**</u>

Case Presentation: A 21-year old woman presented with intermittent left sided abdominal and back pain for 2 weeks. She also reported nausea, subjective fevers and a 15lb weight loss over the same period. Blood work revealed a white cell count of 49 x 109/L (reference range 4-11 x 109/L) as well as anemia and thrombocytopenia. A peripheral smear demonstrated numerous circulating blasts. Bone marrow biopsy confirmed the diagnosis of B-cell acute lymphoblastic leukemia. Cytogenetics studies were normal. Next Gen Sequencing identified a IGH-CRLF2 rearrangement, consistent with Ph-Like B-ALL. She was a Jehovah's Witness (JW) and extensive conversations with the patient, her family, and her spiritual advisors were held. The diagnosis, prognosis, treatment options and potential complications were reviewed. She declined transfusions as supportive measures after understanding the risks and benefits. She was started on weekly rituximab, vincristine and daily prednisone. Romiplostim (1mcg/kg) and darbepoetin alpha (100mcg) were also given every 7 days, on days after each weekly chemotherapy. During induction, her nadir haemoglobin concentration was 5g/dL and nadir platelet count was <5x109/L. With improvement in platelet count, daunorubicin and pegaspargase were added to her regimen. She achieved a complete morphologic remission; flow cytometry was negative for minimal residual disease (MRD). Her treatment was then continued on a pediatric inspired regimen and she remains in an MRD(-) remission over a year after diagnosis. This case report describes the successful achievement of sustained complete remission in an adult JW with Ph-like CD20+ B cell ALL, in the absence of blood product transfusions.

Discussion: The care of JW patients with hematologic malignancies is challenging. Their faith does not allow acceptance of homologous or autologous whole blood, packed red blood cells, plasma, platelets or white blood cells. Given the risk associated with leukemia related/chemotherapy induced cytopenias, physicians may treat JW leukemia patients with less intensive and suboptimal regimens, which may in turn adversely affect outcomes. This case depicts a novel approach to circumvent transfusion needs by off-label use of growth factors. This approach allowed the patient to receive an induction regimen that resembles the CALGB 10403 induction (the preferred regimen at our institution).

Presentation #44

Title: Osimertinib pneumonitis: Case Reports of Asymptomatic Versus Severe Pulmonary Infiltrates

Presenter: Jennifer Wagner

Authors: Jennifer Wagner, MD; Andrew Sumarsono, MD; Tri Le, MD; Jonathan Dowell, MD

Faculty Mentor: Jonathan Dowell

<u>**Abstract**</u>

Case Presentation: We present two polarized cases of pulmonary manifestations on osimertinib -- a kinase inhibitor indicated for metastatic non-small cell lung cancer with EGFR T790M mutation. First, a 58 year old woman with lung adenocarcinoma originally treated with gefetinib but switched to osimertinib after progression. CT scan three months after initiation of osimertinib revealed development of extensive patchy ground glass infiltrate and septal thickening. The patient remained asymptomatic and was continued on osimertinib. In the second case, a 55 year old woman with metastatic lung adenocarcinoma maintained on erlotinib was changed to osimertinib after disease progression. Ten days after starting osimertinib, she developed dyspnea and hypoxemia. CT chest showed diffuse ground glass opacities with an upper lobe predominance in her right lung. She was admitted to the ICU for acute hypoxic respiratory failure for osimertinib induced pneumonitis. Osimertinib was discontinued and she was started on high dose IV steroids and then an oral prednisone taper. On one month follow-up, dyspnea was greatly improved, and hypoxemia resolved.

Discussion: These two cases support the evolving literature on the range of pulmonary adverse events associated with osimertinib. A phase one trial of osimertinib showed 6 potential cases of pneumonitis in 253 patients, and the drug was discontinued in all cases. However at the time of publication, all cases of pneumonitis were gone or resolving. A phase three trial of the drug showed ILD like adverse events in 4% of patients and one death in 279 treated patients. The FDA fact sheet on osimertinib indicates ILD/pneumonitis in 3.3% of patients (0.5% fatal) and advised permanent discontinuation of the drug in all cases. There are several case reports of successful re-challenge of osimertinib in patients after ILD/pneumonitis. Noonan et al (2016), describes a new concept of 'transient asymptomatic pulmonary opacities' that developed in 35% of patient on osimertinib in their study of twenty patients. The median time to first lesion was 8.7 weeks and another 6 weeks to resolution with continued osimertinib treatment. Our two opposite cases show the range of severity of osimertinib induced pulmonary infiltrates- asymptomatic to severe life-threatening pneumonitis.

Presentation #45

Title: Calcitriol-Mediated Hypercalcemia in Borderline Lepromatous Leprosy

Presenter: John Edward Marshall

Authors: John Marshall, MD; Jack Badawy, MD; Naim Maalouf, MD

Faculty Mentor: Naim Maalouf

Abstract

Clinical Presentation: A 39-year-old man with no significant medical history presented with 9 months of progressive hypoesthetic skin lesions on all extremities and 4 weeks of abdominal pain, nausea, vomiting, fatigue, polyuria, and polydipsia. He also noted gradual loss of his eyebrows and eyelashes. He immigrated from Mexico 14 years prior with frequent instances of armadillo hunting, butchering, and consumption before immigrating. On physical examination, he was afebrile with a blood pressure of 130/90 mmHg and a pulse rate of 56 beats per minute. His auricles felt gelatinous on palpation, and skin exam revealed madarosis, alopecia, and desquamating plaques and crusted ulcerations to all extremities. There was mild abdominal tenderness diffusely. Neurologic findings included bilateral hand interossei weakness, diffuse left upper extremity hypoesthesia, and left peroneal nerve thickening. Laboratory testing showed elevated total and ionized calcium at 14.2 mg/dL (reference range: 8.4-10.2 mg/dL) and 7.4 mg/dL (4.6-5.4 mg/dL), respectively. Serum albumin was normal at 3.7 g/dL. Serum parathyroid hormone was depressed at 8.2 pg/mL (15.0-65.0 pg/mL). Parathyroid hormone-related protein was undetectable. Total 25-hydroxyvitamin D level was normal at 27.4 ng/mL, but serum 1,25-dihydroxyvitamin D was elevated at 222 pg/mL (18-64 pg/mL). These findings suggested 1,25-dihydroxyvitamin D-mediated hypercalcemia concerning for lymphoma or granulomatous disease. Computed tomography of his chest, abdomen, and pelvis failed to suggest lymphoma. Skin biopsies revealed epidermal necrosis, granuloma formation around nerves, and numerous bacilli within Schwann cells on Fite staining, consistent with borderline lepromatous leprosy. He underwent aggressive intravenous fluid hydration and received a single dose of intravenous pamidronate. His serum calcium returned to normal levels within 2 days. He began treatment at a Hansen's disease clinic with a course of daily rifampin 600 mg, clofazimine 50 mg, and clarithromycin 500 mg. During the following year, his serum calcium remained normal, and his skin lesions, polyuria, and fatigue improved.

Discussion: This case illustrates classic features of leprosy with an uncommon metabolic manifestation. Despite leprosy's potential to form granulomas, hypercalcemia from leprosy is infrequently described. Though the mechanism is unclear, leprosy may induce hypercalcemia through unregulated 1-alpha-hydroxylase acting on circulating 25-hydroxyvitamin D as occurs in other granulomatous diseases.

Presentation #46

Title: Infected Aortic Graft Presenting with Cardiogenic Shock

Presenter: Stephen Philip

Authors: Stephen Philip, MD; Rich Mills, Megan Milne, MD; Sharon Reimold, MD

Faculty Mentor: Sharon Reimold

Abstract

Case Presentation: This is a 66 year-old man with a recent aortic dissection repair who was brought to the hospital with chest pain. Several weeks after repair of an aortic dissection, this patient initially presented with STEMI and was taken immediately to the catheterization lab for angiography and placement of drug eluting stents. However several hours after his stents were placed, the patient's extremities became cool to palpation and became increasingly tachycardic with the onset of hypotension. A transthoracic echocardiogram showed a moderate-sized pericardial effusion with compression of the right-sided chambers. He subsequently went back to the catheterization lab for pericardiocentesis. Serosanguinous fluid was drained from the pericardial space and cultures grew gram variable rods at less than 24 hours which later speciated as Serratia Marcescens. To investigate for sources of the pericardial bacteria, a CT angiogram of the aorta was obtained. The scan showed a fluid collection around the graft anastomosis, as the likely nidus of infection. Since no surgical treatment was desired, the patient was initiated on a six-week course of IV cefepime followed by lifelong suppressive ciprofloxacin.

Discussion: Pericardial effusions are a common complication after myocardial infarction with rates varying depending on the imaging study used between 6.6 to 66%[1-2]. The majority of effusions are not hemodynamically significant with reported rates of tamponade of less than 1% in STEMI patients[3-4]. In our patient, the signs of hemodynamic effect on the right ventricle prompted urgent pericardiocentesis. The presence of Serratia marcescens, however, was surprising given the patient's lack of infectious sign. In our review of the literature, patients who present with Serratia infections of the of the pericardium, pacemaker pocket, or aortic graft typically have signs and symptoms of infection and sepsis[5-7]. What is unique in this case was that a large aortic wall infection was contained and presented as cardiogenic shock from an infected pericardial effusion causing early tamponade rather than sepsis. To summarize, in patients with signs of hemodynamic compromise post-STEMI, a hemodynamically significant pericardial effusion should be in the differential. Furthermore, in patients with recent surgical intervention and new pericardial effusion, infectious etiologies should be evaluated.

Presentation #47

Title: Skeletal muscle involvement in Systemic Sclerosis

Presenter: Lucas Pineda Bernal

Authors: Lucas Pineda Bernal, MD; Lesley Davila, MD

Faculty Mentor: Lesley Davila

<u>**Abstract**</u>

Background: It has been well stablished that Systemic Sclerosis (SS) can be complicated by muscle involvement. Actually, SS is the rheumatologic condition that more commonly overlaps with inflammatory idiopathic myositis. In spite of this, little is known about the pathological, clinical, serological, or therapeutic features of this entity.

Methods: We reviewed the charts of 11 patients that meet the EULAR/ACR classification criteria for SS with concomitant muscle involvement evaluated in the Rheumatology clinics and in-patient services at Parkland Hospital and UT Southwestern Medical Center between January 2017 and February 2018, and describe, among other variables, demographic, clinical, radiological, and histopathologic features.

Results: 9/11 (81.8%) patients were female; ages ranged between 20-69 years. SS disease duration (from diagnosis to present or date of death) ranged from 0.67 to 13 years (mean of 3.5 years). Most commonly positive antibodies were ANA in 9/11 (81.8%), RNP in 5/11 (45.4%), and Rheumatoid Factor in 5/9 (55%). Myopathy presented before the diagnosis of SS in 4/10 (40%), at the time of diagnosis in 3/10 (30%), and after diagnosis in and 3/10 (30%) where the mean time after diagnosis was 0.48 years. Electromyography reported evidence of myopathy in 7/7 (100%), irritable myopathy in 4/7 (57%), and evidence of neuropathy in 3/7 (43%). Muscle biopsies were done in 4/11 patients and most frequent histopathologic patterns were Neurogenic atrophy in 3/4 (75%), inflammatory in 3/4 (75%), and necrotizing in 2/4 (50%). Most frequently used steroid-sparing agents were mycophenolate mofetil in 9/11 (81.8%), and azathioprine in 5/11 (45.4%).

Conclusions: Because of small sample size and potential selection bias, it is difficult to draw meaningful conclusions. However, we do have some interesting observations. Most patients were females and younger than 50. Muscle disease occurred early in the disease, sometimes before the diagnosis of SS. The most frequently positive antibody was ANA, and always in high titers. Of the muscle biopsies performed, the three main histopathology patterns were neurogenic atrophy, necrotizing and inflammatory myositis. Neurogenic atrophy was not always associated with neuropathy in EMG's, and neither was the inflammatory pattern with irritable myopathy on EMG.

Presentation #48

Title: Diarrhea for Days: GI Disturbance as the Presenting Symptom of Anti-DPPX Encephalitis

Presenter: Mridula Nadamuni

Authors: Mridula Nadamuni, MD; Christina Yek, MD; Samar Harris, MD

Faculty Mentor: Samar Harris

<u>**Abstract**</u>

Anti-DPPX Syndrome is a recently described autoimmune encephalitis characterized by a triad of profuse diarrhea and weight loss, central nervous hyperexcitability, and cognitive changes, with at least 31 cases described in the literature. A 41 year-old female with history of hypothyroidism and recent hysterectomy for uterine prolapse presented with a 6 month history of intractable diarrhea and cramps not improved by dietary modifications, emotional lability, 25 kg weight loss and abdominal distension. Her exam was significant for a cachectic appearance with mild jaw tremor, loss of prosody, flat affect and significant abdominal ascites. Computed tomography revealed bowel wall thickening throughout the colon and duodenum, however colonoscopy with random biopsies showed normal colon and colonic mucosa. Upper endoscopy showed mildly hyperemic mucosa in the stomach with mild chemical gastropathy but no duodenal changes. An abdominal ultrasound showed a nodular liver and liver biopsy was consistent with developing cirrhosis. Workup for an etiology of intractable diarrhea with infectious serologies, stool studies, heavy metal testing, immunologic, paraneoplastic and autoimmune studies was unrevealing. A full-thickness small bowel biopsy was performed, revealing inflammation of enteric autonomic ganglia. She displayed progressively more bizarre behaviors with worsening agitation and neurologic workup with electroencephalogram and cerebrospinal fluid analysis for infectious, paraneoplastic and autoimmune studies was significant only for increased polymorphonuclear leukocytes in cerebrospinal fluid. The possibility of anti-DPPX encephalitis was raised and serum as well as cerebrospinal fluid samples were found positive for the anti-DPPX antibody (1:960 serum; 1:2 CSF). She was treated with high dose steroids with remarkable improvement in both gastrointestinal symptoms and mental status, and was discharged to initiate rituximab as an outpatient. Significant diarrhea distinguishes anti-DPPX encephalitis from other causes of autoimmune encephalitis. Antibodies against the DPPX subunit of Kv4.2 potassium channels predominantly affect intestinal and brain neurons. The mechanism of gastrointestinal involvement is unclear but anti-DPPX antibody mediated neuronal hyperexcitability may be implicated. The onset of symptoms shortly following surgery also invites further discussion of the role of tissue injury in this syndrome. Ultimately, this case illustrates the importance of exploring a unifying diagnosis in patients with non-specific symptoms affecting multiple organ systems.

Presentation #49

Title: Anticonvulsant prophylaxis and survival in patients with primary and metastatic brain tumors: a systematic review and meta-analysis

Presenter: Timothy J Brown

Authors: Timothy J Brown, MD; Christina Zoccoli, MD; Ayesha Ali, BS; Lyndon Kim, MD; Michael Glantz, MD

Faculty Mentor: none

Abstract

Background: Despite high-quality evidence suggesting anticonvulsant prophylaxis in primary and metastatic brain tumors does not improve seizure outcomes, debate persists on the use of anticonvulsants in these patients. Valproic acid is particular interesting due to its histone deacetylase and CYP2C9 inhibitory action. We sought to determine if the body of the world's literature supports the use of anticonvulsant prophylaxis to improve survival in patients with primary or metastatic brain tumors.

Methods: A systematic review of PubMed and EMBase was performed with MeSH headings to identify all studies of anticonvulsant prophylaxis in adult patients with primary or metastatic brain tumors. Data were extracted from the text of included studies or from survival curves. Statistics were performed using Cochrane ReviewManager software. Endpoints of interest were one-year overall survival.

Results: Two-hundred seventy-six studies were reviewed. Eleven studies of 3767 patients with primary and metastatic brain tumors were included in the analysis of survival with any anticonvulsant, while ten studies of 3576 patients provided survival data with valproic acid. Compared to control, any anticonvulsant prophylaxis was associated with a relative risk (RR) of death of 0.88 [95% confidence interval 0.81-0.94, $p=0.0006$] at one year. Valproic acid compared to control was associated with RR of death at one year of 0.86 [95% CI 0.78-0.95, $p=0.003$]. Eight studies of 3194 patients with glioblastoma associated a RR of death at one year of 0.86 [95%CI 0.75-0.99, $p=0.04$] with valproic acid prophylaxis compared to none. Two studies of 344 patients with any brain tumor examined the use of non-valproic acid anticonvulsant prophylaxis did not result in improved RR of death at one year, 0.90 [95%CI 0.79-1.03, $p=0.13$], compared to control.

Conclusions: In this meta-analysis of anticonvulsant prophylaxis in patients with primary and metastatic brain tumors, anticonvulsant prophylaxis was associated with a significant survival benefit at one year. This association is driven primarily by valproic acid prophylaxis.

Presentation #50

Title: Effectiveness and Costs Associated with Biomarker Surveillance after Treatment in Locoregional Breast Cancer

Presenter: Timothy J Brown

Authors: Timothy J Brown, MD; Bernard Tawfik, MD

Faculty Mentor: Bernard Tawfik

Abstract

Background: Utilization of the biomarkers CA 15-3 and CA 27.29 to monitor recurrence or metastases does not improve outcomes after treatment in locoregional breast cancer. We sought to determine the effectiveness and costs of further testing following a positive biomarker test in asymptomatic patients.

Methods: The University of Texas Southwestern breast cancer registry was queried for all CA 15-3 and CA 27.29 tests in stage I-III breast cancer patients from January 1, 2010 to December 31, 2016. A biomarker was determined to lead to further testing if the patient had no symptoms and routine care would not have driven further investigation. Costs were determined by querying the Center for Medicare Services fee schedule.

Results: In total, 5755 biomarker tests were obtained in 1070 patients with stage I-III breast cancer. Four-hundred nineteen tests (7.3%) were positive in 172 patients. Of the patients with positive tests, 116 were asymptomatic and had no further workup while 46 were diagnosed with metastatic disease after undergoing symptom-driven investigations. Furthermore, 10 asymptomatic patients had positive biomarker tests that clearly led to further testing - CT Chest (5), CT abdomen and pelvis (9), PET-CT(1), bone scan (4), ultrasound-guided liver biopsy (3), MRI Pelvis (1), and MRI Brain (1). Recurrent or metastatic breast cancer was diagnosed in only 4 of these 10 asymptomatic patients. Overall, $155,911 was spent on obtaining biomarkers and follow-up testing after positive results, with $38,977 spent for each diagnosis of metastatic breast cancer arising from a positive biomarker test in asymptomatic patients.

Conclusions: In our cohort, very few positive tests led to further testing in the absence of symptoms. Even fewer positive tests ultimately led to a diagnosis of recurrent breast cancer after more intensive investigation and these were obtained with significant cost. The utility of screening biomarkers after definitive treatment for locoregional breast cancer in asymptomatic patients appears to have low utility and a high cost.

Presentation #51

Title: Reconciling beta-blockers and myocardial infarctions - perfecting high quality care

Presenter: Timothy J Brown

Authors: Timothy J Brown, MD; Neil Keshvani, MD; Arjun Gupta, MD; Sandeep R Das, MD; Ambarish Pandey MD

Faculty Mentor: Ambarish Pandey

Abstract

Situation: A 58-year-old man with hypertension and type 2 diabetes mellitus presented to Parkland with 3 days of chest pain. He was diagnosed with a ST-elevation myocardial infarction (STEMI) and underwent percutaneous coronary intervention of the right coronary artery. Post-procedure, the patient was noted to have atrial fibrillation with complete heart block and a junctional escape rhythm. He was admitted to the CCU using the 'STEMI admission order set' but developed worsening shortness of breath, bradycardia, and hypotension post-procedure.

Background: Order sets are pre-formed 'quick orders' designed to increase efficiency and adherence to guidelines. At Parkland, order sets have been established for many conditions. The STEMI order set lists multiple medication classes- antiplatelet agents, nitroglycerin, beta-blockers (BB), statins, ACE inhibitors- that must be selected or manually opted-out. Within the STEMI order set, a clinical decision support (CDS) statement enforced BB within 24 hours as a performance measure following the joint American College of Cardiology/ American Heart Association guidelines in 2006. This was removed from the guidelines in 2008 'due to increased complexity of decision making', however the order set at Parkland did not reflect this change. Assessment: The patient inappropriately received a dose carvedilol 3.125 mg. Interview with the prescribing physician revealed an intention to hold BB in this patient, however the physician was influenced by the perception of performance measure tracking with regards to BB in STEMI. The patient developed cardiogenic shock that briefly required transvenous pacing and inotropic support.

Results: Review of 12 months of cases at Parkland revealed 3 other cases in which BB were inappropriately prescribed, however none developed cardiogenic shock. The CDS statement has since been changed in the STEMI order set and a formal communication mechanism between the interventional cardiologists and CCU has been implemented. Since then, no further adverse events with BB in STEMI have been discovered.

Presentation #52

Title: Intravenous versus Intraosseous Access for Parenteral Drug Administration in Out-of-Hospital Cardiac Arrest: Insight from the Dallas Fort Worth Resuscitation Outcomes Consortium

Presenter: Purav Mody

Authors: Rohan Khera, MD; Ambarish Pandey, MD; Pamela Owens, James de Lemos, MD; Mark Link, MD; Ahamed Idris, MD

Faculty Mentor: Ahamed Idris

<u>**Abstract**</u>

Background: The current guidelines suggest either intravenous (IV) or intraosseous (IO) access for administration of drugs in patients with out-of-hospital cardiac arrest (OHCA). However, their patterns of use in a real-world setting and associated outcomes are not well-studied.

Methods: Using data from the multicenter DFW Resuscitation Outcomes Consortium, we examined the use of different routes of drug administration for individuals with OHCA from 2011 - 2016. The main routes of drug administration examined were initial IV and initial IO.

Results: A total of 8,571 OHCA episodes were identified from 2011-2016 in the DFW area. Initial IV and initial IO access was obtained in 5,694 (66.4%) and 2,877 (33.6%) individuals respectively. Patients receiving initial IV access (compared with initial IO access) were more frequently male (62.4% vs. 52.6%, p<0.001), had a higher proportion of initial shockable rhythm (21.6% vs. 13.2%, p<0.001), witnessed episodes (50.5% vs. 44.1%, p<0.001), less frequently experienced bystander CPR (43.0% vs. 46.9%,p=0.002) and experienced faster times to initial access (9.8 vs. 10.1 minutes, p=0.009). In contrast, there were no differences in age (63.5 vs. 64.1 years, p=0.1) among the two groups. With regards to outcomes, patients receiving initial IV access experienced higher rates of return of spontaneous circulation (ROSC) (25.9% vs. 17.7%, p<0.001), overall survival rate (8.7%vs. 4.6, p<0.001). and survival with good neurological function (3.1% vs. 1.1%, p<0.001). After adjustment for covariates such as age, sex, initial rhythm, bystander CPR, witnessed status and time to initial access, initial IV access (versus initial IO access) was significantly associated with increased survival (OR 1.4, 95% CI 1.1% - 1.9%, p=0.004) , survival with good neurological function (OR 1.7, 95% CI 1.1% - 2.7%, p=0.01) and ROSC (OR 1.5, 95% CI 1.3% - 1.7%, p=0.001).

Conclusion: Both IV and IO access are frequently used in OHCA, with varying time-to-access and patient outcomes. Further study is warranted to explore the optimal means of drug administration in OHCA.

Presentation #53

Title: Direct Comparison of Ultrafiltration to Pharmacological Decongestion in Heart Failure: A Per-Protocol Analysis of CARRESS-HF

Presenter: Spencer Carter

Authors: Spencer Carter, MD; Bradley A. Bart, MD; Steven R. Goldsmith, MD; Mark H. Drazner, MD; W. H. Wilson Tang, MD; Justin L. Grodin, MD

Faculty Mentor: Justin Grodin

Abstract

Background: Despite several studies, the clinical utility of ultrafiltration (UF) in acute heart failure (AHF) remains uncertain. Results from the Cardiorenal Rescue Study in Acute Decompensated Heart Failure trial (CARRESS-HF) did not demonstrate superior decongestive efficacy despite a rise in serum creatinine for UF in comparison to intravenous diuretics - findings possibly influenced by substantial dropout and crossover in the intention-to-treat analysis.

Methods: A per-protocol analysis of CARRESS-HF (N=188) was performed. Participants were included if randomized to UF and had UF output collected, or if randomized to the pharmacological arm and had urine but not UF output collected. Accordingly, there were N=163, 156, 129, and 106 participants at 24 hours intervals. Mixed effects modelling determined the association of treatment on serial parameters.

Results: There were N=71 in the UF arm (age 72y [62-79], 82% male, 48% NICM, Cr 2 [1.7-2.4]) and N=92 in the pharmacological arm (age 66y [58-78], 72% male, 63% NICM, Cr 1.84 [1.08-2.30]) at 24h. UF was associated with higher cumulative fluid loss (Figure A, P=0.003), and higher serum creatinine by 72 hours (Figure B, P<0.05), While there were no differences in aldosterone, cystatin C, or NT-proBNP changes from baseline to 96 hours, UF was associated with an increase in plasma renin activity by 96 hours (P=0.04).

Conclusion: UF was associated with greater decongestion in AHF, but also with rising serum creatinine and an increase in plasma renin activity.

Presentation #54

Title: Disconnection between Volume Loss and Increasing Serum Bicarbonate During Diuretic Treatment for Acutely Decompensated Heart Failure: A Per-Protocol Analysis of CARRESS-HF

Presenter: Spencer Carter

Authors: Spencer Carter, MD; Bradley A. Bart, MD; Steven R. Goldsmith, MD; Mark H. Drazner, MD, MSc; W. H. Wilson Tang, MD; Justin L. Grodin, MD

Faculty Mentor: Justin Grodin

<u>**Abstract**</u>

Background: The evolution of increasing serum bicarbonate is common during decongestive treatment for acute decompensated heart failure. However, animal models of metabolic alkaloses suggest that this evolution is not volume dependent.

Methods: A per-protocol analysis of CARRESS-HF (N=188) was performed. Participants were included if randomized to UF and had UF output collected, or if randomized to the pharmacological arm and had urine but not UF output collected. Accordingly, there were N=163, 156, 129, and 106 participants at 24 hour intervals. Mixed effects models determined the association of daily serum bicarbonate levels and relative weight changes from baseline to 96 hours.

Results: There were N=71 in the UF arm (age 72y [62-79], 82% male, 48% NICM, creatinine 2 [1.7-2.4], bicarbonate 29 [26-31]) and N=92 in the pharmacological arm (age 66y [58-78], 72% male, 63% NICM, creatinine 1.84 [1.08-2.30], bicarbonate 28 [25-31]) at 24 hours. UF was associated with a greater relative reduction in weight over time (P=0.02) than pharmacological therapy (Figure A). However, individuals assigned to the pharmacological arm had higher serum bicarbonate levels over time than did the UF arm at 24 hours (P =0.001), 48 hours, 72 hours, and 96 hours (P <0.001 for all, respectively, Figure B).

Conclusion: The evolution of a metabolic alkalosis during decongestion with loop diuretics is not solely due to intravascular volume depletion but rather a consequence of these pharmacological agents.

Presentation #55

Title: Serum Biomarkers Improve Prognostic Ability of BCLC Staging System

Presenter: Saroja Bangaru

Authors: Saroja Bangaru, MD; Auston Wei, PhD; Myron Schwartz, MD; Neehar Parikh, MD; Mindie Nguyen, MD; Lewis Roberts, MD, PhD; K Rajender Reddy, MD; Alex Befeler, MD; Denise Harnois, DO; Srivastava S, MD; Jo Ann Rinaudo, PhD; Ziding Feng, PhD; Jorge Marrero MD

Faculty Mentor: Jorge Marrero

Abstract

Background: The prognosis of hepatocellular carcinoma (HCC) is critical for the selection of the appropriate treatment. The Barcelona Clinic Liver Cancer (BCLC) staging system allows us to predict survival in HCC reliably. Serum alfa-fetoprotein (AFP), AFP-L3 and des-gamma carboxyprothrobin (DCP) are important biomarkers in HCC but their role in staging is unknown. Aims: To determine if AFP, AFP-L3 and DCP are important prognostic markers for HCC and whether these biomarkers can further stratify the BCLC staging system.

Methods: Patients with HCC were enrolled as part of a multicenter prospective study on HCC biomarkers. Serum biomarker levels had previously been collected. Recursive partition analysis was used to identify cutoff points for serum biomarkers. The GALAD score, a validated score incorporating all 3 biomarkers, was computed for each patient. We performed univariate and multivariate Cox regression analyses to determine predictors of survival. Kaplan-Meier analysis was used to estimate overall survival (OS).

Results: 362 patients with HCC were included in the analysis. The median follow up of the patients was 4.8 years (0.01-10.2 years), and the median OS was 2.2 years. The population had well compensated liver disease and early stage HCC: 71% were Child-Pugh A; 27% Child-Pugh B, and only 2% were Child-Pugh C. Only 10% had portal vein thrombus; only 5% had metastatic disease. 58% of the population had BCLC stage 0/A HCC; 19% had stage B HCC; 21% had stage C. In the univariate analysis, AFP, AFP-L3, DCP, the GALAD score, and Child-Pugh class were significant predictors of survival. Low GALAD score was associated with improved survival (HR = 0.4599, 95% CI 0.3525 - 0.5999, p < 0.0001). Multivariate analysis was performed according to each BCLC stage, and GALAD was an independent predictor of survival in each of BCLC 0/A, B, and C. Kaplan-Meier analysis was performed and demonstrated differential survival of low vs high GALAD in BCLC 0/A HCC.

Conclusions: Our study demonstrates that serum biomarkers can provide further prognostic information for BCLC stages A, B and C. This can lead to improved individualized treatment.

Presentation #56

Title: Muscle diseases of aging and sialic acid biosynthesis

Presenter: Nam Pham

Authors: Nam D. Pham, Poh-Choo Pang, Soumya Krishnamurthy, PhD; Amberlyn M. Wands, Paola Grassi, Anne Dell, Stuart M. Haslam, Jennifer J. Kohler, PhD

Faculty Mentor: Jennifer Kohler

<u>**Abstract**</u>

Background: GNE myopathy is a rare muscle disease of aging that is related to sporadic inclusion body myositis (sIBM), the most common acquired muscle disease of aging. The pathogenesis of sIBM is unknown but the related GNE myopathy is associated with mutations in the enzyme GNE (UDP-GlcNAc 2-epimerase/ManNAc kinase). GNE encompasses a protein with two enzymatic activities required for biosynthesis of the essential carbohydrate sialic acid in mammalian cells. Mutations to both GNE domains are linked to GNE myopathy. However, the correlation between mutation-associated reductions in sialic acid production and disease severity is imperfect.

Methods: To investigate other potential effects of GNE mutations, we compared cell lines expressing wild-type or mutant forms of GNE, by using a combination of flow cytometry, high-performance liquid chromatography (HPLC), and glycan mass spectrometry

Results: GNE deficiency is associated with unanticipated effects on the structure of cell-surface glycans. GNE-deficient cells produced distinct N-linked glycan structures with increased branching and extended poly-N-acetyllactosamine (polyLacNAc). GNE deficiency may also affect levels of UDP-GlcNAc, a central metabolite also associated with aging. Notably, the N-linked glycans produced by GNE-deficient cells displayed enhanced binding to galectin-1, indicating that changes in GNE activity can affect the affinity of cell-surface glycoproteins for the galectin lattice.

Conclusions: These findings suggest an unanticipated mechanism by which alterations in GNE activity might affect signaling through cell-surface receptors. Taken together, this work highlights pathways that may underlie GNE myopathy, sIBM, and other diseases of aging.

Presentation #57

Title: Case Report: CFTR modulators dramatically improve CF-related Bone Disease

Presenter: Nam Pham

Authors: Nam Pham, Raksha Jain, MD

Faculty Mentor: Raksha Jain

<u>**Abstract**</u>

Case Presentation: BR is a 22 year old patient with Cystic fibrosis, Genotrype: Delta F508/S549N. On routine DEXA screening at age of 20, he had Z-score of -1.7 at lumbar spine, -1.9 at left femoral neck, and -2.1 at right femoral neck, despite calcium and vitamin D therapy. Shortly after initiating that screening DEXA, patient was started on the CFTR modulator, ivacaftor. and his repeat DEXA at age 22 revealed Z-scores of -0.7 at lumbar spine, -1.5 at left femoral neck, and -1.5 at right femoral neck. These represent increases of 12.5%, 12.7%, and 14.7% respectively.

Discussion: CF-related bone disease is an early-recognized co-morbidity of CF and a recent meta-analsis suggests that the prevalence of osteopenia, osteoporosis, vertebral and non-vertebral fractures in the CF population is 38%, 23.5%, 15% and 14% respectively 32-34. The cause of CF-related bone disease is likely multifactorial - poor nutrition, vitamin D deficiency, chronic inflammation, chronic steroid exposure, hypogonadism are all likely contributors. Advances in imaging techniques reveal that not only do CF patients have lower bone density they also appear to have altered microarchitecture and imbalanced bone remodeling. Adult CF patients are at great risk from significant morbidity from pathological fractures. Nutritional support is critical in maintaining good bone density and bisphosphonate therapy has shown efficacy in treating osteoporosis in CF patients. A meta-analysis of randomized controlled trials of CF patients on anti-resorptive therapy revealed that bisphosphonates treatment increased bone density by 4.6% at the lumbar spine and 3.3% at the hip. To our knowledge this is the second case report of dramatic improvement of bone mineral density following ivacaftor treatment. Further work is needed to elucidate whether this is due to reduced pulmonary complications or direct improvement in CFTR function in bone homeostasis. Given the high prevalence of bone mineral disease in CF patients and the high risk of morbidity from fractures, this case report suggests that treating underlying CFTR function can potentially improve and reverse demineralization seen patients.

Presentation #58

Title: Impact of EMR-based colonoscopy results reporting and clinical decision support system on guideline-concordant surveillance recommendations

Presenter: Melissa Magrath

Authors: Melissa Magrath, MD; Edward Yang, MD; Caitlin C. Murphy, PhD; Ethan A. Halm, MD; Chul Ahn, PhD; Purva Gopal, MD; Christian Mayorga, MD; Deepak Agrawal, MD; Eric Borton, Celette Sugg Skinner, PhD; Amit G. Singal, MD

Faculty Mentor: Amit Singal

<u>**Abstract**</u>

Background: Surveillance colonoscopy is required in patients with a history of polyps given elevated colorectal cancer (CRC) risk; however, studies suggest substantial overuse and underuse of surveillance colonoscopy. Aims: Identify predictors of guideline-concordant surveillance recommendations after implementation of an electronic medical record (EMR)-based Colonoscopy pathology Reporting and clinical decision support System (CoRS)

Methods: We conducted a retrospective cohort study of patients who had colonoscopy with polypectomy at a safety-net health system before (n=1822) and after (n=1320) implementation of CoRS in December 2013. Recommendations were classified as guideline-concordant or guideline-inconsistent according to the US Multi-Society Task Force on Colorectal Cancer. Surveillance recommendations shorter and longer than guideline recommendations were defined as potential overuse and underuse. We used multivariable generalized linear mixed models to identify correlates of guideline-concordant surveillance recommendations.

Results: The proportion of guideline-concordant surveillance recommendations was significantly higher post-CoRS than pre-CoRS (84.6% vs. 77.4%, p<0.001), with fewer potential overuse and underuse recommendations. In the post-CoRS period, CoRS was used for 89.8% of cases and associated with greater guideline-concordant recommendations (87.0% vs. 63.4%; RR 1.34, 95% CI 1.23-1.42). In multivariate analysis, surveillance recommendations were also more likely to be guideline-concordant in patients with adenomas but less likely among those with fair bowel preparation and those with family history of CRC. Of 203 guideline-inconsistent recommendations, 70.4% were considered potential overuse, 20.2% potential underuse, and 9.4% were not provided surveillance recommendations.

Conclusions: An EMR-based colonoscopy pathology reporting and clinical decision support system was widely used and significantly improved guideline concordance of surveillance recommendations.

Presentation #59

Title: Evidence-Based Medicine and the American Thoracic Society Clinical Practice Guidelines

Presenter: Ross Charles Schumacher

Authors: Ross C. Schumacher, MD; Kaivayla Desphande, MD; Oanh Kieu Nguyen, MD; Anil N. Makam, MD, MAS

Faculty Mentor: Anil Makam, Oanh Kieu Nguyen

<u>**Abstract**</u>

Background: The American Thoracic Society (ATS) issues guidelines to enable healthcare providers to deliver evidence-based care for patients with pulmonary and critical care conditions. Although the usefulness of guidelines depends on the quality of evidence and the manner in which they are presented, the current evidence base for the ATS clinical practice guidelines is unknown.

Methods: We reviewed all ATS clinical practice guidelines listed on the ATS website as of August 1, 2017. For each recommendation, two investigators independently abstracted information on the level of evidence, strength of the recommendation, and a variety of domains to assess whether foundational data for guideline recommendations were presented in a manner to support evidence-based medical decision-making.

Results: We identified 18 guidelines consisting of 222 unique recommendations. Nearly two-thirds (n=141; 63.5%) of recommendations were based on low-quality evidence, 27.9% (n=62) moderate, and only 8.6% (n=19) high-quality evidence. Most 'strong' recommendations were not supported by high-quality evidence (16/86; 18.6%). Of 52 diagnostic testing recommendations, only 46.2% (n=24) provided the test's sensitivity, specificity or likelihood ratios. Of 165 therapeutic recommendations, 56.3% (n=93) either omitted or inconsistently reported the treatment's absolute benefits (absolute risk reduction or number needed to treat). Overall, less than half of recommendations (n= 99/222; 44.5%) included any discussion of patient context (severity of illness, multimorbidity, sociopersonal context, life expectancy, and patient preference).

Conclusions: Despite the prevalence of pulmonary and critical-care illnesses, the evidence base for ATS guidelines is suboptimal. The majority of recommendations are based on expert opinion, including many strong recommendations. Guideline recommendations often did not include necessary diagnostic or therapeutic information or a minimal definition of relevant patient context to support personalized, evidence-based clinical decision-making. Future high-quality research could change more than half of the current guideline recommendations. ATS guidelines should be cautiously applied to patient care, particularly recommendations based on low-quality evidence and those lacking guidance on individualizing care to patient context.

Presentation #60

Title: Ankylosing Spondylitis Presenting as Severe Aortic Valve Regurgitation

Presenter: Ola M Azzouqah

Authors: Ola M Azzouqah, MD; Joel D Taurog, MD

Faculty Mentor: Joel Taurog

Abstract

Case Presentation: A 40-year-old Caucasian man presented to the Parkland ED with congestive heart failure. Workup revealed severe aortic valve insufficiency. Thoracic spine syndesmophytes were seen incidentally on chest imaging. Further investigation revealed that he had advanced ankylosing spondylitis (AS), with fused sacroiliac joints and extensive syndesmophyte formation in the lumbar and thoracic spine. Upon questioning, he admitted to back pain with an inflammatory pattern when in his 20's and early 30's, for which he had not sought medical attention. There was no history of uveitis, psoriasis, or inflammatory bowel disease. A brother was said to have Crohn's disease. HLA B27 testing was negative. EKG showed left atrial abnormality, LVH with strain, but normal conduction.

Discussion: Some degree of pathology of the aortic root and valve is detectable in many patients with AS. of However, moderate-to-severe (i.e., hemodynamically significant) aortic valve insufficiency in AS is usually found only in patients with longstanding disease, and the lifetime prevalence in AS patients has been variably estimated from 2 to 20%. Delay in the diagnosis of AS of a decade or more after the onset of symptoms is not uncommon, but it is rare that the condition is discovered only after severe aortic valve insufficiency has ensued. This case illustrates the relationship between AS and lone aortic valve regurgitation, the most common form of structural heart disease characteristic of AS. Conduction defects, including third degree heart block, also occurs with increased frequency in AS, sometimes together with aortic valve insufficiency.

Presentation #61

Title: Use of QTc interval-prolonging medications among patients with lung cancer: implications for clinical trial eligibility and routine clinical care

Presenter: Tri Le

Authors: Tri Le, MD; Hui Yang, PhD; Sawsan Rashdan, MD; Carlos Alvarez, PharmD; David Gerber, MD

Faculty Mentor: David Gerber

Abstract

Importance: Use of QTc interval-prolonging medications may exclude patients from clinical trials and complicate routine clinical care. Prevalence of QTc-prolonging medication prescriptions among cancer populations is unknown.

Objective: To determine the rate of use of QTc-prolonging medications among individuals newly diagnosed with lung cancer in a national cohort.

Design, Setting, and Participants: We performed a retrospective, cross-sectional study of adult patients in the United States Veterans' Affairs (VA) medical system diagnosed with lung cancer between 2003 and 2016. Data were obtained from the VA Corporate Data Warehouse. Lists and categorization of QTc-prolonging medications were obtained from CredibleMeds®.

Main Outcomes and Measures: The primary endpoint was receipt of a prescription for a QTc-prolonging medication during the three months leading up to and including the date of lung cancer diagnosis. QTc-prolonging medications included those with known or possible risk of causing torsade de pointes.

Results: Overall, 280 068 patients were included in the study. Mean age was 70 years, 98% were male, and 72% were white. Overall, 28.4% of patients received prescriptions for a QTc-prolonging medication. Patients receiving QTc-prolonging medications were slightly younger and more likely to be black. Among the 20 most commonly prescribed QTc-prolonging agents, 35% were antimicrobials, 25% were psychiatric therapies, 10% were cardiovascular agents, and 10% were antiemetics. Over the study period, QTc-prolonging medication use increased approximately 15%.

Conclusions and Relevance: Use of QTc-prolonging medications is common and increasing among patients with lung cancer. This observation has implications for clinical trial accrual and routine clinical care. Further studies to determine the true clinical risk and optimal use of QTc-prolonging medications are warranted.

Presentation #62

Title: Predicting Early Hospital Readmissions Using EHR Data

Presenter: Sameh Saleh

Authors: Sameh N. Saleh, MD; Anil N. Makam, MD, MAS; Ethan A. Halm, MD; Oanh Kieu Nguyen, MD

Faculty Mentor: Oanh Nguyen

Abstract

Background: Due to federal financial penalties, hospitals are focused on preventing 30-day readmissions for a variety of medical conditions. However, early readmissions (within 7 days of discharge) have been shown to be more preventable than later readmissions (8-30 days). We assessed the utility of our previously validated EHR-based multi-condition 30-day readmission risk prediction model in predicting early readmissions.

Methods: Using EHR data, we conducted an observational study on hospitalizations for adult medicine inpatients from 2009-2010 from 6 diverse hospitals in North Texas using a 50-50 split-sample derivation and validation approach. We tested the discrimination and calibration of our original 30-day readmission model on predicting early readmissions in our validation cohort. We then re-derived our model coefficients for the same predictors as in our original 30-day model to optimize prediction of only early readmissions and evaluated changes in coefficients and model performance.

Results: Of 32,922 index hospitalizations among unique patients, 12.7% had a 30-day readmission and 4.4% had an early readmission. Our original model had moderately lower discrimination for predicting early vs. any 30-day readmission (C-statistic of 0.66 vs. 0.69, p≤0.001). Our re-derived model had similar discrimination (C-statistic of 0.66) but improved calibration for predicting early readmissions, particularly for those in the highest risk quintile (new model with 8.1% observed and 9.7% predicted for early readmissions vs. original 30-day model with 8.0% observed and 27.1% predicted). For the re-derived model, certain markers of clinical severity (hyponatremia, hypoalbuminemia, and vital sign instability at discharge) were more predictive of early readmissions, while certain baseline characteristics (Medicaid, widow, prior utilization) were less predictive.

Conclusions: Although early readmissions may be more preventable, they are not optimally predicted using a previously validated 30-day readmission risk prediction model. Some clinical risk factors at discharge were more predictive of early readmissions, while baseline sociodemographic characteristics and utilization history were less predictive. Further improvements in predicting early readmissions will likely require new modeling strategies that incorporate additional novel risk factors.

Presentation #63

Title: A novel approach to chronic antibody mediated rejection in kidney transplantation

Presenter: Stephan Buteau

Authors: Stephane Buteau, MD; Christopher Lu, MD; Mythili Ghanta, MD; Parsia Vagefi, MD; Malcom MacConmara, MD; Jose Torrealba, MD; Allen Hendricks, DO; Bekir Tanriover, MD; Christine Hwang, MD; Justin Parekh, MD

Faculty Mentor: Christopher Lu

<u>**Abstract**</u>

Background: Kidney transplantation (KT) remains the optimal treatment for End stage renal disease. Despite excellent short term KT survival rates, approximately 35% of live donor and 50% of deceased donor transplants fail at 10 years. Chronic active antibody mediated rejection (cAMR) is the leading cause of this late allograft loss. Existing studies have identified antibodies to the HLA Class II antigens, DP and DQ, as major participants in cAMR but expression of DP and DQ target antigens on the renal parenchyma remains unclear. Not much is known about which type of renal cells express these molecules, and what factors regulate their expression. A few studies have shown that while these antigens are not expressed in normal kidney in vivo, renal cells can increase their expression in response to cytokines in vitro. If cytokines increase expression of these antigens during cAMR, we should adopt the novel strategy of inhibiting the expression of these antigens.

Methods: Immunohistochemistry will be performed on 15 human kidney transplant biopsies utilizing antibody against DP antigen. Biopsies performed for work up of graft dysfunction as well as biopsies performed immediately post reperfusion intraoperatively are chosen for the study. Clinical and immunological parameters are collected. DP expression in the allograft biopsies will be correlated with clinical parameters.

Results: The first case of the study is a patient who received a 6-antigen match kidney at ABDR loci with one isolated DP mismatch with the donor. Allograft biopsy revealed Banff 1b Acute Cellular Rejection and immunohistochemistry for DP antigen showed its expression in glomerular capillary and peritubular capillary endothelial cells. When compared to DP expression in a control tissue (Normal kidney tissue obtained from Nephrectomy specimen performed for renal cell carcinoma), there were no differences between the two samples.

Conclusions: This is the first study to characterize DP expression in allograft tissue under various pathological conditions such as rejection and ischemia reperfusion injury. Although DP expression in the index case with cellular rejection and normal kidney did not vary, DP expression in allograft tissue under various pathological circumstances need to be characterized to better determine the factors regulating its expression.

Presentation #64

Title: Deep Phenotyping of HDL Particles: Characterization of Seven HDL Species and Their Relationship to Cardiometabolic Phenotypes in a Multi-Ethnic Population (Dallas Heart Study)

Presenter: Natalie Hoeting

Authors: Natalie Hoeting, MD; Colby R. Ayers, MS; Anand Rohatgi, MD

Faculty Mentor: Anand Rohatgi

<u>**Abstract**</u>

Background: Size-based HDL particle analysis based on small, medium, and large categories has led to inconsistent associations with cardiovascular disease (CVD). A new algorithm expands characterization of HDL-P from three to seven species, but the clinical significance remains unknown. We investigated the relationships between the seven HDL species and traditional risk factors, lipids, and cardiometabolic phenotypes in the Dallas Heart Study, a multiethnic, probability-based, population cohort of Dallas county adults.

Methods: This study included 2,996 DHS participants (56% women, 50% Black), excluding those with prior CVD and statin users. HDL species were determined by nuclear magnetic resonance using the LP4 algorithm, with increasing size from H1P to H7P. Insulin resistance was determined by homeostatic model assessment index (HOMA-IR). Visceral fat was measured by MRI.

Results: The largest HDL species were most directly associated with HDL cholesterol (HDL-C) (H6P: $r = 0.61$, $p < 0.0001$; H7P: $r = 0.66$, $p < 0.0001$). H2P was inversely associated with all HDL species including H1P ($r = -0.19$, $p < 0.0001$) and HDL-C ($r = -0.18$, $p < 0.0001$), but was directly associated with total cholesterol, triglycerides, and LDL-C ($p < 0.0001$). Female gender and Black ethnicity were associated with lower H2P levels ($p < 0.0001$). H2P alone was directly associated with diabetes, hypertension, waist circumference, insulin resistance, and visceral fat (Figure, $p < 0.0001$ for all values)

Conclusion: Our study of a novel 7-species designation of HDL particles revealed that the smallest HDL particle species (H1P and H2P) confer differential associations with cardiometabolic phenotypes. These findings suggest further investigation specifically into the role of H2P and CVD.

Presentation #65

Title: 'Racial and Ethnic Disparities in Non-Alcoholic Fatty Liver Disease Prevalence, Severity, and Outcomes in the United States: A meta-analysis.'

Presenter: Stefany Ifeoma Oji

Authors: Stefany Oji, MD

Faculty Mentor: Amit Singal

Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the United States, affecting 75-100 million Americans. However, its disease burden may not be equally distributed across race/ethnicities.

Aim: We conducted a systematic review and meta-analysis to characterize racial/ethnic disparities in NAFLD prevalence, severity, and prognosis.

Methods: Two investigators searched MEDLINE, EMBASE, and Cochrane databases from inception through August 2016. We identified studies that reported NAFLD prevalence in population-based or high-risk cohorts, NAFLD severity including presence of nonalcoholic steatohepatitis (NASH) and significant fibrosis, and NAFLD prognosis including development of cirrhosis complications and mortality. Pooled relative risks, according to race/ethnicity, were calculated for each outcome using the DerSimonian and Laird method for a random effects model.

Results: We identified 34 studies with 368,569 unique patients that characterized disparities in NAFLD prevalence, severity or prognosis. NAFLD prevalence was highest in Hispanics, intermediate in Whites, and lowest in Blacks, although differences between groups were smaller in high-risk cohorts (range 47.6%-55.5%) than population-based cohorts (range 13.0%-22.9%). Among NAFLD patients, risk of NASH was higher in Hispanics (RR 1.09, 95%CI 0.98-1.21) and lower in Blacks (RR 0.72, 95%CI 0.60-0.87) than Whites; however, the proportion of patients with significant fibrosis did not significantly differ between racial/ethnic groups. Data were limited and discordant regarding racial/ethnic disparities in NAFLD prognosis.

Conclusion: There are significant racial/ethnic disparities in NAFLD prevalence and severity in the U.S., with the highest burden in Hispanics and lowest burden in Blacks; however, data are discordant regarding the presence of racial/ethnic disparities in prognosis among NAFLD patients.

Presentation #66

Title: Jaundice and Volume Overload: Congestive Hepatopathy as a Rare Cause of Severe Hyperbilirubinemia

Presenter: Taylor Derousseau

Authors: Taylor Derousseau, MD

Faculty Mentor: Shannon Tujios

Abstract

A 58-year-old male with end stage renal disease presents after 3 months of jaundice. Liver function testing revealed profound, cholestatic liver injury with initial bilirubin elevated to 24.7 mg/dl. Laboratory work-up and imaging including MRCP, US, and ERCP were non-diagnostic, and notably negative for a large duct obstruction or mass concerning for malignancy. He underwent two separate liver biopsies that showed evidence of significant vascular outflow obstruction. Congestive hepatopathy was determined to be the cause of his jaundice and bilirubin levels decreased with aggressive ultrafiltration.

Discussion: Congestive hepatopathy typically presents with modest elevations in total bilirubin that rarely lead to jaundice. While large duct obstruction and malignancy are more common culprits of cholestatic liver injury and jaundice, congestive hepatopathy can be causative in the right clinical context once more common etiologies have been excluded.

Presentation #67

Title: Re-Challenging with Immunotherapy in Melanoma

Presenter: Bernard Tawfik

Authors: Bernard Tawfik, MD; Yull Arriaga, MD

Faculty Mentor: Yull Arriaga

Abstract

Case Presentation: Mr. JE is a 60-year-old male with history of HIV/AIDS (well controlled on HAART therapy) and melanoma s/p resection in 2012 found to have metastatic melanoma in June of 2015. The original excisional biopsy of his R. back was performed on March, 2012 which showed malignant melanoma, superficial spreading type, with Breslow's thickness of 4.5 mm, Clark's level V. Patient underwent subsequent wide re-excision and R axillary sentinel node biopsy which showed no evidence of residual disease at the tumor bed and 0/9 axillary nodes positive for metastatic disease. JE did well until June 2015 when he presented to Parkland ED with two days of nausea/vomiting, gait instability and dizziness and imaging revealed numerous brain and pulmonary metastasis. Patient was treated with radiation to the brain lesions and started on single agent ipilumumab July 2015 with decreasing size of all lesions. Ipilumumab was continued until January 2016 when he was switched to maintenance nivolumab until July 2016 when his imaging showed progression of pulmonary nodules with new adrenal metastasis. At that time, the decision was made to retreat with immunotherapy given the patient's good functional status, BRAF wild type status and lack of other effective treatments. Patient completed dual immunotherapy with nivolumab and ipilumumab September 2016 and transitioned again to maintanence nivolumab in October with decrease in size of pulmonary and adrenal metastasis. This was continued until progressive disease of the pulmonary and adrenal nodules was found February 2017. Given the patient's previous response, he was retreated a third time with immunotherapy with nivolumab and ipilumumab transitioning to maintenance nivolumab in May 2017 with stable disease on imaging. This continued until August 2017 when the patient again had progressive disease along with rapid decline in functional status and hospice was elected.

Discussion: Rechallenging with immunotherapy is an area of active clinical interest. There is evidence that continue treatment through progressive disease in patients who are clinically benefiting has value in melanoma and renal cell carcioma , . Small case series shows that rechallenge with immunotherapy

Presentation #68

Title: A Fatal Case of Macrophage Activation Syndrome (MAS) in a Patient with Dermatomyositis and Cytomegalovirus Viremia

Presenter: Allison Virginia Lange

Authors: Allison Lange, Salahuddin Kazi, MD; Weina Chen, MD; Arti Barnes, MD

Faculty Mentor: Arti Barnes

Abstract

Case Presentation: We describe a case of an adult with dermatomyositis who presents with a rash, high fevers, tachycardia, and hypotension, initially concerning for an infectious etiology or a dermatomyositis (DM) flare. She was found to have CMV viremia which improved after starting valganciclovir. After extensive workup and lack of improvement with broad-spectrum anti-microbial therapy, IVIG, and steroids, the patient was diagnosed with MAS after bone marrow biopsy and levels of CD 25 and IL-2 were obtained. Unfortunately, despite therapy with dexamethasone, anakinra, and etoposide the patient decompensated and the patient's family opted for comfort care. The patient subsequently expired in the intensive care unit.

Discussion: MAS in patients with dermatomyositis is recognized as a rare phenomenon and has been described only in case reports. Early diagnosis of MAS is beneficial for patients, before inflammatory tissue damage has become irreversible. In our case, rheumatology considered MAS in the differential diagnosis on initial consultation, however biopsy of bone marrow, CD-25 and IL-2 were not pursued initially as the patient's presentation was thought to be due to dermatomyositis flare or CMV viremia and not MAS, and she initially improved with IVIG. Her leukopenia worsened during admission however this was thought to be related to other factors, namely drug side effect of valganciclovir or infection with CMV. The creation of specific guidelines for sepsis management in patients with auto-immune conditions would benefit patients with MAS. Diagnostic criteria specific for MAS in adults would also be beneficial as recognizing these syndromes is challenging. Though clinical trial data is needed to support these practices, the unfortunate rarity of this condition is a major barrier to obtaining this information.

Presentation #69

Title: Parkinsonism Paranoia

Presenter: Ashlin Christensen-Szalanski

Authors: Ashlin Christensen-Szalanski, MD

Faculty Mentor: N/A

Abstract

Case Presentation: A 57 year old man with recently diagnosed Parkinsonism was brought to the emergency department with ten days of progressively intensifying psychotic paranoid delusions. Two weeks prior to presentation he had begun carbidopa-levodopa therapy after a DaT scan confirmed a clinical diagnosis of Parkinsonism. He denied having experienced any fevers, headaches, neck stiffness, falls, recent infections, sick contacts, travel, substance use or misuse, and had experienced no auditory nor visual hallucinations. Aside from obstructive sleep apnea he had no medical history. Though he had no formal psychiatric diagnoses, ten months prior to presentation the patient reported an insidious onset of depressive symptoms including weakness, anergia, weight loss, insomnia and worsening concentration. He had been prescribed a number of sleep aids and antidepressants with minimal adherence. These symptoms had subsequently been attributed to Parkinsonism by the patient and his wife. Upon presentation the patient was noted to have a flat affect with psychomotor retardation a pill-rolling tremor and mild cogwheel rigidity. Carbidopa-levodopa therapy was discontinued and quetiapine therapy was begun. Initial infectious, toxicological and neurological workups were negative. The patient's psychosis persisted seven days after presentation; venlafaxine was initiated and further workups were unrevealing. Two weeks after presentation consent was obtained to begin ECT. After one session of bitemporal ECT the patient experienced significant, but transient, abatement of his symptoms. He continued a thrice-weekly acute series of ECT with continued relief. He remained paranoid but stable for discharge home after his sixth session. After his fifteenth session he reported complete resolution of symptoms after treatments. His venlafaxine was continued, quetipaine tapered, and he was transitioned to bi-weekly maintenance ECT.

Discussion: The likely differential for new-onset psychosis in a 57 year old man with Parkinsonism includes neurocognitive and medication/substance-induced, encephalopathy and primary mood disorder. Though levodopa psychosis typically presents with hallucinations, the temporal association with symptom onset was highly suggestive of a causal relationship. Failure to improve two weeks after levodopa discontinuation necessitated further workup. Ultimately, a thorough psychiatric investigation revealed a mood-induced psychotic disorder which was managed effectively with ECT.

Presentation #70

Title: Early Repolarization Pattern is Associated with Cardiac MR-Derived Left Ventricular Mass

Presenter: Ari Jay Bennett

Authors: Ari J. Bennett, MD; David A. McNamara, MD; Colby R. Ayers, MS; Jarett D. Berry, MD; Mark S. Link, MD

Faculty Mentor: Mark Link

Abstract

Background: Recent studies have shown an association between early repolarization pattern (ERP) and sudden cardiac death. The role of left ventricular mass (LVM) as a potential mediator of this relationship has not been well explored.

Methods: Participants in the Dallas Heart Study who underwent a concomitant electrocardiogram and cardiac MRI (CMR) were assessed for ERP, defined as J-point elevation ≥1 mm in any 2 contiguous leads. LVM was measured by CMR. We compared participants with and without ERP by age, gender, and race/ethnicity; hypertension, diabetes mellitus, and hyperlipidemia; PR interval, QRS interval, and QTc interval; lean body mass and percent body fat; and LVM and LVM/body surface area (BSA) using Student's T-tests and chi-squared tests where appropriate. LVM's and LVM/BSA's associations with ERP were then assessed by multivariable logistic regressions adjusting for the aforementioned variables.

Results: Of the 3019 participants in our study, 286 (9.5%) had ERP. ERP was more prevalent in blacks than non-blacks (14 vs 5%, p<0.00001) and in men than women (18 vs 2%, p<0.00001). Baseline cardiovascular risk factors were not significantly different. Participants with ERP demonstrated higher lean body mass (59±10 vs 52±11 kg, p<0.00001) and lower percent body fat (27±8 vs 36±9%, p<0.00001). The presence of ERP was associated with greater LVM (160±46 vs 128±36%, p<0.00001) and increased LVM/BSA (81±21 vs 65±15%, p<0.00001). Multivariable logistic regressions confirmed the significant associations of ERP with both LVM (OR 1.94 [1.60-2.34]) and LVM/BSA (OR 1.75 [1.49-2.05]).

Conclusions: In a large, multi-ethnic cohort, ERP is associated with increased LVM and LVM/body surface area after adjusting for known confounders. These novel associations may provide insight into the biology of ERP. Future study of LVM's association with ERP and its potential role as a mediator of SCD in ERP is warranted.

Presentation #71

Title: Löffler's Endocarditis: Cardiac MRI Leading to Prompt Initiation of Therapy

Presenter: Ari Jay Bennett

Authors: Ari Bennett, MD; Sefik Gokaslan, MD; Yasmeen M Butt, MD; Susan Matulevicius, MD; Amit Khera, MD; David McNamara, MD

Faculty Mentor: Amit Khera

<u>**Abstract**</u>

Case Presentation: A 52-year-old woman with a past medical history of late-onset asthma, chronic rhinosinusitis, and discoid lupus presented to the hospital with two weeks of dyspnea on exertion and progressive substernal chest pain radiating to the jaw with associated diaphoresis. Electrocardiogram revealed normal sinus rhythm with a left axis and low voltages. Pertinent labs included a cardiac troponin T of 0.36 ng/mL, NT-proBNP of 3,963 pg/mL, a white blood cell count of 16.93/mL, an eosinophil count of 9.95/mL, and erythrocyte sedimentation rate of 74 ng/mL, and a C-reactive protein of 30.9 ng/mL. Transthoracic echocardiogram showed an ejection fraction (EF) of 26% with mid-distal inferoseptal, inferior, and inferolateral akinesis and a small pericardial effusion. Cardiology was consulted by the ER with concern for acute coronary syndrome. In lieu of left heart catheterization (LHC), an urgent cardiac MRI was performed, which revealed foci of mid-myocardial late gadolinium enhancement and diffuse pericardial thickening, consistent with myopericarditis. Endomyocardial biopsy demonstrated innumerable eosinophils in a background of acute and healed myofibril damage, consistent with severe eosinophilic myocarditis (EM). The patient was diagnosed with ANCA-negative eosinophilic granulomatosis with polyangiitis (EGPA). Pulse steroids and goal-directed heart failure therapy were initiated. Four months into therapy, the EF improved to 41%, and the eosinophilia and symptoms resolved. The patient was transitioned to mepolizumab, a novel IL-5 antagonist recently shown to be a viable alternative to long-term steroids in patients with EGPA.

Discussion: This case highlights the role that early cardiac MRI played in the rapid diagnosis of a patient with EM. Recognition of the signs and symptoms of myocarditis followed by the decision to bypass LHC and pursue urgent cardiac MRI led to prompt initiation of therapy. Our patient demonstrated subsequent improvement of her symptoms, ejection fraction, and EGPA disease course.

Presentation #72

Title: Erythromelalgia Gets Misdiagnosed Again and Again

Presenter: Ari Jay Bennett

Authors: Ari Bennett, MD; Joseph Tejan, MD; Travis Vandergriff, MD; Abey Thomas, MD

Faculty Mentor: Abey Thomas

Abstract

Case Presentation: A 72-year-old man with a past medical history of polycythemia vera developed right hallux pain, swelling, and erythema days after stopping daily aspirin. Cellulitis was diagnosed, and symptoms improved with antibiotics. One month later, the symptoms returned. Lancing did not elicit drainage, and, despite weeks of multiple antibiotics, symptoms continued. MRI showed osteoarthritis of the right first metatarsophalangeal joint (MTP); labs were significant for a hemoglobin of 16.8 g/dL, platelets of 608,000/uL, normal ESR and CRP, and a serum uric acid of 8.9 mg/dL. The patient was diagnosed with gout and started on allopurinol and prednisone without improvement. The next month, arthrodesis of the right first MTP was performed to no avail. In a follow-up visit, splinter hemorrhages were noted on finders of his right hand. The patient was admitted and started on daily aspirin for primary prevention and a heparin drip given the concern for thromboembolic disease. Workup-which included an autoimmune panel, c3, c4, ANCA, fibrinogen and D-dimer, blood cultures, a transthoracic echocardiogram, and a punch biopsy of the right foot-was noncontributory. Three days into the admission, the symptoms began to improve. Given the (1) dependent painful swelling and erythema of the extremities; (2) the significant thrombocytosis; and (3) the improvement of symptoms with aspirin; the patient was diagnosed with erythromelalgia. The patient received phlebotomy and was started on 325 mg daily aspirin with complete resolution of symptoms.

Discussion: Erythromelalgia is a rare condition consisting of intermittent pain, erythema, and swelling of dependent extremities that typically occurs in the setting of thrombocytosis and resolves with aspirin; its rarity has led to numerous misdiagnoses reported in both medical journals and newspapers. This case demonstrates the multiple superfluous and potentially detrimental interventions-including arthrodesis, clinical lancing, numerous antibiotics, a punch biopsy, and IV anticoagulation-that were performed after recurrent misdiagnoses of erythromelalgia. The lack of recognition of erythromelalgia is likely related to availability heuristic given the prevalence of the differential diagnoses, namely arthritis and cellulitis. Earlier recognition related to more widespread knowledge of this condition could hopefully lead to improved patient care.

Presentation #73

Title: Systemic Reaction Rates with Omalizumab, Subcutaneous Immunotherapy, and Combination Therapy in Children with Allergic Asthma

Presenter: Daniel Har

Authors: Daniel Har, MD; Min Jung Lee, MD

Faculty Mentor: Min Jung Lee

Abstract

Background: Subcutaneous immunotherapy (SCIT) is contraindicated in poorly controlled asthma. Our study compares the safety of combining omalizumab and SCIT versus omalizumab alone in children with moderate-severe persistent asthma. We hypothesize that the rate of systemic reactions (SR) in children receiving SCIT and omalizumab combination therapy is comparable to omalizumab alone.

Methods: We performed a retrospective study of children ages 6-18 years old with allergic asthma from 07/2010-06/2017 who received SCIT, omalizumab, or combination therapy in our Children's allergy clinic. All patients receiving omalizumab or combination therapy had moderate-severe persistent asthma. The rate of SR was compared among each of these categories.

Results: We reviewed 79 patients: 30 SCIT patients (1550 injections), 30 omalizumab patients (729 injections), and 29 combination therapy patients (954 injections). In the SCIT group, 19 SR (1.2% of injections) occurred in 10 patients (33%). In the omalizumab group, 3 SR (0.4% of injections) occurred in 3 patients (10%). Similarly in the combination group, 3 SR (0.3% of injections) occurred in 3 patients (10%). Compared to SR in SCIT group, both omalizumab and combination groups had significantly lower SR, p=0.045 and 0.011, respectively. Rate of SR in children receiving omalizumab and combination therapy was not statistically different (p=0.73).

Conclusions: Children with moderate-severe persistent allergic asthma receiving omalizumab or combination therapy had significantly lower SR compared to allergic asthmatic children receiving SCIT therapy. SCIT treatment in omalizumab-treated children is safe and may serve as an endpoint to omalizumab therapy with long-lasting immune modulating benefits.

Presentation #74

Title: AL Amyloidosis Presenting as Peripheral Neuropathy

Presenter: Ethan Tobias

Authors: Ethan Tobias, MD; Carlos Cardenas, MD; Bret Evers MD, PhD; Jonathan Dowell, MD

Faculty Mentor: Jonathan Dowell

Abstract

Case Presentation: A 45 year old male with ESRD, hypertension, and MGUS presented with 6 months of progressive weakness and numbness in all four extremities leading to multiple falls. Review of systems was notable for a 20 lb weight loss over this same time period. Physical examination revealed muscle atrophy, decreased tone, and diminished strength in all four extremities. Deep tendon reflexes could not be elicited. Sensation was also diminished to vibration and pinprick in a stocking-glove distribution. Labs showed pancytopenia (WBC 3.4, Hgb 9.3, Plts 146). HgbA1c and Vitamin B12 levels were normal. SPEP showed two M-components in the beta region that were too small to be quantified. Serum free light chain analysis revealed elevated kappa and lambda with a kappa/lambda ratio of 0.22. Nerve conduction studies (NCS) and electromyography (EMG) were consistent with a peripheral sensorimotor axonal polyneuropathy. Gastrocnemius muscle and sural nerve biopsies were performed. Both were consistent with the diagnosis of amyloidosis and mass spectrometry confirmed the presence of AL amyloid. Bone marrow biopsy revealed a minute population (0.8%) of what was felt to be aberrant plasma cells, consistent with the diagnosis of AL amyloidosis.

Discussion: Peripheral neuropathy is a common neurological complaint. Often it is mild in severity, slowly progressive with only sensory deficits, and has an etiology self-evident from the history, such as diabetes, alcohol abuse, or chemotherapy. These do not require further evaluation. Otherwise, initial laboratory testing with the highest yield are serum B12, HgbA1c, and serum protein immunofixation electrophoresis. EMG and NCS can be useful to differentiate myopathy, neuropathy and radiculopathy. In this case, the patient developed a neuropathy with motor predominance and rapid progression, which warranted further investigation and led to the diagnosis of AL amyloidosis. AL amyloidosis is a plasma cell disorder characterized by the deposition of immunoglobulin light chains leading to organ dysfunction. The most common presentations are proteinuria with renal failure, congestive heart failure, and peripheral neuropathy. The diagnosis of AL amyloid is a pathological diagnosis and requires a biopsy of an affected organ or a surrogate site, such as the abdominal fat pad or bone marrow.

Presentation #75

Title: Prescribing Patterns for FOLFIRINOX in the Real World

Presenter: Chad Guenther

Authors: Chad Guenther, MD; Nizar Bhulani, MD, MPH; Adam Korenke PAC; Jenny Li, MD; Leticia Khosama, NPC; Samira Syed, MD; Syed Kazmi MD; Naga Cheedella MD; Sirisha Karri, MD; Jay Lohrey, MD; Aravind Sanjeevaiah, MD; Udit Verma, MD; John Cox, DO; Yull Arriaga, MD; M. Shaalan Beg, MD

Faculty Mentor: Muhammad Shaalan Beg

Abstract

Background: FOLFIRINOX therapy is associated with improved outcome in patients with gastrointestinal cancers. The regimen can be associated with significant toxicity and empiric dose modifications are often used. We analyzed 1) real-world prescribing patterns of FOLFIRINOX and 2) toxicity of therapy.

Methods: Patients undergoing FOLFIRINOX chemotherapy at an academic, NCI-Designated Comprehensive Cancer Center were identified and electronic medical records reviewed. Patients who received at least one dose of FOLFIRINOX were included. Chemotherapy dose, growth factor use and toxicity data was abstracted for the first 8 weeks. 'Standard FOLFIRNOX' was defined as the regimen utilized by Conroy et al (NEJM 2011). Any empiric reduction/withholding of drug dose for cycle 1 was classified as 'modified FOLFIRINOX'. Bivariate analysis was performed on the data.

Results: There were 111 patients seen between 5/2011-3/2017 and 94% had pancreatic cancer. Age range was 29-87 years and 52% were female. 59% received 'modified FOLFIRINOX' and 20% received empiric growth factors. Line of therapy for standard vs modified respectively was 71.1% vs 45.5% for 1st, 17.8% vs 36.4% for 2nd, and 11.1% vs 18.2% for beyond 2nd (p = 0.03). Patients with 'modified FOLFIRINOX' were more likely to have metastatic disease (p = 0.01), have received second line or beyond, and higher ECOG score (p = 0.03). Patients with 'modified FOLFIRINOX' had a trend toward fewer treatment-related ED visits or hospitalization vs 'standard FOLFIRINOX' (27.2% vs 42.2% p = 0.10) and fewer treatment delays (25.8% vs 42.2% p = 0.07).

Conclusions: In our cohort, a majority of patients on FOLFIRINOX received empiric dose modifications. There were no significant differences in toxicity between standard and modified regimens.

Presentation #76

Title: Telephone Reminder Program to Improve DAPT Adherence

Presenter: Jeffrey Paul Chidester

Authors: Jeffrey Chidester, MD; Danny Bennett, MD; Laurie Beall, RN; Tiffany Denkins, RN; Kristin Alvarez, PharmD; Chris Mathew, PharmD; Rebecca Vigen, MD; Sandeep Das, MD; Michael Luna, MD; Tayo Addo, MD

Faculty Mentor: Sandeep Das

<u>**Abstract**</u>

Background: Khalili (2016) and Shemisa (2017) previously demonstrated proportion of adherence rates >80% to P2Y12 inhibitors (e.g. clopidogrel) at Parkland range between 50-60% following percutaneous coronary intervention (PCI). Rinfret et al. (2013) demonstrated improvement in median adherence with patient phone calls at multiple time intervals following PCI. Improper use of medications can lead to adverse events such as rethrombosis or bleeding. Method: A nursing-led patient phone call initiative was implemented at the following intervals following PCI: within 1 week, 30 days, and 90 days. Multidisciplinary algorithms were put in place to address medication related issues identified during the call. The primary objective was to improve adherence as measured by proportion of days covered (PDC). The secondary objective was to identify system-level processes affecting medication adherence or address side effects.

Results: Of all patients who underwent PCI from 9/1/2017-10/31/2017, a nurse was able to contact 30 patients (45%) within seven days, left messages for 22 (30%), had incorrect or incomplete contact information for eight (12%), and another six patients were unreachable. Patient contact rates were similar at 30 and 90 days. We limited PDC analysis to patients (n=43) who filled P2Y12 inhibitor prescriptions only at a Parkland Pharmacy and calculated a median PDC rate of > 90%. Twelve patients were identified as either not taking their medications at all; not taking medications as instructed; being discharged without medications; or unable to secure adequate funding for refills. Interventions for these patients included one-on-one education by a pharmacist or coordination of refills with pharmacy; physician phone calls and medication substitutions; provision of coupons; and collaborative meetings between different nursing area administrators.

Conclusions: A nursing-led patient phone call system in collaboration with physicians and pharmacists improved medication adherence rates to P2Y12 inhibitors following PCI and identified areas for process improvement to improve patient access to medication.

Presentation #77

Title: Reversible ECG Changes in the Setting of Chronic Cocaine Use

Presenter: Jeffrey Paul Chidester

Authors: Jeffrey Chidester, MD; Nicholas Brownell, MD; Jarett Berry, MD

Faculty Mentor: Jarett Berry

Abstract

Case Presentation: We present a case of a 59-year-old female with a past medical history of self-reported cocaine abuse, hypertension, pancreatitis, and ventricular fibrillation cardiac arrest who presented with a one-year history of non-exertional left-sided chest pain, increasing in frequency over the past several months. She described the pain as a tightness associated with diaphoresis and nausea. On initial examination in the Emergency Department, the patient was symptom-free with an unremarkable electrocardiogram and an undetectable troponin, as well as a negative urine toxicology screen. She admitted to cocaine use for several years prior to presentation, but none recently. While in the ED she experienced a transient episode of chest pain. ECG during this time demonstrated 2:1 AV block, ST elevation in leads II, III, and aVF, as well as ST depression in leads I and aVL. A repeat ECG obtained twenty seconds later, at a time when her pain had resolved, demonstrated reversal of these findings. The patient was admitted to the CCU service and started on treatment for ACS, followed by emergent coronary catheterization. Coronary angiography demonstrated no obstructive coronary lesions. Administration of oral calcium channel blockers led to complete resolution of her symptoms.

Discussion: This patient presented with chest pain and reversible ECG findings compatible with the diagnosis of an ST elevation myocardial infarction, likely due to vasospastic angina in the setting of chronic cocaine use. Her urine toxicology was negative for cocaine; however, she self-reported a several-year history of cocaine use, and one month prior to arrival had an episode of ventricular fibrillation arrest in which cocaine was found among her belongings. While ingestion of cocaine can acutely cause vasospasm and predisposes users to experience an acute coronary syndrome, in the case of this patient, chronic cocaine abuse appears to have predisposed her coronary arteries to vasospasm in the absence of acute intoxication. Her ECG demonstrates a dramatic example of the reversibility of ischemic changes that can be caused by coronary vasospasm.

Presentation #78

Title: Intravenous Immunoglobulin is Effective in Persistent Heparin-induced Thrombocytopenia

Presenter: Bryan Park

Authors: Bryan Park, MD; Monika Kumar, MD; Srikanth Nagalla, MD; Nicole De Simone, MD; Kavitha Donthireddy, MD; Richard H Aster, MD; Anand Padmanabhan, MD, PhD; Ravi Sarode, MD; Siayareh Rambally, MD

Faculty Mentor: Siayareh Rambally

Abstract

Background: Heparin induced thrombocytopenia (HIT) is a serious adverse drug reaction caused by transient antibodies against platelet factor 4-heparin complexes, resulting in platelet activation and potentially fatal arterial and/or venous thrombosis. Most cases of HIT respond to cessation of heparin and administration of an alternative non-heparin anticoagulant, but there are rare cases of persistent HIT, defined as thrombocytopenia due to platelet activation/consumption for greater than seven days on standard therapy. These patients remain at high risk for thrombotic events. Intravenous immunoglobulin has been used as an adjunct therapy for these refractory cases based on its ability to saturate FcγRIIa receptors on platelets, thus preventing HIT antibody binding and platelet activation.. Here we describe 2 cases of persistent HIT (ELISA OD >2.0, SRA strongly positive and persistent thrombocytopenia >7 days) with rapid response to IVIg with in-vitro experiments supporting the proposed hypothesis.

Methods: Pooled washed O blood group normal platelets (1 x 10e6) were treated with PF4 (3.75 mg/mL) for 20 min followed by 1-hour incubation with patients' sera. Platelet activation before and after addition of IVIg was evaluated by P-selectin expression.

Results: Decreased platelet activation was demonstrated in-vitro after the addition of IVIg to both patient samples, which corroborated with the rapid clinical response that each patient experienced.

Conclusion: Our study mechanistically supports the use of IVIg as an adjunct therapy for persistent HIT.

Presentation #79

Title: Primary Angiosarcoma Of Thyroid: Clinical Recognition May Help Early Diagnosis And Individualized Treatment Plan

Presenter: Ananya Kondapalli

Authors: Ananya Kondapalli, MD; Yin Htwe Oo, MD

Faculty Mentor: Yin Oo

<u>**Abstract**</u>

Angiosarcomas are malignant vascular tumors of endothelial origin and commonly seen in the skin and superficial soft tissue. Primary angiosarcoma at other sites including thyroid are less common and cytological diagnosis is challenging due to paucity of cells, presence of necrosis and rarity of disease. However, the cytological diagnosis is possible with high index of clinical suspicion and immunohistochemistry stain. A 55-year-old Caucasian man with atrial fibrillation on Rivaroxaban and hypothyroidism presented with sudden onset of left neck pain and swelling. Neck CT showed bilateral thyroid masses with displacement of trachea to the right. Thyroid ultrasound showed 3-4 cm irregular margin thyroid masses in both thyroid lobes with a diffuse micro-calcification and increased vascularity on right side and ring shaped macro-calcification inside the left thyroid mass. While waiting for FNA, he presented to the hospital with hemoptysis, changes in voice, increased fullness of the neck and odynophagia. FNA of bilateral thyroid masses showed malignant epithelioid cells with differential diagnosis of medullary thyroid cancer versus metastasis. Stains for calcitonin, TTF-1, thyroglobulin, CEA, and synaptophysin along with serum tumor markers such as CEA, chromogranin A and calcitonin were negative. PET-CT scan showed bilateral FDG avid thyroid lesions, FDG avid cervical and superior mediastinal lymphadenopathy, and FDG accumulation in the manubrium. The diagnosis of poorly differentiated sarcoma was made after positive stain for thrombomodulin, CD99, CD31, CD30 and SMA of cells from biopsy of manubrium. Majority of thyroid malignancies are epithelial in origin. Mesenchymal origin of primary thyroid angiosarcomas are rare and comprise 2-10% of all thyroid cancers. Thyroid angiosarcomas are more common in European Alpine region with iodine deficiency. Typical age of presentation is between 50 and 80 years of age and some have longstanding history of goiter. The presence of extrathyroidal extension (ETE) and distant metastasis at the time of presentation carry poor prognosis. Although diagnosis is commonly made after thyroidectomy, the awareness of this disease entity and requesting appropriate immunohistochemistry staining make early diagnosis possible and prevent surgical complications. Early diagnosis may have impact on clinical outcome and prognosis by enabling an individualized treatment plan.

Presentation #80

Title: What Defines an 'Adequate' Urine Collection?

Presenter: Ananya Kondapalli

Authors: Ananya Kondapalli, MD; Beverley Adams-Huet, MS; Naim Maalouf, MD

Faculty Mentor: Naim Maalouf

Abstract

Objective: 24-hour urine collections are widely ordered for measuring a variety of nutrients, hormones, and other analytes. Concomitant measurement of creatinine excretion adjusted for body weight (BW) is utilized to determine adequacy of 24-hour urine collection. However, use of reference ranges for daily creatinine excretion/BW that were established prior to the rising prevalence of obesity has resulted in a large proportion of contemporary individuals to appear to have an 'incomplete' urine collection. Our objective was to evaluate the range of creatinine excretion in adults by reviewing results of collections done in an inpatient research setting (to overcome the problem of incomplete collection) by individuals with a wide range of age, BW, and BMI. We analyzed data from participants in inpatient research studies conducted by the Center for Mineral Metabolism and Clinical Research at UT Southwestern from 2000-2017. We selected participants who completed two consecutive 24-hour urine while consuming a fixed metabolic diet of normal protein content. Linear regression models were constructed to predict 24-hr urine creatinine excretion from sex, age, weight, and height across a wide spectrum of BW and BMI. We reviewed 115 pairs of 24-hr urine collections from 50 female and 65 male participants. Urine creatinine excretion ranged 716-2018 mg/24-hr. Urine creatinine excretion/BW was within the widely used reference ranges of 15-20 mg Cr/kg BW for females and 20-25 mg Cr/kg BW for males in only 24.3% of all collections. The proportion of participants with creatinine excretion/BW below these reference ranges increased with greater BMI (45% for BMI 18-25 Kg/m2, 78% for BMI 26-30 Kg/m2, 70% for BMI 31-40 Kg/m2, and 100% for BMI > 40 Kg/m2). Reliable prediction of urine creatinine (within 85 mg/24-hr) was achieved from a linear combination of sex, age, weight and height by linear regression ($R^2=0.82$). Despite having monitored 24-hour urine collections in an inpatient setting, a majority of participants had creatinine/BW below the laboratory reference range. We propose revision of currently used criteria of adequacy of urine collection to account for the impact of obesity using our model. These findings have wide implications on patient care and research studies.

Presentation #81

Title: 'Biological Determinants of Circulating hs-cTnT and NT-proBNP in the Dallas Heart Study'

Presenter: Christopher W. Puleo

Authors: Christopher W. Puleo, MD; Colby Ayers, MS; James de Lemos, MD

Faculty Mentor: James de Lemos

Abstract

Background: The development of highly sensitive assays for cardiac troponin has demonstrated a significant prevalence of highly sensitive cardiac troponin T (hs-cTnT) in the general population, even in the absence of acute pathology. Several of these large general population studies have shown a continuous relationship between circulating hs-cTnT levels and the incidence of first cardiovascular event, heart failure and cardiovascular death. Similarly, prior work in a large general population cohort has shown that brain natriuretic peptide (BNP) and NT-proBNP are significantly associated with left ventricular hypertrophy (LVH) and left ventricular systolic dysfunction (LVSD). Moreover, multiple independent risk factors for elevated NT-proBNP (black race, LVH, LVSD, ESRD) also appear to be associated with increased circulating hs-cTnT. While additional large general population cohorts without history of cardiovascular disease have shown a correlation between hs-cTnT and NT-proBNP, the underlying mechanisms behind this association remain unclear. There has been limited available data comparing circulating levels of hs-cTnT and NT-proBNP in the same general population cohort. We measured circulating hs-cTnT and NT-proBNP in a contemporary multi-ethnic cohort with extensive cardiovascular phenotyping, with the goal of identifying their respective pathophysiological determinants in a population without known cardiovascular disease or active cardiac symptoms.

Methods: NT-proBNP and hs-cTnT were measured in 1877 individuals enrolled in both the Dallas Heart Study Phase 1 (2000 to 2002) and the Dallas Heart Study Phase 2 (2007 to 2009), a multi-ethnic, population-based cohort study with extensive cardiovascular phenotyping. Individuals with prior documented history or symptoms of CVD were excluded. Univariable analysis and linear regression models were used to identify associations between each biomarker.

Results: (in process) A Spearman correlation coefficient of 0.179 indicated that NT-proBNP and hs-cTnT are not directly correlated. However, when monitoring respective change for each biomarker between study phases, both were significantly correlated with age, coronary artery calcium score, BMI, and multiple measured correlates for LVH on MR. NT-proBNP and hs-cTNT were both inversely related to GFR and discordant with regard to LDL and systolic blood pressure.

Conclusion: Although not directly correlated, hs-cTnT and NT-proBNP share multiple mutual pathophysiological determinants which may indicate common biological mechanisms of production.

Presentation #82

Title: Efficacy, dysfunction, and mortality of endoscopic gastroduodenal stenting in patients with malignant gastric outlet obstruction

Presenter: Daniel Markowski

Authors: Daniel Markowski, MD; David Tang, MD; Deepak Agrawal, MD

Faculty Mentor: Deepak Agrawal

<u>**Abstract**</u>

Malignant gastric outlet obstruction (GOO) is highly morbid and can be treated with endoscopic gastroduodenal stenting. Stent placement has been widely established, yet the question of technical and clinical success remains unanswered. We aim to assess long term efficacy of gastroduodenal stenting, predictors of stent dysfunction, and overall mortality of these patients. We performed a retrospective cohort study of all patients referred for endoscopy for malignant GOO from 2011 through 2016 at a single center and followed until death or November 15, 2016. Clinical success was defined as a gastric outlet obstruction score ≥ 2. Stent dysfunction is defined as return of symptoms after initial stenting necessitating another endoscopic or surgical procedure. Kaplan Meier (KM) analyses of stent dysfunction and overall mortality were performed. Patients were censored at death, loss of follow up, or end of study. Cox proportional hazards modeling was used to assess for predictors of stent dysfunction. 56 of 57 patients (98%) received technically successful initial placement of 63 stents. 6 patients (11%) received multiple stents at initial EGD. No adverse events or deaths were directly due to endoscopy. 35 patients (62.5%) achieved clinical success. Presence of liver metastases was a negative predictor of clinical success on multivariate logistic modeling. 10 patients (18%) suffered stent dysfunction. Of the 9 patients to receive repeat endoscopy for stent dysfunction, 6 received 1 more stent, 1 received 2 more stents, and 1 received 3 more stents. KM stent dysfunction curve yielded a median dysfunction time of 292 days. Cox proportional hazards modeling did not identify any predictors of stent dysfunction among age, sex, presence of ascites, presence of liver metastases, or length of initial stenting. Only 3 patients (5%) were confirmed alive at the end of the study and 32 patients (57%) were confirmed dead. KM survival curve yielded a median overall survival after initial stenting of 102 days. Gastroduodenal stenting for malignant GOO is highly technically successful. Only a small minority of patients suffer from eventual stent dysfunction. Overall mortality from baseline malignancy remains high and most patients are able to be palliated with one stent before death.

Presentation #83

Title: Epidemiology of Invasive Fungal Disease in Lung Transplant Recipients

Presenter: Christina Yek

Authors: Christina Yek, MD; Xie D, Barros N, Liu T, B. Adams-Huet, MS; Ricardo La Hoz, MD

Faculty Mentor: Ricardo La Hoz

Abstract

Introduction: The incidence of invasive fungal disease (IFD) in lung transplant (LT) recipients is reported at 4-13%. Despite advances in diagnostic and therapeutic tools, mortality remains high. This study aimed to describe the epidemiology of IFD in LT recipients at a large academic center.

Methods: This retrospective single center cohort study included all first-time LT recipients transplanted between 2010 and 2016 at the University of Texas Southwestern Medical Center in Dallas, TX. Data mining tools were used to extract data from electronic medical records and merge it with information from the Scientific Registry of Transplant Recipients (SRTR). Medical records of subjects with positive fungal serologies, cultures or histopathology were manually adjudicated using EORTC/MSG Consensus Group definitions. The 1-year cumulative incidence was calculated using the Kaplan-Meier method.

Results: A total of 397 patients met inclusion criteria. The cohort was predominantly male (60%) and white (84%) with median age 60 (interquartile range 51-66). The most common pre-transplant diagnosis was interstitial lung disease (51%), followed by chronic obstructive lung disease (26%) and cystic fibrosis (10%). Incidence of IFD at 365 days post-transplant was 17% (n=69). Proven cases (n=47) constituted 68% while probable cases (n=22) made up 32% of all IFD cases. Aspergillus (n=34, 49%) was the most common fungal pathogen, followed by Candida (n=24, 35%). IFD locations included pulmonary parenchymal (n=26, 38%), tracheobronchial (n=17, 25%), pleural/pericardial (n=10, 14%), bloodstream (n=7, 10%), skin/soft tissue (n=5, 7%), and intra-abdominal (n=4, 6%). Patients who developed IFD were more likely to be male (75% vs 56% with no IFD, p=0.004) and CMV discordant with their donor (62% vs 44%, p=0.005). Mortality at 12 weeks after diagnosis of IFD was 12%. Incidence of IFD was associated with incidence of CMV disease within 365 days of transplant (p=0.001), as well as all-cause mortality (p=0.05).

Conclusion: IFD is a frequent complication after lung transplantation. Efforts to identify risk factors may help guide the development of targeted interventions to reduce the burden of IFD in this vulnerable population.

Presentation #84

Title: Elevated Plasma Lymphotoxin Beta Receptor Levels and Subsequent Diagnosis of Gastrointestinal Cancer

Presenter: Colin Bergstrom

Authors: Colin Bergstrom, Muhammad Beg, MD; Colby Ayers, MS; Arjun Gupta, MD; Ian J. Neeland, MD

Faculty Mentor: Ian Neeland

Abstract

Background: Lymphotoxin beta receptor (LTBR) is a member of the tumor necrosis factor receptor superfamily. LTBR is expressed on several cell types including mucosal epithelium but not T or B lymphocytes. Immune activation of LTBR with resultant signaling mediates pathways of cell death and proliferation. In vitro studies have implicated LBTR signaling in carcinogenesis. The relationship of LTBR with cancer diagnosis in a large population-based cohort is unknown.

Methods: 3,119 participants with and without history of cancer enrolled in the Dallas Heart Study (DHS) between 2000 to 2002 and underwent a baseline measurement of plasma LTBR. Participants (3,032) without a diagnosis of cancer at the time of enrollment were followed longitudinally for 12 years for a new diagnosis of cancer. The Texas Cancer Registry was linked to the DHS allowing for identification of prevalent cancer (diagnosis within 1 year of enrollment) or incident cancer (diagnosis after 1 year of enrollment).

Results: 191 participants had prevalent cancer history (PC+) and 178 participants without baseline cancer developed a cancer (IC+) at follow-up. LTBR (median, ng/mL) levels were higher in subjects with PC+ compared to subjects without prevalent cancer (PC-): 1.20 vs 1.00, p<0.001 as well as in those with IC+ compared to IC-: 1.10 vs 1.00, p<0.002. After adjustment for age, sex and race/ethnicity these relationships were no longer significant. When analyses were performed by type of cancer: gastrointestinal (GI), breast, and prostate, LTBR remained associated with GI PC+ vs GI PC-: HR, 95% CI: 2.64, 1.23-5.68, p=0.013 and GI IC+ vs GI IC-: 2.65, 1.27-5.54, p=0.009 after adjustment for age, sex, and race/ethnicity. Relationships for breast and prostate cancer were not significant. Median follow-up for GI IC+: 5.9[IQR:2.8,8.9] years.

Conclusions: Elevated plasma LTBR levels are associated with both prevalent and incident GI cancer. Moreover, the antecedent elevated LTBR level years prior to the diagnosis of GI cancer combined with in vitro studies by other investigators suggests a role for LTBR in the pathogenesis of GI cancer. This finding may provide insight into the tumor microenvironment and be potentially useful for risk stratification of GI cancer by utilizing a circulating immune biomarker.

Presentation #85

Title: Revascularization Patterns of Systolic Heart Failure in a Large Urban County Hospital

Presenter: Christopher B. Scoma

Authors: Christopher Scoma, MD; Kimberly Berger, MD; Rebecca Vigen, MD; Sandeep Das, MD

Faculty Mentor: Sandeep Das

Abstract

Background: Coronary angiography is frequently performed after heart failure diagnosis to determine etiology and revascularization strategy. Surgical revascularization conveys a mortality benefit as compared to medical therapy, and the role of percutaneous coronary intervention (PCI) is not established. The aim of this study is to describe revascularization patterns among patients presenting with systolic heart failure.

Methods: We evaluated patients with symptomatic heart failure with reduced ejection fraction (HFrEF) without acute coronary syndrome (n=150; average left ventricular ejection fraction of 25%) who underwent coronary angiography between 2011 and 2015. Primary outcomes included intervention (PCI, CABG, or medical therapy [MT] alone) as well as referral for CABG.

Results: Among patients presenting with clinical evidence of HFrEF who were sent for coronary angiography, 78% (n=78) had evidence of CAD. Thirty-six percent of patients with CAD (n=28) were classified as having surgical disease (two-vessel disease including left-main or proximal left anterior descending artery, or three-vessel disease), while 64% had non-surgical CAD. Among patients with non-surgical disease, 78% (n=39) underwent PCI, while 22% (n=11) received medical therapy (MT) only. Of patients with surgical CAD, 78.6% (n=22) underwent PCI, 35.7% were referred for CABG, 14.3% (n=4) underwent CABG, and 7.1% (n=2) received MT only.

Conclusion: Patients with HFrEF sent for cardiac catheterization have a high prevalence of significant CAD. The majority of patients with evidence of either surgical or non-surgical CAD during coronary angiography underwent revascularization, with PCI being the dominant revascularization method.

Presentation #86

Title: Pilot Study of a Half-Day Mini-Curriculum to Improve Resident Confidence In Conducting Goals of Care Discussions

Presenter: Dheepa Sekar

Authors: Dheepa R. Sekar, MD; Lauren N. Smith, MD; Caitlin Siropaides, MD; Oanh K. Nguyen, MD

Faculty Mentor: Oanh Nguyen

Abstract

Background: Although goals of care discussions are an integral component of patient care, and require proficiency in patient communication skills, residents receive limited observation, feedback, or experiential training in these skills. Existing goals of care curricula include training modules spanning multiple days, limiting broad dissemination and implementation given the time constraints of many residency programs. Thus, we sought to develop, pilot, and evaluate the effect of a focused, half-day mini-curriculum on resident attitudes and confidence in conducting goals of care discussions.

Methods: We conducted a single-site pilot study in the internal medicine residency program at UT Southwestern in Dallas, Texas from March through April 2017. Our curriculum consisted of: 1) a didactic lecture to introduce the 'SPIKES' framework for breaking bad news (1-1.5 hours); and 2) small group breakout sessions for guided practice in: a) succinctly summarizing a complex hospital course for patients and families; b) anticipating and responding to emotional responses with empathy; and c) eliciting patient priorities to make code status recommendations (1.5-2 hours). We conducted a pre-post survey analysis of resident attitudes towards training and confidence in leading goals of care discussions, with survey responses reported on a five-point Likert scale.

Results: Of 184 total residents, 109 residents (59%) participated in the curricular intervention. Residents reported an improvement in their overall confidence in leading goals of care discussions after the intervention (3.6 ± 0.9 vs. 4.1 ± 0.6, $p<0.001$), with the largest improvements in confidence responding to emotions (3.5 ± 0.9 vs. 3.9 ± 0.6, $p=0.005$), making care recommendations to families (3.5 ± 1.0 vs. 3.9 ± 0.7, $p<0.001$), and quickly conducting an effective code status discussion (3.6 ± 1.0 vs. 4.0 ± 0.7, $p<0.001$). Additionally, residents reported an increased in desire for supervision (3.7 ± 1.0 vs. 4.0 ± 1.0, $p=0.03$) and feedback (4.0 ± 0.9 vs. 4.2 ± 0.8, $p=0.05$) during goals of care discussions

Conclusions: A single session mini-curriculum improves resident confidence in goals of care discussion skills and attitudes towards supervision and feedback during these discussions, creating a foundation for additional training interventions. Additional experiential training opportunities and observation are likely needed to influence resident competence in these communication skills.

Presentation #87

Title: Be still, my beating heart! A perplexing confusion, a confounding effusion

Presenter: Allexa Allyn Hammond

Authors: Allexa Hammond, MD; Wanpen Vongpatanasin, MD

Faculty Mentor: Wanpen Vongpatanasin

<u>**Abstract**</u>

Case Presentation: A 32 year old male with Down Syndrome (DS) and a ventral hernia presented with 3 months of dyspnea, behavioral changes and abdominal pain. He was noted by family to be less communicative and combative. A lacy-appearing rash appeared on both legs, for which he was given antibiotics without relief. He did not have fevers, chest pain, vomiting or hematochezia. On admission, the patient was hypothermic and bradycardic. Distant cardiac sounds, reducible hernia and livedo reticularis rash were found. X-ray incidentally noted an enlarged cardiac silhouette; EKG revealed bradycardia with low voltage QRS. Echocardiogram showed a large pericardial effusion with evidence of compression of the right ventricle's free wall, consistent with cardiac tamponade. Pericardiocentesis yielded 1950 cc of serous fluid. Diagnostic work-up identified a TSH of 285.9 and a free T4 of 0.1. Intravenous levothyroxine was given with eventual transition to the oral form after evidence of recovery in thyroid function. The patient was back to his baseline upon follow-up in Endocrinology clinic, and was then lost to follow-up before an echocardiogram could be performed after discharge.

Discussion: The estimated prevalence of hypothyroidism in DS (13% to 63%) is much greater compared to the general population (1% to 2%). Although many cases are diagnosed by adolescence, there are some that do not manifest until adulthood. Many signs of hypothyroidism share similar features to those of DS, which makes the diagnosis more challenging. For example, the presence of short stature, macroglossia or delayed cognition may be found in both conditions. In addition, studies have argued that the presence and size of a pericardial effusion relates to the chronicity and severity of hypothyroidism. In this case, the patient likely had hypothyroidism for a long period. Barriers to diagnosis may have included atypical signs of hypothyroidism (i.e. irritability, muted speech, rash) and difficulty in obtaining a history. Thus, in addition to yearly screening for hypothyroidism in DS patients, the internist should have a lower threshold for suspecting hypothyroidism in this population, and promptly treat after diagnosis to avoid the dangerous sequelae associated with this condition.

Presentation #88

Title: A violaceous neck mass in an HIV patient- lymphoma or red herring?

Presenter: Allexa Allyn Hammond

Authors: Allexa Hammond, MD; Nilum Rajora, MD

Faculty Mentor: Nilum Rajora

<u>**Abstract**</u>

Case Presentation: A 45 year old male with HIV/AIDS (CD4 109 cells/microliter, viral load 5573 copies/milliliter, recently started on anti-retroviral therapy) presented with a one month history of an enlarging, non-tender, right-sided neck mass associated with fevers. He had been treated with doxycycline without effect. On admission, the patient was febrile (100.4° F) and tachycardic with a ten centimeter, erythematous and fluctuant right-sided neck abscess. Cervical, retropharyngeal and supraclavicular lymphadenopathy were confirmed on CT imaging. A lymph node biopsy obtained via fine needle aspiration in addition to two out of three acid fast bacilli sputum cultures were positive for Mycobacterium avium-intracellulare complex (MAC). The patient was thus diagnosed with MAC lymphadenitis with pulmonary involvement and started on rifabutin, ethambutol and azithromycin. The patient was discharged in stable condition; upon follow-up in clinic, there was a noted decrease in the size of the abscess with ongoing active drainage exhibiting appropriate response to therapy.

Discussion: Found in soil- and water-rich environments, MAC is an opportunistic infection often affecting HIV/AIDS patients with a CD4 count below 50 cells/microliter. Although one may commonly treat for MAC in the setting of active pulmonary infection, one may not commonly encounter a patient with lymphadenitis in the setting of MAC infection as the primary symptom. Also known as scrofula, mycobacterial lymphadenitis (historically more commonly associated with mycobacterial tuberculosis) characteristically presents as a painless and violaceous mass with slow growth over a period of several weeks. The mass eventually becomes fluctuant and may start to openly drain; the patient may also experience low grade fevers. Given the relatively non-specific physical examination findings, the provider may be inclined to consider more commonly diagnosed conditions before considering mycobacterial infection, such as lymphoma or pyogenic abscess due to S. aureus or Streptococcus species; however, this may lead to a misdiagnosis and delay in proper treatment. In all, the clinician should take note that mycobacterial infections may imitate many of the clinical features associated with other pathologies. To avoid a misdiagnosis, there should be a very low threshold to evaluate for mycobacterial infection in HIV/AIDs patients, particularly in the appropriate clinical context.

Presentation #89

Title: Bacterial infection or a diagnosis more elusive? Discovering a case of HLH in a febrile patient with abdominal pain

Presenter: Allexa Allyn Hammond

Authors: Allexa Hammond, MD; Catherine Chen, MD

Faculty Mentor: Catherine Chen

Abstract

Case Presentation: A 54 year old male with end stage renal disease and recently diagnosed Clostridium difficile colitis on oral vancomycin presented with recurrent diarrhea, abdominal pain and fevers. The patient denied any sick contacts or recent travel. The patient was febrile to 103°F with tachycardia and hypotension; physical exam findings were notable for jaundice, diffuse abdominal pain and hyperactive bowel sounds. Lactate was 4.4 with transaminitis (AST 253 U/L, ALT 115 U/L), pancytopenia, elevated triglycerides and significantly elevated ferritin (37,523 ng/mL). The patient was initially admitted to the floor and placed on broad spectrum antibiotics for presumed bacterial infection, however quickly decompensated and was transferred to the intensive care unit for pressor support, continuous renal replacement therapy and intubation in the setting of multi-organ system failure. Clostridium difficile PCR, bacterial and fungal cultures returned negative. Concerns for hemophagocytic lymphohistiocytosis (HLH) encouraged further diagnostic work-up, with a bone marrow biopsy showing erythrophagocytosis and an exceedingly rare lymphoma known as systemic EBV-positive peripheral T-cell lymphoma of childhood. The patient was emergently started on dexamethasone, however the patient passed before full initiation of chemotherapy.

Discussion: HLH is a macrophage-driven immune hyperactivation more commonly diagnosed in the pediatric population, however can manifest in adults as well. HLH in adults arises most often from a secondary cause, such as infection (i.e. EBV, HIV), malignancy or autoimmune conditions. Those who have a malignancy-associated HLH generally have a poorer prognosis, particularly T-cell lymphomas as was the case in our patient. Five out of eight criteria must be met for diagnosis (including fevers, pancytopenia, hypertriglyceridemia, elevated ferritin, splenomegaly, elevated soluble CD25, erythrophagocytosis and depressed NK cell activity). Many of the criteria are non-specific, and thus affected patients are often mistaken to have a systemic infection rather than HLH, ultimately delaying diagnosis and appropriate treatment. Such an error may be fatal, as HLH is a condition with a rapid course of progression and high risk for mortality if not promptly addressed. Given the fulminant course of this condition, it is thus prudent to have a low threshold to evaluate for HLH in the appropriate clinical context.

Presentation #90

Title: Symptomatic Hypocalcemia due to Plasma Exchange for Hyperlipidemia-Induced Pancreatitis

Presenter: James Keeton

Authors: James Keeton, MD; Vivek Patel, MD

Faculty Mentor: Vivek Patel

Abstract

Case Presentation: A 48-year-old Hispanic man with a self-reported history of gastrointestinal cancer status post right hemicolectomy 25 years ago and recurrent small bowel obstructions presented with 2 days of midepigastric abdominal pain worse with eating and associated nausea and vomiting. Of note, he reported moderate alcohol use but no recent binges. Vital signs were significant for tachycardia, fever and mildly overweight body mass index. Noteworthy findings on physical exam included no jaundice, non-icteric sclera, tachycardic rate, and severe tenderness to the midepigastrium without signs of peritonitis. Remarkable laboratory studies include white blood cell count of 14x109/L, total calcium of 7.7 mg/dL, lipase greater than 600 units/L, and triglyceride level greater than 4425 mg/dL. Computed tomography of the abdomen and pelvis with contrast revealed pancreatic edema with diffuse peripancreatic inflammation and hepatic steatosis with hepatomegaly. There was no evidence of cholestasis or choledocholithiasis. He was subsequently started on therapeutic plasma exchange (TPE) with 5% albumin infused with calcium gluconate using a citrate-based anticoagulant. However, he experienced chest pressure, worsening abdominal pain, and severe bilateral arm pain and contractures during the procedure. The total calcium drawn during the procedure was 6.3 mg/dL and required replacement. Ultimately, the procedure was discontinued prematurely due to severe hypocalcemic symptoms and around 3 liters of milky white plasma was removed. A repeat lipid panel the following morning showed a triglyceride level of 1315 mg/dL. He was then started on gemfibrozil 600 milligrams twice a day, which was eventually changed to fenofibrate 67 milligrams daily due to elevated transaminase enzymes with improvement in triglyceride levels to 327 mg/dL on discharge.

Discussion: Acute pancreatitis is a common condition, but is much less commonly precipitated by very severely elevated triglyceride levels, usually greater than 1000 mg/dL. There is a role for TPE to decrease circulating triglycerides leading to symptomatic improvement and possibly decreased mortality. However, as was experienced in this patient, symptomatic hypocalcemia is a relatively common complication of TPE. Therefore, calcium levels should be closely monitored and prophylactically included in the replacement fluids during the procedure to decrease the incidence of hypocalcemic toxicity.

Presentation #91

Title: Reducing Wait Time Between Admission and Chemotherapy Initiation

Presenter: Jenny Jing Li

Authors: Jenny J Li, MD; Arjun Gupta, MD; Bernard Tawfik, MD; Thao M Pham, PharmD; Sudarshan S Pathak, RN; Prabhjyot Singh, RN; Esmaeil Porsa, MD; Navid Sadeghi, MD; Hsiao C Li, MD

Faculty Mentor: Hsiao Li

Abstract

Background: Reducing the length of stay (LOS) is a high priority objective for all healthcare institutions. Delays in chemotherapy initiation for planned pre-admissions lead to patient dissatisfaction and prolonged LOS.

Methods: A multidisciplinary team was formed as part of the ASCO Quality Training Program. We aimed to reduce the time to initiation of chemotherapy from patient arrival to Parkland Hospital from a median of 6.2 hours at baseline, to 4 hours over a 6-month period (35% reduction). The team identified inconsistency in blood work requirements, poor communication, and non-standard patient arrival times as key delays in the process. Plan-Do-Study-Act (PDSA) cycles were implemented based on identified improvement opportunities. The outcome measure was time from arrival to chemotherapy start. Data were obtained from time stamps in the electronic health record.

Results: The first PDSA cycle included patient reminders to arrive at a specific time, improved communication using a smartphone secure messaging application, and the oncology fellow writing a pre-admit note detailing whether fresh labs were needed on admission prior to starting chemotherapy. Baseline data from 36 patients and postimplementation data from 28 patients were analyzed. Median time from admission to chemotherapy initiation pre-process change was 6.2 hours and 3.2 hours post-change. A sustained shift in the process was apparent on a control chart.

Conclusion: Delays in initiation of chemotherapy can be prevented using classic quality improvement methodology and a multidisciplinary team. We aim to further refine our PDSA cycles and to ensure sustainability of change.

Presentation #92

Title: Exploring the metabolism of acetate in early stage breast cancer

Presenter: Jenny Jing Li

Authors: Jenny Jing Li, MD; Tomoyuki Mashimo, PhD; Kumar Pichumani, PhD; Vamsidhara Vemireddy, MD; Barbara Haley, MD; Venetia Sarode, MD; Roshni Rao, MD; Craig Malloy, MD; Robert Bachoo, MD, PhD; Elizabeth Maher, MD, PhD

Faculty Mentor: Elizabeth Maher

<u>Abstract</u>

Background: A hallmark of cancer involves the reprogramming of metabolic pathways. Historically, studies of cancer metabolism have focused on the breakdown of glucose. However, recent studies have shown that acetate can also serve as a bioenergetic substrate for the citric acid cycle in aggressive brain tumors. ACSS2 (acyl-CoA synthetase short-chain family member 2), a downstream target of SREBP (sterol regulatory element-binding proteins), is an enzyme that converts acetate into acetyl-CoA and is elevated in the brain tumors that oxidize acetate. It is unknown whether overexpression of ACSS2 and oxidation of acetate is an adaptation in aggressive tumors or a more general feature of cancer. To address this question, we undertook a metabolic study in early stage non-metastatic breast cancer patients in vivo.

Methods: Patients with a diagnosis of early stage breast cancer were enrolled in an IRB-approved clinical protocol. Patients were infused with either [U-13C]glucose or [1,2-13C]acetate during surgery for 120-180 minutes. 13C-NMR and ACSS1, ACSS2, SREBP1, SREBP1/2 immunohistochemistry were performed on resected tumor samples. Blood was collected for determination of circulating labeled substrate. Fraction of infused substrate that was present in glutamate was calculated from 13C-NMR since it reflects entry of substrate into the citric acid cycle. Immunohistochemistry scoring was based on area of staining and staining intensity (H score). Tumor stage, histology, cellular proliferation, and estrogen receptor (ER)/progesterone receptor (PR)/HER2 status were collected.

Results: Twenty patients were enrolled; half each received 13C-glucose or 13C-acetate. In striking contrast with 13C-glucose, 13C-acetate was readily oxidized in the citric acid cycle whereas almost all infused glucose was converted to lactate. Immunohistochemical analysis demonstrated significantly increased ACSS2 staining in all cases (H score: ACSS2, 153.1±38.3 vs ACSS1, 29.6±7.4, SREBP1, 48.1±12.0, SREBP1/2, 12.3 ± 3.1, p<0.001). No significant differences were found among histological subtypes for glucose and acetate oxidation or immunohistochemistry of ACSS2.

Conclusion: Metabolic reprogramming of substrate utilization appears to be an early event in breast cancer, independent of histological subtype and tumor aggressiveness. The uniform elevation of ACSS2 suggests that this pathway may be a potential treatment target.

Presentation #93

Title: Effective use of electronic medical record (EMR) data in analysis of association between KRAS mutations and depression in colorectal cancer patients

Presenter: Jenny Jing Li

Authors: Jenny Jing Li, MD; Jessica Harper, Hong Zhu, PhD; Nizar Bhulani, MD; Chad Michael Guenther, MD; Alejandra Madrigales, MS CTR; Samantha Gates, Syed Kazmi, MD; Udit Verma, MD; Marisa Toups, MD; M. Shaalan Beg, MD

Faculty Mentor: Muhammad Shaalan Beg

Abstract

Background: Previous studies have demonstrated that KRAS mutations were associated with higher rates of depression in patients with metastatic colorectal cancer (CRC). The objective of this study was to evaluate the feasibility of extracting EMR data to examine the association between KRAS mutations and positive screening test for depression in CRC patients.

Methods: Retrospective review of stage I to IV CRC patients seen between 2011and 2015 at an academic, NCI-Designated Comprehensive Cancer Center was performed. At each clinic visit, depression was assessed using the Patient Health Questionnaire-2 (PHQ-2), which is part of the institution's universal Distress Screening tool. PHQ-2 score of 2 and above was considered positive screening test for depression. PHQ-2 and KRAS mutation data were extracted from the EMR via the Clinical Data Exchange Network bioinformatics tool and confirmed by retrospective chart review. Chi-square test was used to assess the association between KRAS mutation and depression. Multiple imputation was used to impute the missing values.

Results: Of the 484 CRC patients, KRAS status was known in 45 cases: 22 (49%) were KRAS mutated and 23 (51%) were KRAS wild type. PHQ-2 score was 0 in 42 cases (93.3%), 1 in 2 cases (4.4%), and ≥2 in 1 case (2.3%). The rate of positive PHQ-2 for KRAS mutated vs wild type was 4% vs 0% (p = 0.36). The result based on 50 imputed datasets suggests a trend towards an association between KRAS mutation and depression (p = 0.09).

Conclusions: This study did not demonstrate an association between KRAS mutation and depression in patients with colorectal cancer, probably due to a high proportion of missing data. Bioinformatics studies that extract and analyze EMR data are a feasible and effective platform to assess the association of genomic data with clinical outcomes. Additional validated algorithms and data are needed to further optimize such studies.

Presentation #94

Title: Sedentary Behavior and Subclinical Cardiac Injury: Results from the Dallas Heart Study

Presenter: Josephine Harrington

Authors: Josephine L Harrington, MD; Colby Ayers, MS; Jarrett Berry, MD; Tobjorn Omland, MD, PhD; Ambarish Pandey, MD; Stephen Seliger, MD, MS; Christie Ballantyne, ND; Jacquelyn Kulinski, MD; Christopher deFilippi, MD; James de Lemos, MD

Faculty Mentor: James de Lemos

Abstract

Background: Subclinical myocardial damage, detectable as chronic elevations in high-sensitivity troponin T (hs-cTnT) and I (hs-cTnI), is associated with higher rates of new-onset heart failure and mortality, even in patients without symptoms or known cardiovascular disease. Multiple studies have observed that increased physical activity and higher fitness reduce both high sensitivity troponin levels and incident heart failure. 1-4 Recent research suggests that time spent in sedentary behavior may contribute to heart failure risk independent of time spent performing moderate to vigorous physical activity (MVPA).3,5 We therefore hypothesized that increased sedentary time would be associated with higher levels of hs-cTnT and hs-cTnI.

Methods: To test this hypothesis, we performed a cross-sectional study using participants from Phase 2 visit of the Dallas Heart Study who worn an accelerometer to measure their activity levels, and with plasma measurements of either hs-cTnT or hs-cTnI. Participants with known CVD or cardiovascular symptoms including chest pain, shortness of breath, or recurrent lower extremity edema were excluded. Associations between sedentary time and hs-cTnT and hs-cTnI were assessed in linear regression analyses adjusting for age, sex, race/ethnicity and time spent in MVPA (Model 1), and then additionally adjusting for chronic kidney disease, BMI, hypertension, and diabetes (Model 2), and finally adjusting for left ventricular mass and end diastolic volume (Model 3).

Results: Sedentary activity positively correlated with hs-cTnI (Rho = 0.09, p<0.0001) and hs-cTnT (Rho =0.10, p=0.001).Associations between sedentary time and hscTnT as well as hsTnI remained statistically significant after adjusting for the demographic, comorbidity and cardiovascular risk factors described above (Model 3, hs-cTnI: Beta 0.076 p=0.04; hs-cTnT: Beta 0.087, p=0.02) . Associations between MVPA and hs-cTnI and hs-cTnI did not persist after adjusting for confounders (Model 3, hs-cTnI: Beta -0.012 p=0.74 and hs-cTnT: Beta 0.047 p=0.2).

Conclusions: Our results suggest that increased sedentary time is associated with chronic myocardial injury, as evidenced by increases in high-sensitivity troponin, independent of MVPA and other potential confounders. Additional studies are necessary to assess whether reducing sedentary time may reduce myocardial injury and therefore diminish the risk of future heart failure.

Presentation #95

Title: Does Acute Hepatitis C Ever Lead to Acute Liver Failure?

Presenter: Giuliana Cerro

Authors: Giuliana Cerro Chiang, Daniel Ganger, R. Todd Stravitz, A James Hanje, Michelle Gottfried, Jody Rule, William M Lee, MD

Faculty Mentor: William Lee

Abstract

Background: While hepatitis A and B commonly cause acute liver failure (ALF), hepatitis C rarely appears to do so, at least in the United States. Given the 4 million carriers of hepatitis C in the US alone, it seems surprising that clear-cut cases of HCV-related ALF have not been described. The ALFSG registry contains detailed clinical and serological data on more than 3,000 patients enrolled between 1998 and 2016 with ALF or acute liver injury (ALI). We probed this database for cases that might be attributed to hepatitis C and adjudicated these based on data available.

Methods: All patients enrolled in the ALFSG registry who also had had hepatitis C antibody or RNA testing were reviewed; those with positivity for either or both were further examined to determine whether acute hepatitis C was present and might have been responsible for their ALF. Demographic information, etiology, transplant, comorbidities, complications, vital signs, imaging and lab data were reviewed on those positive for hepatitis C antibody and/or RNA. Results Of the 3015 patients included in the cohort, 2546 were tested for HCV antibody, of whom 144 were positive (5.65%). Of these, 85 were tested for HCV RNA and 42 were positive. Among this group, 27 (64%) were determined to have acute liver failure/injury secondary to acetaminophen (APAP) toxicity, 13 were classified as either shock liver, indeterminate or another etiology and 3 as possible hepatitis C. However, only one case was believed to represent primary acute hepatitis C as the cause of the ALF (0.033%). Even this patient was complicated by severe NAFLD on biopsy (not cirrhosis); the other one was confounded by concomitant APAP use, while the 3rd patient was both hep C antibody and RNA positive prior to admission and negative for both during the hospitalization <1 week later (possible lab error).

Conclusion: Many ALF patients are hepatitis C antibody positive or have chronic hepatitis C; however, hepatitis C virus virtually never causes ALF primarily, but may play a combined role, with fatty liver, APAP or other hepatic diseases.

Presentation #96

Title: Granulomatosis with Polyangiitis Masquerading as Hypertension at a Health Fair

Presenter: Emmanuel Terance Johnson

Authors: Emmanuel Johnson, MD

Faculty Mentor: Henry Quinones

<u>**Abstract**</u>

Case Presentation: Hypertension is a common comorbidity in patients presenting for acute care that can be part of a constellation of common diagnoses representing a devastating multi-system autoimmune disease. A 64 year old female with hypothyroidism was diagnosed with hypertension at a health fair two months prior to presentation and treated with Metoprolol, Amlodipine, and Losartan by her PCP. She reported a lifetime of good health and normotension. She presented to an outside hospital, diagnosed with pneumonia, and treated with pipercillin-tazobactam. Hospitalization was complicated by worsening acute kidney injury. She was transferred to Clements. Initial physical examination significant only for cough. Admission creatinine 3, UA with protein, blood, and WBCs. Subsequent examination of urine sediment showed muddy brown cast, no RBC casts. Admission CXR with a LLL infiltrate. Serologic workup positive for C-ANCA and proteinase-3 antibodies. She was later transferred to the ICU for rapidly increasing oxygen requirements, renal failure (creatinine peaked 8) and worsening infiltrates on CXR that progressed to DAH. She received broad spectrum antibiotics, stress dose steroids, plasma exchange, 3 sessions of hemodialysis, and Rituximab. Kidney biopsy showed PR3-ANCA associated necrotizing cresentic glomerulonephritis. With marked renal recovery she was discharged off hemodialysis, started on Azathioprine with a creatinine of 2.3 on outpatient follow up.

Discussion: Heuristic are mental algorithms we as physicians employ to make decisions in patient care. Under pressure of time, stress, and fatigue they are integral to contemporary medicine. Influenced by what is typically true and prejudiced by what easily comes to mind, common symptoms and signs often lead to common diagnoses. But what happens when a patient doesn't fit into our mental templates? In this case, availability and representativeness error could have cost this patient her life. The arrogation in medicine is that we know how to think, but often we don't. We must make it incumbent upon ourselves as physicians to be aware of cognitive bias and in every patient encounter ask ourselves could it be something else?

Presentation #97

Title: A Retrospective Analysis of Mantle Cell Lymphoma in the First Remission

Presenter: Danny Guidot

Authors: Daniel Guidot, MD; Jeffrey Switchenko PhD; Loretta Nastoupil MD; Jean Koff MD; Kristie Blum MD; Joseph Maly MD; Christopher Flowers MD; Jonathon Cohen MD

Faculty Mentor: Jonathan Cohen

Abstract

Background: Mantle cell lymphoma (MCL) is a heterogeneous disease with high rates of relapse. There are limited data guiding the use of surveillance imaging in MCL following successful initial treatment. We evaluated surveillance imaging in MCL patients in first remission in a multi-center analysis.

Methods: We constructed a retrospective cohort from two academic institutions that included patients with previously untreated MCL who completed first-line therapy and underwent follow-up to evaluate relapse patterns and test characteristics of surveillance imaging. Patients were stratified by whether relapse was diagnosed by clinical signs/symptoms or by surveillance imaging; the two groups were compared using Kaplan-Meier survival curves. Additionally, 801 surveillance imaging studies for patients in first remission were evaluated for positive predictive value (PPV) and number needed to treat (NNT) to detect one asymptomatic relapse.

Results: Of 217 patients, 102 had a fully documented relapse, with 38 (37%) diagnosed by surveillance imaging and 64 (63%) by non-imaging clinical surveillance. There was no significant advantage in overall survival (OS) from diagnosis date (hazard ratio [HR] 0.80, p=0.39) or relapse date (HR 0.72, p=0.22) when relapse was detected by surveillance imaging. Of 801 surveillance images, PET/CTs had a PPV of 24% and NNT of 51, and CTs had a PPV of 49% and NNT of 24.

Conclusions: Surveillance imaging by PET/CT or CT for MCL after successful first-line therapy lack clinical benefit, and routine use is discouraged. Novel approaches are needed for monitoring these patients to establish strategies that can impact survival.

Presentation #98

Title: Racial and Ethnic Differences in Cardiac Biomarkers

Presenter: Eddie Hackler III

Authors: Eddie Hackler III, MD; Colby R Ayers, MS; Jeanney Lew, MD; Kamakki Banks, MD; Darren K McGuire, MD, MHSc; Amit Khera, MD, MSC; Anand Rohatgi, MD; Ian Neeland, MD; James A. de Lemos, MD

Faculty Mentor: James de Lemos

<u>**Abstract**</u>

Background: The incidence and clinical manifestations of cardiovascular disease (CVD) differ between blacks and whites. Blacks have increased rates of heart failure, PVD, DVT and stroke but decreased rates of atrial fibrillation. Whites have more advanced coronary atherosclerosis but similar or lower rates MI. Currently there is limited understanding of pathophysiological mechanisms underlying these racial differences. Investigation of racial and ethnic differences in biomarkers associated with CVD may provide insights into biological pathways contributing to these racial and ethnic differences.

Methods: A cross-sectional analysis was performed using data from the Dallas Heart Study, a multi-ethnic probability based cohort study. Participants with existing CVD were excluded. Associations between race/ethnicity (African American, Caucasian and Hispanic) and 30 distinct biomarkers were evaluated using multivariable linear regression adjusting for age, race, traditional CVD risk factors, MRI and DEXA measures of body composition and fat distribution, renal function, insulin resistance, LV mass by MRI, and socioeconomic factors.

Results: The study population included 3,214 individuals, mean age 43, 51% African American and 18% Hispanic. Significant race/ethnicity based differences were seen in multiple categories of biomarkers, including lipids, adipokines, and biomarkers of inflammation and myocyte injury and stress. In fully adjusted models, AA women had higher levels of Lp(a), Leptin, D-Dimer, OPG, ANA, SDMA and Homoarginine in comparison with Caucasian women, and AA men had higher levels of HDL-c, Lp(a), Leptin, D-Dimer, hs-CRP, ANA, SDMA, Homoarginine, hsTnT and ST2 in comparison with Caucasian men (Table).

Conclusion: Black and white adults demonstrate substantial differences in biomarker profiles after accounting for risk factors, body composition, and socioeconomic factors. These findings yield information that could be used clinically to risk stratify at-risk populations earlier in the treatment and prevention of CVD. Future studies are needed to distinguish whether pathophysiological processes delineated by these biomarkers contribute to racial and ethnic differences in the development and complications of CVD.

Presentation #99

Title: Ethyl Chloride Inhalation and Neurologic Impairment

Presenter: Garrett Seth Greenan

Authors: Garrett Greenan, MD

Faculty Mentor: Roohi Cheema

Abstract

Case Presentation: The patient is a 67 year-old male with a PMH of HIV (on HAART, with an undetectable VL and a CD4 count of 429), CKD, and anxiety. He was brought to the ED by his friend, due to AMS. The patient's last known normal was the morning prior to the day of presentation. The patient had visited a bar the night before presentation. On the morning of presentation, the friend visited the patient at home and noted that he seemed confused and had slurred speech. As the patient's mental status did not improve throughout the day, the friend brought the patient to the ED. The patient was initially difficult to interview given his AMS. It was ascertained that he had no recent travel history, and the friend didn't believe that the patient may have recently ingested anything other than alcohol. VS were unremarkable. The patient was alert and oriented only to self, was able to follow some commands, and wasdiffusely tremulous. There were no focal neurologic deficits. SHx was negative for tobacco use. The patient endorsed drinking 2 beers/week. He denied illicit drug use. However, the day after presentation he revealed a 6 month history of inhaling 'Amsterdam' solvent cleaner. He noted recently increased usage, citing a motive of increased sexual pleasure upon inhalation. FHx was negative for neurologic disease. Labs were unremarkable, with lactate 0.8, blood alcohol level negative, Utox negative, UA unremarkable, and RPR negative. LP was negative for CMV, Cryptococcus, VDRL, WNV, and Ehrlichiosis. CT and MRI brain were unremarkable. The patient's AMS, slurred speech, confusion, tremulousness, and weakness slowly improved over ten days, in the setting of supportive care. He was discharged at his baseline, without neurologic deficits, and with a recommendation to abstain from 'Amsterdam' inhalation.

Discussion: There are numerous case reports of acute, reversible neurologic deficits in the setting of ethyl chloride inhalation. Ethyl chloride is found in many cleaning solvents, and its inhalation can lead to confusion, tremulousness, impaired concentration and memory, weakness, and slurred speech; these deficits are usually reversible, with treatment featuring supportive care and future abstinence from use.

Presentation #100

Title: Recreational marijuana use is not associated with worse outcomes after renal transplantation

Presenter: Garrett Seth Greenan

Authors: Garrett Greenan, MD; Sarwat Ahmad, MD; Megan Anders, MD; Alexia Leeser, Jonathan Bromberg, MD, PhD; Silke Niederhaus, MD

Faculty Mentor: Silke Niederhaus

Abstract

Background: As marijuana (MJ) legalization is increasing, kidney transplant programs must develop listing criteria for marijuana users. However, no data exist on the effect of MJ on kidney allograft outcomes, and there is no consensus on whether MJ use should be a contraindication to transplantation.

Methods: We retrospectively reviewed 1225 kidney recipients from 2008 to 2013. Marijuana use was defined by positive urine toxicology screen and/or self-reported recent use. The primary outcome was death at 1 year or graft failure (defined as GFR<20 mL/min/1.73 m2). The secondary outcome was graft function at 1 year. Using logistic regression analyses, we compared these outcomes between MJ users and non-users.

Results: Marijuana use was not associated with worse primary outcomes by unadjusted (odds ratio 1.07, 95% CI 0.45-2.57, P=.87) or adjusted (odds ratio 0.79, 95% CI 0.28-2.28, P=.67) analysis. Ninety-two percent of grafts functioned at 1 year. Among these, the mean creatinine (1.52, 95% CI 1.39-1.69 vs 1.46, 95% CI 1.42-1.49; P=.38) and MDRD GFR (50.7, 95% CI 45.6-56.5 vs 49.5, 95% CI 48.3-50.7; P=.65) were similar between groups.

Conclusions: Isolated recreational MJ use is not associated with poorer patient or kidney allograft outcomes at 1 year. Therefore, recreational MJ use should not necessarily be considered a contraindication to kidney transplantation.

Presentation #101

Title: 'Light up': Towards more exact detection and imaging of cancer

Presenter: Esther de Boer

Authors: Esther de Boer, MD, PhD; Jason M. Warram, PhD; Margaret S. Brandwein-Gensler, MD; Baran D. Sumer, MD; Jinming Gao, PhD; Gooitzen M. van Dam, MD, PhD; Kurt R. Zinn, DVM, MS, PhD; Eben L. Rosenthal, MD

Faculty Mentor: Eben Rosenthal

Abstract

Background: The primary treatment for many solid cancers remains surgical resection with negative margins which requires accurate identification of cancer in real-time. Currently surgeons and pathologists lack adequate and reliable tools to consistently discriminate tumor from normal tissue. This has resulted in high rates of positive margins with associated high rates of local recurrence. Accurately identifying close or positive margins in real-time permits re-excision during surgical procedures. To effect change, we hypothesize that epidermal growth factor receptor (EGFR) can be targeted for safe and specific real-time localization of cancer.

Methods: A dose escalation study of cetuximab conjugated to IRDye800 was performed in patients (n=12) undergoing surgical resection of squamous cell carcinoma (SCC) arising in the head and neck. Safety and pharmacokinetic data were obtained. Multi-instrument fluorescence imaging was performed in the operating room and in surgical-pathology. To evaluate feasibility of the fluorescence-guided pathology approach, we evaluated head and neck SCC tumor specimens and margins resected from animals and patients after systemic injection of cetuximab-IRDye800CW in a surrogate margin study.

Results: Fluorescence imaging successfully differentiated tumor from normal tissue during resection with an average tumor-to-background ratio of 5.2. Fluorescence positively correlated with EGFR levels. In a preclinical model of luciferase-positive tumor resection using bioluminescence as the gold standard, fluorescence accurately predicted the presence of disease in 33/39 positive margins yielding an overall sensitivity of 85%, specificity of 95%, positive predictive value (PPV) of 94% and a negative predictive value (NPV) of 87%, which was superior to both surgical assessment (54%, 61%, 57% and 58%) and pathological assessment (49%, 95%, 91%, 61%), respectively. When the sensitivity and specificity of fluorescence-guided pathology was determined using traditional histological assessment as the gold standard in human tissues obtained during the clinical trial of fluorescence-guided surgery, the technique was strongly accurate with a sensitivity of 91%, specificity of 85%, PPV of 81%, and NPV of 93% through 90 human-derived samples. Conclusion We demonstrate that optical-imaging provides an opportunity for more precise identification of tumor during the surgical procedure and during the pathological analysis of tissues ex-vivo which has the potential to improve outcomes in clinical oncology.

Presentation #102

Title: Characteristics and Outcomes among Patients with Failed Extubation after Lung Transplantation

Presenter: Lauren Nichole Smith

Authors: Lauren N. Smith, MD; Rohan Kanade, BS; Luke D. Mahan, MSN; Srinivas Bollineni, MD; Jessica Mullins, MD; Vaidehi Kaza, MD; Manish Mohanka, MD; Michael Wait, MD; Fernando Torres, MD; Amit Banga, MD

Faculty Mentor: Amit Banga

<u>**Abstract**</u>

Background: Previous studies have reported an association of worse outcomes among critically ill patients with failed extubation. However there is lack of data on characteristics and outcomes among patients with lung transplantation (LT) who develop this complication after transplant surgery.

Methods: We reviewed charts of all patients who underwent lung transplantation at UTSW between January 2012 and December 2014 (n=186; age 56.2±13.3 yrs, M:F 109:77). Demographic and clinical variables before and after the LT, including the last pre-LT 6-minute walk test (6MWT) and lung functions at one year post LT were recorded. Development of failed extubation after the transplant surgery was the primary outcome variable. Variables were compared among patients with and without failed extubation. Lung functions at one year along with survival at one and three years were compared between the two groups.

Results: Incidence of failed extubation after LT surgery was 6.5% (12/186). Patients with failed extubation had significantly lower heart rate recovery (HRR, calculated as the change in the heart rate between the end of 6MWT and 1 minute post) on their last pre-LT 6MWT (median with IQR: 10, 5-14 vs 14, 10-20; Mann Whitney U p value: 0.016) with 12 as the best cut-off per the ROC analysis. Although, patients with failed extubation were more likely to be younger (median age 54 vs 58 years), African American (incidence 11.1%) and to have undergone bilateral LT (all 12 patients with failed extubation had bilateral LT), none of these associations were statistically significant. Other baseline variables including medical co-morbidities, acuity of illness determined by the lung allocation score at match, need of bridging strategies including mechanical ventilation or ECMO support did not have an association with failed extubation. Patients with failed extubation had prolonged ICU and hospital length of stay and experienced significantly worse survival at one year (58.3% vs 90.2%, p=0.007) and three years post LT (33.3% vs 67.8%, p=0.025).

Conclusions: A significant proportion of LT patients experience failed extubation. Patients with a HRR<12 during the last pre-LT 6MWT are at an increased risk of this complication. Early and late outcomes are significantly worse among patients with failed extubation after LT.

Presentation #103

Title: Predictors of Placement of Inpatient Palliative Care Consult Orders Among Patients With Breast, Lung, and Colon Cancer in a Safety Net Hospital System

Presenter: Lauren Nichole Smith

Authors: Lauren N. Smith, MD, Ramona L. Rhodes, MD, MPH, Lei Xuan, PhD, and Ethan A. Halm, MD, MPH

Faculty Mentor: Ramona Rhodes

<u>**Abstract**</u>

Background: The provision of palliative and end-of-life care to patients who are underrepresented and underserved provides unique challenges and opportunities. Objectives: To examine predictors of placement of inpatient palliative care consult orders among patients with breast, lung, and colorectal cancer hospitalized in a safety net hospital in 2010.

Methods: Simple and multivariable logistic regression of data on selected patients with cancer was performed to identify predictors of placement of inpatient palliative care consult orders.

Results: Of 979 patients, 56% had colorectal cancer, 23% had lung cancer, and 21% had breast cancer. Of those patients, 16% received an order for inpatient palliative care consultation during the study period. Patients who had more than 20 prescriptions for opioids ordered (adjusted odds ratio [AOR]: 9.10, 95% confidence interval [CI]: 4.62-17.95), had an order for a radiation oncology consult (AOR: 2.60, 95% CI: 1.50-4.49), or had low albumin (AOR: 2.75, 95% CI: 4.71) were more likely to have an order for an inpatient palliative care consult placed. Race and ethnicity were not statistically significant predictors.

Conclusion: In this cohort of patients in a safety net hospital, markers of pain, advanced disease, and poor prognosis were associated with placement of inpatient palliative care consult orders.

Presentation #104

Title: VIPoma: Diagnosis and Management

Presenter: Nathaniel Milburn

Authors: Nate Milburn, MD Michael Burton, MD Maria Yu

Faculty Mentor: Michael Burton

Abstract

A 39 year old man without significant past history presented with cramping, abdominal pain, and chronic watery diarrhea of 9 months duration. He had previously attempted a change in diet, avoided lactose, and received empiric antibiotics, desipramine and a probiotic, without any improvement in symptoms. Thorough infectious workup was negative, and an EGD/colonoscopy did not reveal any significant abnormalities. CT abdomen showed an enlarged heterogeneously enhancing vascular mass on the superior aspect of the pancreatic mid-body measuring 4.7x4.8x4.5cm. Several 8-9mm enhancing structures within both the right and left hepatic lobes and a 4-5mm flash enhancing structure in the right lobe were also seen. Pathology of the pancreatic lesion was consistent with neuroendocrine differentiation. In addition, the patient was noted to be hypokalemic (K 2.9) below his baseline of 4.0. In addition to potassium supplementation, he was initially treated with sandostatin LAR (octreotide) injections several times daily, with limited improvement. Octreotide scan showed single focus of disease in the area of the pancreas. VIP level was noted to be elevated to 895 pg/mL (nl <75 pg/mL); chromogranin A normal at 59 ng/mL (nl <225 ng/mL); urine 5-HIAA 3.6mg/24h (normal <6mg/24h). The patient underwent distal pancreatectomy with splenectomy, abdominal regional lymphadenectomy and cholecystectomy. Hepatic lesion resection was deferred as lesions did not appear consistent with metastasis at the time of operation. Pathology demonstrated a well-differentiated pancreatic endocrine tumor (T3N0M0), and at 7 month follow-up repeat VIP was 18 pg/mL. Patient was then stable for 2 years following his initial surgical procedure, but returned 3 years post-op with recurrence of diarrhea and multiple new enhancing liver lesions (R>L lobe) consistent with hepatic metastasis. VIP level was elevated to 254 pg/mL. He was started on monthly octreotide depot injections (later transitioned to subcutaneous octreotide TID with better symptom control) and underwent bland embolization and later Y90 radioembolization of both hepatic lobes with improvement of symptoms.

Presentation #105

Title: Predictors of Global Well-Being and Dyspnea Changes During Treatment for Acute Decompensated Heart Failure

Presenter: Nicholas Hendren

Authors: Nicholas Hendren, MD; Mark H. Drazner, MD; W.H. Wilson Tang, MD; Justin L. Grodin, MD

Faculty Mentor: Justin Grodin

<u>**Abstract**</u>

Background: The goal of treating acute decompensated heart failure is to safely and efficiently relieve symptomatic congestion. However, symptomatic relief is complex and may be dependent on non-treatment related factors. We hypothesize that factors outside net-fluid loss will be associated with symptomatic relief as assessed by global well-being and dyspnea visual assessment scales (GVAS and DVAS, respectively).
Methods: In the Diuretic Optimization Strategies Evaluation in Acute Heart Failure (DOSE-AHF) and Renal Optimization Strategies Evaluation in Acute Heart Failure (ROSE-AHF) datasets, we performed mixed effects modelling to determine the impact of baseline VAS score on serial VAS scores (both GVAS and DVAS) over 72 hours. Additionally, a backwards stepwise linear regression algorithm (P-removal >0.1 and P-entry<0.05) with bootstrapped oversampling was used to identify significant predictors of VAS change from baseline to 72 hours. Thirty-six candidate variables (including trial participation) representing demographic, clinical, physical examination, inpatient treatment, treatment response, changes in cardiorenal parameters, and serologic characteristics (including NTproBNP) of ADHF severity hospitalization were selected for model inclusion.

Results: In our study cohort (N=549, age 68±13 y, 75% male, 58% ischemic, LVEF 35±17 %, creatinine 1.6±0.6 mg/dl, and NTproBNP 4,723 [2,427-10,184] pg/mL), baseline and 72-hour changes in GVAS and DVAS scores were 49±24 and 20±26; and 54±27 and 19±26; respectively. Multivariable predictors of 72-hour changes in GVAS per 10 units were: baseline GVAS, 72-hour creatinine change, ICD presence, change in 72-hour NTproBNP, baseline loop diuretic dose, and 72-hour total loop diuretic dose. Multivariable predictors of 72-hour changes in DVAS per 10 units were baseline DVAS score and change in 72-hour NTproBNP.

Conclusions: Changes in GVAS and DVAS were dependent on their baseline levels despite adjustment for net-fluid loss and other treatment-related factors. Independent predictors of GVAS were loop diuretic dose (baseline and cumulative), NTproBNP change during treatment, ICD presence, and creatinine change; and for DVAS change, only NTproBNP change during treatment. These findings highlight that the potential for symptomatic improvement appears to be heavily influenced by initial symptom severity.

Presentation #106

Title: Intensive Blood Pressure Control and Body Size: Insights from SPRINT

Presenter: Nicholas Hendren

Authors: Nicholas Hendren, MD; Dharam Kumbhani, MD; Mark H. Drazner, MD; W.H. Wilson Tang, MD; Ian J. Neeland, MD; Justin L. Grodin, MD

Faculty Mentor: Justin Grodin

<u>**Abstract**</u>

Background: Targeting systolic blood pressure (SBP) <120 mm Hg in patients at high-risk for cardiovascular events but without diabetes reduces cardiovascular morbidity and mortality. Whether body size effects this relationship needs further clarification. Methods. This is a post-hoc analysis of the Systolic Blood Pressure Intervention Trial (SPRINT). We sought to determine whether there was interaction between body mass index (BMI) and the benefit of intensive blood pressure control (targeting SBP<120 mm Hg) vs. standard care (targeting SBP<140 mm Hg) on the primary composite outcome of myocardial infarction, acute coronary syndrome, stroke, acute decompensated heart failure, or cardiovascular death.

Results: In the study cohort (N=9,284, age 68±9 [years], 64% male, SBP 140±16 [mm Hg], creatinine 1.1±0.3 [mg/dL], and Framingham Risk Score 18 [12-26]) the average BMI was 30±6 [kg/m2]. BMI was weakly correlated to SBP (rho=-0.07, P<0.001) and not associated with the primary composite outcome (HR per kg/m2 0.99, 95% CI 0.97-1.00, P=0.08). After adjustment for baseline SBP, the effect of intensive blood pressure control was consistent across BMI levels for the primary composite outcome (Figure, HR 0.59, P-interaction=0.5) and for the primary composite outcome or death (HR 0.79, P-interaction=0.6).

Conclusion: Intensive blood pressure control in non-diabetic individuals at high-risk for cardiovascular events confers benefits across a broad range of BMI.

Presentation #107

Title: Association of Number of Live Births with Electrocardiographic and Cardiac Structural Changes

Presenter: Elizabeth Harris

Authors: Elizabeth Harris, MD; Colby Ayers, MS; James de Lemos, MD; Monika Sanghavi, MD

Faculty Mentor: James de Lemos

Abstract

Background: Pregnancy causes marked hemodynamic changes that may have a 'legacy effect' beyond the gestational period. Whether parity is associated with long term cardiac remodeling and electrocardiogram (ECG) changes warrants further investigation.

Methods: Using the Dallas Heart Study, a multiethnic population cohort study of Dallas county adults, we evaluated the association between number of live births and cardiac magnetic resonance imaging (MRI) and ECG parameters. We used linear regression analysis and sequential multivariable regression models, adjusting for age, race, education level, income, hypertension, smoking, and body size.

Results: 3,019 women were included in the study, divided into categories of 0, 1, 2, 3, 4, and 5+ live births. Increasing parity was associated with longer PR intervals (β 1.12 +/- 0.38, p = 0.0032), with no correlation between parity and QRS, QT, or ventricular rate. Increasing parity was also associated with increased left ventricular end diastolic volume (LVEDV, β 1.29 +/- 0.41, p < 0.002), left ventricular end systolic volume (LVESV, β 0.81 +/- 0.24, p < 0.001), and left ventricular mass (LV mass, β 1.05 +/- 0.40, p = 0.032). No significant association was found with wall thickness, ejection fraction, or concentricity.

Conclusions: This is one of the first studies to correlate ECG parameters with parity. Increased parity was associated with prolongation of the PR interval, and an increase in LVEDV, LVESV, and LV mass in a multiethnic population. Our results show that parity is associated with changes in cardiovascular structure and electrical activity later in life, though whether these changes are pathologic and increase the risk of heart failure or arrhythmias requires further investigation.

Presentation #108

Title: The Effects of Acute and Chronic Incretin Therapy on Endothelial Function in Humans with Prediabetes

Presenter: Kayla Riggs

Authors: Kayla Riggs, MD; Amy Dursteler, BA; Sara Coverdale, BA; Heinrich Taegtmeyer, MD, PhD; Absalon Gutierrez, MD

Faculty Mentor: Absalon Gutierrez

<u>Abstract</u>

Background: Studies show conflicting data regarding the effect in incretin therapies on endothelial function in insulin-resistant humans. We investigated the efficacy of acute and chronic incretin therapy on postprandial endothelial function and hypertriglyceridemia in prediabetic humans.

Methods: Fifteen adult prediabetic subjects (age 51 ± 2 years, BMI 32.5 ± 0.4 kg/m2, HbA1c 5.96 ± 0.05 %) participated in a single center, randomized, crossover, placebo-controlled double-blinded prospective trial utilizing the following medications: exenatide, saxagliptin, and placebo. For each study arm, fasting patients presented to the Clinical Research Unit. Forearm blood flow (FBF) was measured via strain gauge venous occlusion plethysmography. Blood was drawn for lipid levels. Study medication was given and subjects ate a standardized high-fat test meal. Blood was collected every 2 hours, and FBF was measured every three hours, for a total of 6 hours. These procedures were repeated for the remaining study arms. Subsequently, seven patients participated in an open-label extension study. Exenatide extended release (ER) was administered for six weeks, after which the above procedures were repeated.

Results: Single doses of exenatide and sitagliptin improved postprandial hypertriglyceridemia, but showed no significant changes in resting or peak postprandial FBF when compared to placebo. Six weeks of exenatide ER, compared to single dose exenatide, improved fasting resting but not peak FBF, but did not improve postprandial resting or peak FBF.

Conclusions: The data show that chronic exenatide ER therapy led to mild improvements in fasting but not postprandial endothelial function in prediabetic humans, via FBF measurements. Acute exenatide and saxagliptin did not improve endothelial function, though postprandial triglyceride levels were reduced with both drugs. Long-term administration of exenatide may offer cardiovascular protection beyond glucose control in prediabetes.

Presentation #109

Title: Variation in Physician Perceptions of Readmission Risk by Physician Specialty and Perceived Reason for Readmission

Presenter: Colin Washington

Authors: Oanh Kieu Nguyen, MD; Vivek R. Patel, MD; Colin Washington, MD, MPH; Anil N. Makam, MD

Faculty Mentor: Oanh Nguyen

Abstract

Background: Physician specialty and clinical judgement may be important predictors of patients' 30-day hospital readmission risk. However, the influence of these factors on physician perceptions of patient readmission risk is unknown. METHODS We conducted a prospective study of physicians caring for hospitalized adults on inpatient medicine and cardiology services in a large, urban safety-net hospital in Dallas, Texas from September through October 2017. We asked physicians to predict patients' risk of 30-day readmission, rate their confidence in each prediction on five-point Likert scales (for both measures, 'low' = score of 1-3, and 'high' = 4 or 5) and to select a primary reason (medical, social, or mental health) for potential readmission. Surveys were conducted in-person on the day of anticipated discharge.

Results: We surveyed 106 physicians on 1,248 hospitalizations. Of physicians surveyed, 29.3% identified as hospitalists; 51.9% identified as general internists and 18.8% identified as other types of clinical subspecialties. Overall, physicians reported 26.0% as being high risk, and did not differ by physician specialty (hospitalists identified 27.7% as high risk vs. 24.9% by other specialties, p=0.21). Overall, physicians were more confident in predictions of high risk versus low risk (65.1 vs 45.2%, p<0.001). Hospitalists were more confident in their perceptions of readmission risk (56.4 vs 46.6%, p<0.001). There were no differences in perceived reason for potential readmission by specialty (overall, 76.2% medical, 13.4% social, 10.4% mental health). Perceived high readmission risk was more likely to be associated with social (21.6 vs 10.6%, p<0.001) or mental health reasons (18.7 vs 7.3%, p<0.001) for readmission compared to low-risk predictions.

Conclusions: Physicians overall are more confident in predicting patients as being high risk for readmission than low risk. Hospitalist physicians are more confident in their predictions than other physicians, which may be related to greater experience in discharging patients. In a safety-net hospital, physicians reported medical illness as being the most common reason for potential readmission. However, if physicians thought a readmission would occur because of socioeconomic or mental health reasons, they were more likely to rate their patients' readmission risk as high.

Presentation #110

Title: Contemporary Epidemiology of Atrial Fibrillation Among Medicare Beneficiaries, 2004-2013

Presenter: Joshua Parker

Authors: Joshua Parker, Rohan Khera, Ambarish Pandey, Daniel Cheeran, Colby Ayers, MS; Sandeep R Das, MD, MPH; Mark S Link, MD; James A de Lemos, MD; Jarett D Berry, MD

Faculty Mentor: Jarett Berry

<u>**Abstract**</u>

Background: Atrial fibrillation (AF) is the most common dysrhythmia in clinical practice, and is a significant contributor to morbidity and mortality. Prior reports have projected a large increase in AF burden over time. A contemporary assessment of epidemiology is needed to assess if an emphasis of prevention strategies over the last decade has been effective in alleviating this risk.

Methods: We used a 5% national sample of all Medicare beneficiaries in the US from 2002 through 2013 to construct a longitudinal cohort of 2.3 million fee-for-service Medicare beneficiaries administratively followed for ≥2 years using claims data. Trends in incident and prevalent AF were assessed for 2004 through 2013. Using ICD-9 codes, encounters with AF were identified from inpatient, outpatient, and physician claims. AF during the first 2 years of entry into the cohort was defined as pre-existing AF. Incident AF was defined as having either 1 inpatient claim with a diagnosis of AF or 2 outpatient or physician claims with AF. Calendar-year prevalence comprised pre-existing and incident AF for the respective years as well as those with incident AF in preceding years. Age-adjusted time trends were assessed using Poisson regression.

Results: Between 2002 and 2013, 219,570 patients had incident AF. At incidence, mean age was 79 years, 55% were women, and 92% and 5% were white and black, respectively. Age-adjusted AF incidence decreased by 0.4/1000 per year between 2004 (20/1000) and 2013 (17/1000). While incidence declined for white men and women (P<.05), it has remained unchanged for black men and women. Proportion of incident events in the outpatient setting increased from 26% to 40%. One-year mortality was 9%, and remained unchanged throughout the study period. Over this period, the overall prevalence of AF decreased by 0.9/1000 per year (p<.05), however, there was a relative increase in AF prevalence among black men.

Conclusions: Between years 2004 and 2013, the overall incidence and prevalence of AF among a 5% sample of Medicare beneficiaries stabilized. There were, however, differences across racial groups, with a slight decline in incidence among white men and women, which was not observed in black men.

Presentation #111

Title: Mycoplasma Pneumonia-Induced Rash and Mucositis in a 23-Year-Old Female

Presenter: Roy Elias

Authors: Roy Elias, MD; Timothy Brown, MD; Nilofar Syed, MD

Faculty Mentor: Nilofar Syed

Abstract

Case Introduction: The patient is a 23-year-old African American female with no past medical history who presented to the emergency department for worsening rash and mucositis one week after the development of cough, low grade fevers, and malaise. The rash had started two days prior to admission with rapid progression of lesions in the oropharynx and spreading of the rash to involve the trunk and extremities. The patient had not started any new medications or supplements and was not taking any medications at home. Physical exam was notable for superficial confluent erosion of the lips with involvement of the tongue, as well as scattered tense vesicle and bullae along the trunk, back, and all extremities. The involved mucositis was painful and prevented adequate oral intake. Tzanck smear of peripheral lesions was negative for acantholytic cells. Respiratory viral panel was positive for mycoplasma pneumonia, and the diagnosis of Mycoplasma Pneumonia induced Rash and Mucositis (MIRM) was made. The patient was treated with azithromycin for the underlying pathogen, and supportive care including barrier creams for her oral rash. After three days the patient was able to tolerate an adequate oral diet and was discharged home.

Discussion: Mycoplasma pneumoniae is a common cause of atypical pneumonia, however up to 25% of patients can experience extra-pulmonary involvement. MIRM is a rare and often misdiagnosed complication of mycoplasma pneumoniae infection. The disease process falls within the spectrum of Stevens-Johnson syndrome, erythema multiforme, and toxic epidermal necrolysis. The presentation is variable with most patients presenting with polymorphic lesions, with severe mucositis alone in up to 34% of cases. The average age at presentation is 12 with nearly all patients exhibiting prodromal symptoms. Treatment is targeted towards the underlying infection as well as supportive care for the rash. Complications can arise with ophthalmic or vaginal involvement due to significant scaring of these organs and MIRM warrants detailed physical exam and expert consultation.

Presentation #112

Title: Rapid Progression followed by psueduoprogression in Renal Cell Carcinoma Treated with Nivolumab

Presenter: Roy Elias

Authors: Roy Elias, MD; Payal Kapur, MD; Ivan Pedrosa, MD; James Brugarolas, MD PhD

Faculty Mentor: James Brugarolas

<u>**Abstract**</u>

Introduction: Immunotherapy is a rapidly growing tool in the management of cancer patients. With the adoption of immune checkpoint inhibitors (ICI) such as the PD-1 antibody Nivolumab, many patients have demonstrated lasting remissions of disease. In contrast to molecularly targeted therapies and traditional chemotherapy, immune checkpoint inhibitors have been shown to have variable and unpredictable response patterns in patients. Here we present a case of rapid progression following the administration of Nivolumab in renal cell carcinoma (RCC), followed by a marked and durable response.

Case Description: The patient is a 70 year-old man diagnosed with metastatic clear cell RCC two years prior who had progressive disease after sequential treatment with pazopanib, followed by an investigational agent (PT2385), and axitinib. The patient had a fair functional status despite heavy disease burden with a level three tumor thrombus in addition to tumors in the lungs, bone, liver, and several soft tissue lesions. The decision was made to pursue Nivolumab with simultaneous radiotherapy to a dominant lung lesion and bothersome shoulder metastasis. After two infusions, the patient began to experience severe fatigue and a rapid decline in functional status. Restaging scans demonstrated marked progression of his disease, most notably in the lungs with the development of innumerable new metastatic lesions. Faced with declining functional status and progressive disease, the patient elected to pursue hospice care. Remarkably, five months later the patient returned to clinic stating he had experienced a significant improvement in his overall health and functioning. Radiologic assessment demonstrated a dramatic response when compared to pre-hospice scans. Nivolumab was reinitiated but was ultimately held four months later secondary to a Grade IV acute interstitial nephritis. He was subsequently treated with everolimus and levatinib, where he survived an additional two years before unfortunately passing away from complications of pneumonia.

Discussion: Here we report a dramatic case of psuedoprogression following the administration of Nivolumab. Checkpoint inhibitors have been shown to have unique response patterns that create challenges for clinicians, researchers, and patients. Continued investigation is required to develop tools to differentiate psuedoprogression from true progression in this rapidly growing field.

Presentation #113

Title: Identifying Predictors of Response to Immunotherapy in Renal Cell Carcinoma

Presenter: Roy Elias

Authors: Roy Elias, MD; Nicholas Levonyak, MD; Joseph Formella, Payal Kapur, MD; Ivan Pedrosa, MD; Raquibul Hannan, MD; James Brugarolas, MD, PhD

Faculty Mentor: James Brugarolas

Abstract

Background: Harnessing the body's immune system to defeat cancer has long held promise, and decades of effort have led to recent successes. Particularly impactful in RCC have been immune checkpoint inhibitors (ICI), of which Nivolumab (anti PD-1) has already been approved by the FDA as second line therapy after the results of the phase III randomized trial CHECKMATE 025. Here we review a cohort of patients with metastatic Renal Cell Carcinoma (mRCC) treated with ICI at the Harold C. Simmons Comprehensive Cancer Center (SCCC).

Methods: This study is a retrospective chart review of 46 patients who received ICI at the SCCC from 2014 until March 2018. Baseline patient characteristics were summarized using count and percentage for categorical variables. Progression free survival (PFS) and objective response rate (ORR) were defined by the RECIST v1.1 radiological criteria. Overall survival was defined as the time from initial treatment with ICI until death.

Results: 46 patients were identified. 34 (74%) of these patients were men, 42 (91%) were non-Hispanic. The average age at diagnosis was 58.3 years (14-75). 85% demonstrated clear cell histology. The objective response rate was 17/46 (37%), with the median progression free survival of 17.5 weeks. Median overall survival was 54.2 weeks. 23/46 (50%) patients received concurrent radiation. 19 (41%) of patients were treated beyond progression on nivolumab with nivolumab or nivolumab and ipilimumab. Immune-related adverse events (irAE) were experienced by 20 (43%) patients and grade III/IV resulting in cessation of treatment were experienced by 8 (17%) of patients.

Conclusions: The use of ICI in RCC is rapidly increasing since the approval of Nivolumab in late 2015. At SCCC we have treated 46 patients with metastatic renal cell carcinoma with ICI. Our experience has demonstrated similar results with respect to overall response rates, progression free survival, overall survival, and immune related adverse events. Further investigation is warranted to identify predictive variables associated with response in this cohort of patients.

Presentation #114

Title: Surveillance Imaging and Alpha Fetoprotein for Early Detection of Hepatocellular Carcinoma in Cirrhosis: A Meta Analysis

Presenter: Joseph Obi

Authors: Joseph Obi, MD; Kristina Tzartzeva, MD; Nicole E. Rich, MD; Neehar D. Parikh, MD; Jorge A. Marrero, MD; Adam Yopp, MD; Akbar Waljee, MD; Amit G. Singal, MD

Faculty Mentor: Amit Singal

Abstract

Background and Aims: Professional society guidelines have discordant recommendations for the most effective surveillance strategy to detect hepatocellular carcinoma (HCC) at an early stage. Our study's aim was to compare the performance of surveillance imaging with or without alpha fetoprotein (AFP), for early stage HCC detection in patients with cirrhosis.

Methods: Two reviewers searched MEDLINE and SCOPUS from January 1990 to August 2016 and determined sensitivity and specificity of surveillance strategies for overall and early HCC detection. Pooled estimates were calculated and compared using the DerSimonian and Laird method for a random effects model. The study was conducted in accordance with Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines.

Results: Thirty-two studies (n=13367) characterized sensitivity of imaging with or without AFP for HCC detection in cirrhosis patients. Ultrasound sensitivity for any stage HCC was 84% (95%CI 76-92%); however, sensitivity for early detection was only 47% (95%CI 33-61%). In studies comparing ultrasound with or without AFP, ultrasound had lower sensitivity than ultrasound plus AFP for any stage (RR 0.88, 95%CI 0.83-0.93) and early stage (RR 0.81, 95%CI 0.71-0.93) HCC detection but exhibited higher specificity (RR 1.08, 95%CI 1.05-1.09). Sensitivities of ultrasound with and without AFP for early detection were 63% (95%CI 48-75%) and 45% (95%CI 30-62%), respectively (p=0.002). The benefit of using AFP in combination with ultrasound was consistent across subgroups including prospective studies (RR 0.78, 95%CI 0.66 - 0.92), studies conducted in the United States (RR 0.59, 95%CI 0.41 - 0.85), studies exclusively enrolling patients with cirrhosis (RR 0.76, 95%CI 0.60 - 0.95), and studies conducted after year 2000 (RR 0.79, 95%CI 0.66 - 0.95). Only four studies evaluated CT or MRI-based surveillance, but available data suggest MRI has high sensitivity (84%; 95%CI 70-92%) and specificity (89%, 95%CI 87% - 91%) for early stage HCC detection.

Conclusion: Ultrasound alone demonstrates poor sensitivity for early HCC detection in patients with cirrhosis. Using AFP with ultrasound significantly increases early HCC detection, suggesting the combination should be the preferred surveillance strategy for patients with cirrhosis until better surveillance strategies are available.

Presentation #115

Title: Cardiac Injury, Malignant left ventricular hypertrophy and risk of heart failure in African Americans: The Jackson Heart Study

Presenter: Neil Keshvani

Authors: Neil Keshvani, MD; Ambarish Pandey, MD; Colby Ayers, MS; James de Lemos, MD; Jarett D. Berry, MD

Faculty Mentor: Jarett Berry

<u>**Abstract**</u>

Background: African Americans have a disproportionately greater burden of heart failure (HF) risk factors and clinical HF and are more likely to have left ventricular hypertrophy and subclinical myocardial injury, as determined by high sensitivity cardiac troponin (hs-cTn) measurements. However, the contribution of these subclinical phenotypes toward HF development in African Americans is not well characterized. We aimed to examine the independent and joint effects of LVH and chronic myocardial injury on risk of HF in African Americans.

Methods: The Jackson Heart Study is a prospective study of African American adults without prevalent HF at baseline (2000-2004). Participants were stratified into categories based on the presence of absence of LVH (measured through echocardiography) and the burden of myocardial injury as measured by hs-cTnI, where levels above 4 ng/L in women and 6 ng/L in men were considered elevated. The risk of incident HF across different LVH and chronic myocardial injury groups was assessed using adjusted Cox proportional hazards models.

Results: We included 3,796 participants (mean age 54 years, 64% women, 6.1% with LVH, 17.2% with chronic myocardial injury, and 3.7% with both LVH and chronic myocardial injury). Median follow up was 9.8 years with 285 incident HF events observed. In adjusted analyses, LVH and higher burden of chronic myocardial injury as identified by hs-cTnI levels at baseline were independently associated with risk of HF [HR (95% CI): LVH (vs. no LVH): 2.05 (1.50 - 2.80); chronic myocardial injury (highest vs. lowest category HR 3.52 (2.44 - 4.87)]. A significant interaction was observed between LVH and hs-TnI for the risk of HF (p-interaction < 0.0001) with the highest risk among individuals with both LVH and myocardial injury [Absolute incidence 35%; HRadj 5.35 (3.66 - 7.83)]. In contrast, LVH without chronic myocardial injury was not associated with significantly increased HF risk [1.81 (0.94 - 3.50)]

Conclusions: The combination of LVH and chronic myocardial injury identifies a malignant, preclinical HF phenotype in African Americans with a remarkably high absolute risk of HF over a 10-year f/u period. Targeting individuals with this high-risk preclinical phenotype may offer an important strategy to mitigate HF risk in African Americans.

Presentation #116

Title: Improving Respiratory Rate Measurement Accuracy in the Hospital: A Quality Improvement Initiative

Presenter: Neil Keshvani

Authors: Neil Keshvani, MD; Kimberly Berger, MD; Arjun Gupta, MD; Sheila DePaola, RN; Sudarshaan Pathak, RN; Shirly Koduvathu, RN; Oanh Kieu Nguyen, MD; Anil N. Makam, MD

Faculty Mentor: Anil Makam

<u>**Abstract**</u>

Introduction: Respiratory rate (RR) is a predictor of adverse outcomes and an integral component of many risk prediction scores for hospitalized adults. Despite its clinical value, measured RRs are often inaccurate and may lead to misclassification of disease severity. We sought to improve inpatient RR measurement by patient care assistants (PCAs) through a multipronged quality improvement (QI) initiative in a single inpatient unit of Parkland Hospital.

Methods: We observed PCA vital sign measurements to assess RR accuracy compared to 'gold-standard' measurement by two trained study team members. We identified two logistical barriers to RR measurement: absence of a time-keeping device and perceived lack of time to measure RR. Our intervention addressed these errors by: a) adding a time-keeping device to vitals carts; b) creating a time-neutral workflow modification calling for RR measurement during automated blood pressure measurement; c) implementing RR measurement skill labs during PCA orientation; d) retraining existing PCAs on RR measurement during monthly unit staff meetings and daily PCA & nursing huddles; and e) employing regular vital sign audits. We assessed RR accuracy and time to vital sign completion both before and after the intervention.

Results: Before the intervention, median gold-standard RR was 16 (IQR 12-18) versus 18 (IQR 18-20) for PCAs (n=100), and the vital sign completion time was 2:36 minutes (n=50, IQR, 2:04-3:20). Only 62% of PCA-measured RRs were 'accurate', defined as being ±4 breaths/minute of the gold-standard RR. After the intervention, the median gold-standard RR was 18 (IQR, 14-20) versus 18 (IQR, 15-20) for PCAs, and the frequency of accurate PCA-measured RRs increased to 82% (p<0.01). Time to complete vital signs post-intervention decreased to 2:05 minutes (IQR, 1:39-2:09; p<0.001).

Conclusion: Through a continuous QI initiative, we improved both RR accuracy and vital sign efficiency among PCAs. Our next steps will be to assess for changes in risk-prediction scores (i.e. SIRS) post-intervention, assess sustainability of the intervention, and to disseminate the modified workflow and training to other inpatient hospital units. We hope to create a lasting culture change to overcome our collective long-standing complacency for human error in RR measurement to ultimately improve patient outcomes.

Presentation #117

Title: Reducing Hospitalizations: Institution of Outpatient Infusional EPOCH-based Chemotherapy at a Safety-Net Hospital

Presenter: Neil Keshvani

Authors: Neil Keshvani, MD; Arjun Gupta, MD; Corbin Eule, MD; Eileen Marley, PharmD; Navid Sadeghi, MD; Hsiao C. Li, MD

Faculty Mentor: Navid Sadeghi

<u>**Abstract**</u>

Background: EPOCH-based chemotherapy regimens have traditionally been administered inpatient because they include a continuous 96-hour infusion. These routine admissions are costly, disrupting, and isolating to patients.

Methods: We aimed to transition EPOCH-based chemotherapy regimens to an ambulatory infusion model at our safety-net hospital and quantify the effects of avoided hospitalization and outpatient administration of medications on overall healthcare costs. Guidelines for chemotherapy administration and educational materials were developed through a multidisciplinary collaboration with hematology/oncology, nursing, and pharmacy. Data were collected through chart review and the finance department.

Results: From 1/30/2017 through 1/30/2018, 87 cycles of EPOCH-based chemotherapy were given to 23 individual patients. Sixty-one cycles (70%) were administered in the outpatient setting to 18 individual patients. There was a 57.6% reduction in drug cost per cycle due to the lower cost of drug acquisition in the outpatient setting. Of the 26 cycles that were administered in the hospital, 18 (69%) were the first cycle of treatment. In one patient due to poor performance status and lack of transportation, all 6 cycles were administered inpatient, accounting for 23% of inpatient treatments. Per previous published data, an additional $3,291 per cycle was saved from each prevented 5-day admission, totaling $200,751. An estimated 336 days of hospital stay were avoided. Rates of inappropriate prophylactic antimicrobial prescription and laboratory draws were markedly lower in the outpatient setting.

Conclusions: Multiday EPOCH-based regimens can be successfully and safely administered in an ambulatory setting in our safety net urban hospital. Outpatient therapy allows patients to receive treatment in their own environment and leads to significant savings through avoided hospitalizations and reduction in drug acquisition cost.

Presentation #118

Title: RESOLUTION OF IMMUNE THROMBOCYTOPENIA FOLLOWING RESECTION OF KIDNEY CANCER: A CASE REPORT

Presenter: Namrah Siddiq

Authors: Kavita Donthireddy, MD; Namrah Siddiq, MD; Naga Koteswari Sucharita Cheedella, MD

Faculty Mentor: Kavitha Donthireddy, Naga Cheedella

<u>**Abstract**</u>

We present this case of a 62- year old African American male patient with severe thrombocyto-penia and a renal mass. After thorough work-up for causes of the thrombocytopenia and an im-provement in platelet count after initiation of IVIG, the patient was diagnosed with ITP. The pa-tient's CT scan revealed an incidental renal mass which was then biopsied and was consistent with papillary renal cell carcinoma. Following a partial nephrectomy, patient had normalization of his platelet counts. We suspect the patient had secondary ITP which is an immune mediated phenomenon that can lead to resolution of ITP if the underlying cause, in this case a renal malignancy, is treated.

Presentation #119

Title: Paraproteinemia in Multiple Myeloma: a case of acquired dysfibrinogenemia

Presenter: Namrah Siddiq

Authors: Namrah Siddiq, MD; Colin Bergstrom, MD

Faculty Mentor: Srikanth Nagalla

Abstract

We present a case of a 63 year old man who presented for work up of bleeding diathesis and was noted to have a low fibrinogen activity level with a normal fibrinogen antigen level. Further studies revealed elevated lambda free light chains, leading to the diagnosis of multiple myeloma. Despite initiating treatment with velcade/dexamethasone, the patient continued to have recurrent bleeds along with hypofibrinogenemia noted on labs. This refractoriness to treatment prompted a switch in medications to kyprolis/dexamethasone. The patient responded with improvement in bleeding symptoms, normalization of fibrinogen, and a decrease in serum free light chains.

Presentation #120

Title: Statin-Associated Autoimmune Myopathy: The importance of early recognition

Presenter: Megan Milne

Authors: Megan Milne, MD; Sarah Cossich, MD

Faculty Mentor: Guillermo Quiceno and Carlos Cardenas

Abstract

Case Presentation: A 58 year-old woman with Type II Diabetes Melliltus, Hyperlipidemia, Subclinical Hypothyroidism, and Coronary Artery Disease with prior NSTEMI presented with diffuse body weakness. The patient fell 3 weeks prior, breaking her coccyx. She then developed diffuse myalgias and weakness. Her medical history was notable for persistent transaminitis first noticed in June when she was started on Ezetimibe. She was taking Atorvastatin for years without complication. On evaluation, the patient had 3/5 strength in upper and lower extremities bilaterally. Proximal muscles were more severely affected than distal. Laboratory evaluation revealed an AST of 401, ALT of 582, and creatinine kinase of 7,531. Atorvastatin and Ezetimibe were discontinued. Muscle biopsy and autoimmune serologies were obtained. While awaiting results, the patient was treated with IV fluids to prevent acute kidney injury. Her course was complicated by urinary retention and constipation. This was attributed to abdominal muscle weakness affecting her ability to bear down. Additionally, the patient had a near-choking event despite passing her initial speech evaluation. Muscle biopsy revealed necrotizing myositis. ANA, CCP, Jo-1, RNP, SCL, Smith, SSA, and SSB antibodies were negative. Anti-HMG CoA reductase antibody resulted as strongly positive, confirming Statin-associated autoimmune myopathy. She was started on daily high-dose prednisone and completed a five-day course of IVIG therapy. Her urinary retention and constipation resolved. Her weakness improved to 4/5 in upper and lower extremities symmetrically. Creatinine kinase levels responded well to prednisone, and she will continue both prednisone and monthly IVIG therapy outpatient.

Discussion: Statin-associated autoimmune myopathy is a rare cause of autoimmune polymyositis. Patients develop antibodies against 3-hydroxy-3-methylglutaryl coenzyme (HMG-CoA) reductase, diffuse weakness, elevated creatinine kinase, and myonecrosis on biopsy[1]. Older patients often develop the disease after chronic exposure to statins.[2] The majority of patients will require immunosuppressive therapy to prevent persistent weakness from muscle atrophy[2]. Chronic under-treatment may result in fatty muscle infiltration [1]. Timely recognition and treatment are critical for optimal outcomes in patients with statin-associated autoimmune myopathy.

References 1.   Mammen, AL. Statin-Associacted Autoimmune Myopathy. N Engl J Med 2016;374:664-9. 2.   Karunaratne, K et al. Autoimmune necrotising myopathy and HMGCR antibodies. Pract Neurol 2018; 0:1-5.

Presentation #121

Title: Clinical translation of 2HG MR spectroscopy for IDH-mutant glioma patient clinical care and clinical research trials

Presenter: Johanna Busch

Authors: Johanna Busch, MD, PhD; Divya Mella, MD; Changho Choi, PhD; Joseph Maldjian, MD; Marco Pinho, MD; Elizabeth Maher, MD, PhD

Faculty Mentor: Elizabeth Maher

Abstract

Background: Proton magnetic resonance spectroscopy (MRS) can detect and quantitate 2-hydroxyglutarate (2HG), the oncometabolite produced in isocitrate dehydrogenase (IDH)-mutant gliomas. Using a dedicated research scanner at UTSW in a longitudinal study, 2HG MRS was validated as a reliable clinical biomarker. Clinical translation of 2HG MRS has been undertaken with the goal of establishing patient selection criteria, clinical workflow, data acquisition parameters, and an immediate analytic pathway to enable incorporation into clinical scanning and reporting.

Methods: 2HG MRS was incorporated into the clinical flow on Phillips 3T MR scanners at UTSW. For each scan, a single voxel was placed after routine acquisition of T2/FLAIR images and proton spectra acquired. Data was automatically processed by an algorithm developed in the ANSIR lab at UTSW and sent to the clinical imaging system, PACS. The metabolite spectrum, concentrations of 2HG, GABA, tCholine (mM) were displayed graphically with a screen shot of voxel placement.

Results: 205 scans were performed in 91 patients (74 IDH mutant, 17 IDH WT). 42 IDH-mutant patients had serial scans (range 2-5). The clinical flow worked well and data was obtained without complications from each scan. Scans/data were subgrouped by IDH status (mutant vs WT) and timing relative to treatment (pre-, during, post-treatment). Technical assessment of spectral quality was a major component of the analysis. 35% of the scans did not meet minimum cutoff due to either small voxel size or inadequate spectral signal and were not included in further analysis. IDH WT scans were used to develop a minimum threshold for 2HG detection since the metabolite is produced only in patients with an IDH mutation (mean 1.5 mM, range 0-2.8 mM). Biological reproducibility was established in patients who had measureable disease and 2HG concentration above the threshold. Clinical reliability was established in stable patients and in patients with radiographic documentation of response and decrease in 2HG over the treatment course.

Conclusions: Availability of 2HG MRS on routine clinical scanning will be an important tool for clinical management of patients with IDH mutant gliomas and can be evaluated as a surrogate biomarker endpoint in clinical trials of IDH mutant glioma patients.

Presentation #122

Title: Electrophysiology Study and Catheter Ablation Procedural Characteristics in Patients with Pulmonary Hypertension and Supraventricular Tachycardia

Presenter: Nimesh Patel

Authors: Wei Shan Tsui, BS; Nimesh Patel, MD; Nitin Kulkarni, MD; Curtiss Moore, MD; Richard Wu, MD

Faculty Mentor: Richard Wu

<u>Abstract</u>

Background: Pulmonary hypertension (PH) is a debilitating disease that results in right ventricular dysfunction and right atrial enlargement. This disruption in cardiac architecture can lead to various supraventricular tachycardias (SVTs), including atrial tachycardia, atrial flutter, and AVNRT. Tachyarrhythmias are poorly tolerated by patients with PH, and these patients are often referred for electrophysiology study (EPS) and ablation. There is a scarcity of data on the types of SVT identified by EPS in patients with PH and the efficacy of catheter ablation in this patient population.

Methods: We performed a retrospective review of all patients diagnosed with pulmonary hypertension patients that underwent EPS and ablation at UT Southwestern University Hospital from January 1,2011 to July 1,2015. Eligible patients' charts were reviewed to abstract demographic, baseline clinical data, arrhythmia characteristics, and EPS procedural characteristics. Lastly, the procedural outcomes were determined by identifying arrhythmia recurrence at three months and mortality rate in 6-month and 1 year.

Results: We identified a total of 83 arrhythmias in 63 EP studies procedures that were perfomed in 59 patients with PH. The most common SVT identified in patients with PH who underwent EPS was typical atrial flutter (43%), followed by atrial tachycardia (18%), atrial fibrillation (16%), atypical atrial flutter (13%), and AVNRT (10%). Immediate procedure success was 93.7%. Freedom from arrhythmia recurrence at 3 months was 71.4%. 87.9% of patients survived at 6 months post-procedure.

Conclusion: There is a high rate of immediate procedural success for catheter ablation in patients who under EPS for SVT in patients with PH, however recurrence rates are higher than in the general population. The relatively high frequency of atrial arrhythmias (typical and atypical atrial flutter, atrial tachycardia, and atrial fibrillation) as the cause of SVT in the population studied is consistent with distortions in right atrial remodeling due to right atrial pressure overload.

Presentation #123

Title: Ventricular Pacing Burden after Permanent Pacemaker Implant after Transcatheter Aortic Valve Replacement

Presenter: Nimesh Patel

Authors: Nimesh Patel, MD; James Daniels, MD; Phi Wiegn, MD; Subhash Banerjee, MD; Sarah Gualano, MD; Michael Jessen, MD; Dharam Kumbhani, MD

Faculty Mentor: Dharam Kumbhani

Abstract

Background: Permanent pacemaker (PPM) implant frequently occurs after transcatheter aortic valve replacement (TAVR) for new conduction abnormalities including bundle branch block/fascicular block (BBB/FB). There are no guidelines regarding indication for PPM implant after TAVR and follow-up pacemaker utilization has not been described in these patients.

Methods: We performed a retrospective study of patients undergoing TAVR and subsequent in-hospital PPM implant at UTSW and Dallas VA medical centers from 2013-2017. Data abstracted included indication for pacemaker implant, pacemaker programming, and follow-up device interrogation. We compared follow-up ventricular pacing (VP) % depending on indication for PPM implant: a new BBB/FB alone versus any other indication for implant (including atrioventricular block, slow atrial fibrillation, sick sinus syndrome).

Results: Patients who underwent PPM for a new BBB/FB alone compared to other indications had a significantly lower mean VP % (19% to 46%, $p = 0.007$) and higher likelihood to have <0.1% VP (56% to 14%, $p < 0.0001$) on follow-up device interrogation.

Conclusion: Patients who undergo PPM after TAVR for a new BBB/FB alone compared to other indications have a substantially lower burden of VP on follow-up. Further studies are needed to identify subsets of patients with a new BBB/FB who will require a greater degree of VP and would greater benefit from PPM implant.

Presentation #124

Title: Independent predictors of anastomotic dehiscence and its association with survival among patients with lung transplantation: An analysis of UNOS database

Presenter: Omer Mirza

Authors: Omer B Mirza, MD; Amit Banga, MD

Faculty Mentor: Amit Banga

Abstract

Background: There is lack of data regarding pre-transplant variables associated with airway complications such as anastomotic dehiscence (AD) after lung transplantation (LT). The current study was conducted to identify recipient, donor and procedure related variables that are independently associated with AD and evaluate its impact on 1 year and 5 year survival.

Methods: We queried the United Network of Organ Sharing (UNOS) database for adult patients (≥ 18 years of age) undergoing LT between 1989 and 2014. We excluded patients with simultaneous dual organ transplantation and where data regarding AD was not available (final n=23859). With AD as the dependent variable, donor, recipient and procedure related characteristics were analyzed as potential predictors. Multivariate logistic regression analysis was conducted to determine independent associations. Kaplan Meier survival curves were constructed to compare the 1 year and 5 year survival among patients with and without AD (log-rank analysis).

Results: Overall frequency of AD for the period of study was 1.41% (n=337). AD was more common in the post-lung allocation score (LAS) era (1.54% vs 1.23%; OR, 95% CI: 1.26, 1.01-1.57; p=0.048). Following variables emerged as independent predictors of AD (adjusted OR, 95% CI): older age (1.01, 1.00-1.02; p=0.049) , male gender (1.70, 1.34-2.16; p<0.001), admission to the hospital (1.69, 1.17-2.44; p=0.005) or intensive care unit (2.02, 1.46-2.78; p<0.001) in comparison to outpatient status at the time of transplant and bilateral LT (3.27, 2.21-4.83; p<0.001) or right single LT (1.99, 1.27-3.12; p<0.001) in comparison to left single LT. Patients with AD had significantly increased mortality at 1 year (n=22585; 47.6% vs 16.9%; OR, 95% CI: 4.47, 3.58-5.59; p<0.001, Figure 1A) as well as 5 year follow up (n=15734; 70.6% vs 46.3%; OR, 95% CI: 2.79, 2.07-3.75; p<0.001, Figure 1B).

Conclusions: Overall prevalence of AD after LT is low although it appears to have increased in the post LAS era. Several recipient and procedure related characteristics are independently associated with AD. Development of AD is associated with significantly lower 1 year and 5 year survival after LT.

Presentation #125

Title: A Case of Bias

Presenter: Melanie Holtrop

Authors: Melanie Holtrop, MD; Nagendra Pokala, MD; Shan Luong, MD

Faculty Mentor: Shan Luong

<u>**Abstract**</u>

A 19 year-old woman with no past medical history presented with one month of shortness of breath and unintentional 20 lb weight loss. The shortness of breath was constant, but also worse with exertion. Deep inspiration triggered sharp chest pain and a dry cough. She denied fevers, recent travel, sick contacts, tobacco, or illicit drug use. On exam, she appeared well with oxygen saturation 98% on room air. Respiratory exam demonstrated mild tachypnea, no accessory muscle use, and decreased breath sounds at the right lung base. The anterior cervical lymph nodes were enlarged, but non tender. CRP was 3.4; ESR was 95. CT angiography demonstrated diffuse bulky lymphadenopathy, splenomegaly, and a small right pleural effusion. Excisional lymph node biopsy demonstrated benign pathology and flow cytometry. Upon further questioning, the patient endorsed intermittent swelling and pain in her finger and wrist joints for the past two years. Joint exam demonstrated swelling of the proximal interphalangeal, metacarpophalangeal, and radiocarpal joints with rheumatoid factor elevated at 24. The patient was diagnosed with rheumatoid arthritis and initiated on prednisone and methotrexate with significant improvement. Shortness of breath is a common problem for the internist. When there is a significant finding, it is important to not anchor on one diagnosis. In our young patient with diffuse lymphadenopathy and pleural effusion, lymphoma was thought to be inevitable. The findings of hand and wrist synovitis were not considered initially, and the diagnosis was missed. This case demonstrates the importance of maintaining a broad differential. In particular, autoimmune diseases are systemic diseases that may have varying presentations. Rheumatoid arthritis affects approximately 1 in 100 individuals. The typical presentation is joint pain and morning stiffness. Extra-articular manifestations are common, with symptomatic pleural disease occurring in 5% of patients. There is generally no correlation between the timing of pleural effusion development and synovitis; 25% of cases precede or develop simultaneously with onset of articular disease. Factors associated with the development of rheumatic pleural effusions include male sex, age older than 45 years, subcutaneous nodules, and high-titer RF. Pleural effusion and lymphadenopathy should be recognized as extra-articular manifestations of rheumatoid arthritis.

Presentation #126

Title: Validating Patient Reported Outcomes in Older Veterans with Chronic Back Pain

Presenter: Rabih Nayfe

Authors: Rabih Nayfe, MD; Matthieu Chansard, MCRC; Katharine McCallister, BA; Thiru Annaswamy, MD; Una Makris, MD

Faculty Mentor: Una Makris

<u>**Abstract**</u>

Background: Chronic back pain is a prevalent condition among older adults, incurring high physical and psychosocial burden. Identifying appropriate, efficient and reliable patient reported outcome (PRO) measures is critical for research and clinical purposes. The NIH's Patient Reported Outcomes Measurement Information System (PROMIS) instruments provide robust PRO measures; however, these have not been compared to validated 'legacy' instruments in older adults with chronic back pain. This study aims to evaluate convergent validity and time to completion (TTC) of PROMIS as compared to 'legacy' instruments.

Methods: We enrolled older Veterans (age 60+) with chronic back pain (≥3 months) scheduled for lumbar epidural steroid injections. Participants completed PROMIS computer adaptive test (CAT) item banks and corresponding 'legacy' instruments in the following domains: pain interference, behavior and intensity; functional status; depression and anxiety; fatigue; sleep and social functioning. Convergent validity between PROMIS and 'legacy' instruments was evaluated using Pearson correlation coefficients in a correlation matrix. Paired sample t-tests compared average TTC between both instruments.

Results: Participants included 71 Veterans who were on average 67 years old, 94% men, 73% non-Hispanic white, 16.9% African American. The average BMI was 32, 25% reported multi-site pain and 59% were diagnosed with depression, anxiety and/or PTSD. The majority (69%) reported pain duration >5+ years with ~ 93% reporting associated radiculopathy. Pearson correlations showed a strong convergent validity between PROMIS and 'legacy' instruments in all the domains (correlation coefficients >0.5) except for social functioning (0.35). PROMIS items had significantly shorter total TTC than 'legacy' items (8m10s vs 26m44s).

Conclusion: PROMIS measures, especially for pain, depression, anxiety, fatigue and sleep domains, have strong convergent validity in older Veterans with chronic back pain. Moreover, PROMIS measures require less time to complete. Given time efficiency of using PROMIS, along with strong convergent validity, PROMIS instruments are a valid and practical choice for both research and clinical purposes.

Presentation #127

Title: The Impact of Impaired Renal Function on Associations Between HDL Particle Number and Cholesterol Efflux Capacity with Incident Cardiovascular Events (Observations from the Dallas Heart Study)

Presenter: Shahzad Chindhy

Authors: Shahzad Chindhy, MD; Parag Joshi, MD; Amit Khera, MD; Colby R. Ayers, MS; S. Susan Hedayati, MD; Anand Rohatgi, MD

Faculty Mentor: Anand Rohatgi

Abstract

Background: High-density lipoprotein (HDL) becomes dysfunctional in the setting of CKD, but the clinical relevance of this is unknown. Cholesterol efflux capacity (CEC) and total HDL particle number (HDL-P) each inversely associates with incident CV events, independent of HDL-C. We sought to assess the impact of renal dysfunction on the association of CEC and HDL-P with incident CV events in a multiethnic population-based cohort.

Methods: 2,805 participants without a known history of CVD from the Dallas Heart Study were included in the analysis. CKD was defined as impaired renal function at a single time point based on an estimated glomerular filtration OR gender-based albumin-to-creatinine ratio (ACR) as defined by NHANES. Cox proportional hazards models were used to assess the associations of CEC and HDL-P. Pre-specified outcomes were ASCVD (nonfatal MI, nonfatal stroke, or death from CV), total CVD (ASCVD + coronary revascularization by percutaneous coronary intervention or coronary-artery bypass grafting, and hospitalizations for atrial fibrillation, heart failure, or peripheral arterial disease), CV death and non-CV death. Interactions of CEC and HDL-P with CKD were tested in models adjusted for age, sex, race, diabetes, hypertension (HTN), smoking, total cholesterol, HDL cholesterol, log eGFR, body mass index (BMI), hs-CRP, and ACR.

Results: The median HDL-C, CEC, and HDL-P were not significantly different between groups. In multivariate Cox models, there was a significant interaction between CEC and CKD on associations with ASCVD (p=0.01) and total CVD (p=0.05). Specifically, in those without CKD, CEC was inversely associated with incident ASCVD and total CVD. However, in those with CKD, CEC was directly associated with ASCVD and CV death but not with total CVD. HDL-P was inversely associated with each of the CV events with no evidence of interaction by CKD status.

Conclusion: CKD modified the inverse association between CEC and CV events such that higher CEC may actually connote paradoxically increased CV risk in those with CKD. HDL-P remained inversely associated with events regardless of CKD status. Further studies are warranted to elucidate the mechanisms by which CKD impacts these relationships.

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Presentation #128

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Title: Extreme elevations in both HDL-C and Lp(a), adiposity, and subclinical atherosclerosis in a multi-ethnic population-based cohort: observation from the Dallas Heart Study

Presenter: Nimish Shah

Authors: Nimish N. Shah, MD; Ian J. Neeland, MD; Parag H. Joshi, MD; Amit Khera, MD; Colby Ayers, MS; Anand Rohatgi, MD

Faculty Mentor: Anand Rohatgi

<u>**Abstract**</u>

Introduction: Higher HDL-C is considered atheroprotective; however, extremely elevated HDL-C may confer increased atherosclerotic cardiovascular disease (ASCVD) risk. Elevated lipoprotein (a) [Lp(a)] is a known independent risk factor for ASCVD. We hypothesized that those with both extremely elevated HDL-C and Lp(a) would have accentuated adverse metabolic and atherosclerosis phenotypes.

Methods: Participants were included from the probability-based multi-ethnic Dallas Heart Study who had risk factor measurements, MRI, DXA, and coronary calcium (CAC). High HDL-C was defined as greater than the 90th race- and sex-specific percentile, and high Lp(a) was defined as greater than the 80th race- and sex-specific percentile. Four groups were constructed to compare risk factors: high HDL-C/high Lp(a), high HDL-C alone, high Lp(a) alone, and neither high. Multivariable adjusted linear regression models were used to assess the cross-sectional association between high HDL-C/high Lp(a) relative to the neither high group and each of the following: DXA-derived lower body fat, MRI-derived liver and visceral fat, MRI-derived aortic wall thickness, and CAC.

Results: Of 2554 participants, 63% were black and 56% were women. The prevalence of high HDL-C/high Lp(a) was 1.9%. HDL-C/Lp(a) groups varied significantly by family history of MI, BMI, waist-to-hip ratio, DXA and MRI-derived fat mass, insulin resistance, total cholesterol, adiponectin, and lipid particle distribution. High HDL-C/high Lp(a) compared to the neither high group was not associated with any subclinical atherosclerosis measure but was directly associated with MRI-derived visceral fat in fully adjusted models ($p < 0.01$, Table 1). Conclusion In a large multi-ethnic cohort, high HDL-C/high Lp(a) was directly associated with visceral adiposity, a measure linked to increased ASCVD risk. These findings warrant further investigation into the metabolic perturbations in this group as it related to ASCVD.

Presentation #129

Title: Hypophosphatasia among patients presenting for osteoporosis evaluation

Presenter: Roger Fan

Authors: Roger Fan, MD; Ananya Kondapalli, MD; John Poindexter, Naim M. Maalouf, MD; Khashayar Sakhaee, MD

Faculty Mentor: Naim Maalouf

Abstract

Background: Hypophosphatasia is a rare heritable disorder characterized by deficiency of tissue non-specific alkaline phosphatase leading to accumulation of phosphorylated molecules, including inorganic pyrophosphate, which causes impaired bone mineralization and fractures. Hypophosphatasia is overlooked among adults diagnosed with osteoporosis. The distinction is important because bisphosphonate use is associated with atypical femoral fractures (AFF) in hypophosphatasia. A low serum alkaline phosphatase level (ALP) is the hallmark of hypophosphatasia. We sought to characterize patients presenting to an osteoporosis clinic with a low ALP and assess for features of hypophosphatasia.

Methods: Our population included all patients presenting to the UT Southwestern (UTSW) Mineral Metabolism clinic for osteoporosis from 7/1/2006-6/30/2016 with initial ALP ≤40 IU/L. We collected information on fracture history, bone mineral density (BMD), laboratory studies, medications, and secondary causes of low ALP. These patients were compared to controls matched for age, gender, race, and date of initial visit. We further compared features of patients with persistently vs. transiently low ALP, and patients in whom hypophosphatasia was suspected (based on clinic notes).

Results: Of 2810 patients presenting to clinic for osteoporosis, 159 patients had initial ALP ≤40 IU/L (5.66%). Compared to matched controls, low ALP patients had significantly lower BMI (p=0.00012) and lower BMD at the femoral neck (p=0.017) but not at other skeletal sites. Only 23 patients (14.5%) had a persistently low ALP, defined by ≥2 ALP values, with all values ≤40 IU/L. Of 10 patients suspected of having hypophosphatasia, vitamin B6 was checked in 9 patients, and was only elevated in one patient with hypophosphatasia confirmed by genetic analysis. Compared with the 149 patients not suspected of having hypophosphatasia, the 10 patients with suspected hypophosphatasia had significantly higher prevalence of AFF (20% vs. 0.67%), foot fractures (40% vs. 12.1%) and a history of unusual tooth loss/decay (20% vs. 1.34%).

Conclusions: Most patients evaluated for osteoporosis with persistently low ALP were not suspected of having hypophosphatasia. Patients suspected of having hypophosphatasia had higher rates of AFF, foot fractures and unusual dental history. Additional genetic and metabolic studies are planned for patients with suspected and/or proven hypophosphatasia in the UTSW Mineral Metabolism Clinic.

Presentation #130

Title: Role of Igfbp3 in Neonatal Heart Regeneration

Presenter: Shah Ali

Authors: Shah R. Ali, MD; Nicholas T. Lam, PhD; Hesham A. Sadek, MD, PhD

Faculty Mentor: Hesham Sadek

Abstract

Neonatal mice exhibit healthy myocardium with minimal scar formation following an apical resection injury or myocardial infarction (MI) due to expansion of cardiomyocytes, in stark contrast to adult mice. In order to define the molecular basis for this regenerative response, we sought to identify secreted proteins whose expression increases after neonatal MI through a microarray screen. After further confirmation with real-time PCR, in-situ hybridization, and immunofluorescence, we discovered that IGFBP3 is a secreted factor that is upregulated following neonatal MI. Our data suggests a possible role for IGFBP3 to promote cardiomyocyte cell division. IGFBP3 belongs to a family of proteins that participates in the IGF signaling pathway by binding, stabilizing, and transporting insulin-like growth factors (IGFs) in the serum, although IGF-independent effects on cell division and cell death have been described. To date, the role of IGFBP3 in neonatal cardiac regeneration is not characterized. Our work demonstrates that IGFBP3 is abundant in the border zone after neonatal MI at the mRNA and protein level but rare in the adult heart after MI. Remarkably, delivery of recombinant IGFBP3 protein into older mouse hearts leads to an increase in cardiomyocyte cell division. Our data suggests that IGFBP3 plays a key role in the robust cardiomyocyte mitosis that occurs after neonatal MI and may present a therapeutic opportunity for heart disease in humans.

Presentation #131

Title: Cirrhosis and TIPS in Pregnancy: A Case Report

Presenter: Shruti Chandramouli

Authors: Shruti Chandramouli, MD; William H. Lee, MD; Julie Lo, MD; Seth Toomay, MD; Shannan Tujios, MD

Faculty Mentor: Shannan Tujios

Abstract

Case Description: A 40-year old G2P1 female with cirrhosis and history of esophageal varices, encephalopathy, and ascites presented with enlarging caput medusae and decompensated cirrhosis at 22 weeks gestation. On exam, she had multiple caput medusae on her abdomen, with the largest one in her epigastric region accompanied by a palpable and audible thrill. MRI abdomen showed a massively dilated paraumbilical vein (~4cm) with multiple anterior abdominal wall collaterals and ascites. She underwent a TIPS procedure with reduction of her portosystemic pressure gradient from 16 mm Hg to 8 mm Hg. She experienced improvement in ascites and decompression of collateral vessels. She had a Caesarean section at 30 weeks gestation with delivery of a healthy male infant but developed a wound infection and hepatic encephalopathy post-partum, that were ultimately well-controlled. Since discharge, she has been maintained on the liver transplant list with a MELD score of 15, well-controlled ascites, and medically-managed encephalopathy. Her TIPS is monitored with ultrasound regularly and remains patent five years later. Her son remains healthy with no developmental delays.

Discussion: Pregnant women with cirrhosis are at risk of complications. There is an increased risk of hepatic encephalopathy, especially in hypotension or infection. There is also risk of splenic artery rupture due to increased splenic blood flow from both pregnancy and portal hypertension, which can lead to rapid intra-abdominal bleeding and high maternal-fetal mortality. There is an increased risk of bleeding esophageal varices during the second and third trimesters of pregnancy, due to increasing pressure of the growing fetus on the inferior vena cava. While sclerotherapy and banding of varices are considered safe in pregnancy, TIPS can be used as a rescue technique when a pregnant patient develops refractory bleeding varices. TIPS procedures are safer later in pregnancy, after fetal organogenesis and critical brain development are complete. Radiation levels in TIPS are about 5 mGy, which is below the 50 mGy threshold for an increased risk of fetal malformations. Our case shows that TIPS can be performed safely in pregnancy but close monitoring by a multidisciplinary team of hepatologists, maternal-fetal medicine specialists, and interventional radiologists is necessary.

Presentation #132

Title: Pacs-1 is a novel regulator of antigen receptor signaling and B cell homeostasis

Presenter: Evan Nair-Gill

Authors: Evan Nair-Gill, MD, PhD; Xue Zhong, PhD; Aijie Liu, Bruce Beutler, MD

Faculty Mentor: Bruce Beutler

<u>**Abstract**</u>

Background: Mechanisms that regulate the number of lymphocytes in the body are incompletely understood. Defective lymphocyte homeostasis drives primary immunodeficiencies, autoimmunity, and lymphoid malignancies. Through forward genetic screening of mice mutagenized with N-ethyl-N-nitrosourea (ENU), we found that phosphofurin acidic cluster sorting protein-1 (Pacs-1) is a critical regulator of B lymphocyte homeostasis. Mice deficient for Pacs-1 (Pacs-1-/-) have ~50% fewer circulating B cells. Pacs-1 is a sorting protein that mediates intracellular protein traffic between membrane-bound compartments. It has no previously described role in the immune system. Here, we define Pacs-1's function in B cells and measure its contribution to the development of autoimmune and lymphoproliferative diseases.

Methods: We used flow cytometry to identify B cell subsets dependent on Pacs-1 and to measure their response to B cell receptor (BCR) stimulation. Immune competence in Pacs-1-/- mice was tested through immunization using well-characterized model antigens. We combined the Pacs1 deletion with genetic models of disrupted cell-intrinsic and cell-extrinsic apoptosis to assess Pacs-1's role in dysregulated lymphocyte proliferation and autoimmunity.

Results: Pacs-1-/- mice had ~4-fold reduction in splenic follicular B cells. These cells showed blunted calcium flux after BCR crosslinking, indicating a defect in antigen receptor signaling. Despite this, Pacs-1-/- mice mounted normal humoral responses after immunization. Bcl2 reduces cell death through cell-intrinsic apoptosis and is frequently overexpressed in B cell lymphomas. Transgenic expression of Bcl2 overrode the B cell deficiency in Pacs-1-/- mice. Humans and mice carrying loss of function mutations in the Fas gene lack cell-extrinsic apoptosis. They develop bulky lymphadenopathy and lupus-like autoimmunity due to an accumulation of autoreactive lymphocytes. In mice carrying mutant Fas (Faslpr), Pacs-1 deletion strikingly suppressed the development of lymphadenopathy and the expansion of autoreactive cells.

Conclusions: Pacs-1 regulates B cell homeostasis by enhancing antigen receptor signaling and reducing B cell death from cell-intrinsic apoptosis. While Pacs-1 deletion does not block normal humoral responses, it impairs lymphoproliferation resulting from defects in cell-extrinsic apoptosis. Targeting the intracellular trafficking machinery represents a novel way to disrupt antigen receptor signaling. This approach may be leveraged to treat certain autoimmune or lymphoproliferative disorders while avoiding toxicity to beneficial immune functions.