34th Annual

EVMS Research Day

Friday, October 14, 2022

Support for research travel and publications for trainees at Eastern Virginia Medical School are made possible by funding mechanisms managed by EVMS Research and Student Affairs. Of special note, we would like to highlight the following resources:

EVMS Community Faculty Designated Student/Resident Research Award Fund
Specifically created as a funding mechanism for student and resident professional travel to present research findings, up to eight $1,000 awards are offered per fiscal year. To qualify for funding, applicants must have a publication-quality manuscript ready for submission to a professional journal within three months of travel. Through this fund, made possible by a Community Faculty donor, over 45 students and residents have been able to present their research at national conferences in a wide variety of specialties and areas of research.

Student Affairs Award-Travel and Publication Fees
Students are able to utilize a new EVMS funding source for travel and publication fees, administered by Student Affairs. Travel awards of up to $1,500 per student are given to support attendance at a conference to present research findings. This travel award can be used to cover the conference registration fee for either virtual or in-person conferences, so actual travel is not required. Additionally, through this mechanism, students are able to apply for separate funds to cover manuscript publication fees for submission to professional journals.

For more information about these awards or the application process, students and residents can email ***EVMSResearch@evms.edu***.

34th Annual EVMS Research Day
October 14, 2022
Timeline of Events

Connection information and more on the Research Day Website:

https://www.evms.edu/research/research_day/

Oral Presentations

In person: Waitzer Hall, room 300

Overflow/Remote viewing: Waitzer Hall, rooms 989 & 1031

Virtual: (***click here to join*** or join directly on the website)

Opening Remarks

12:00-12:15 PM Eva Forgacs-Lonart, PhD, EVMS Research Advisory Committee Co-Chair
Alfred Abuhamad, MD, EVMS President, Provost, and Dean of the School of Medicine

Keynote Speaker

12:15-1:15 PM Introduction of Keynote Speaker
Paul Harrell, PhD, EVMS Research Advisory Committee Co-Chair

Milton L. Brown, MD, PhD
EVMS Professor of Internal Medicine and Vice Dean for Research
Prudence and Louis Ryan Chair of Research
Subject: Discovering New Medicines for the Future

Platform Presentations

1:15-1:29 PM Esther Jones, Biomedical Sciences Graduate Student
Title: Glycosylated RNA - A Potential Marker for Prostate Cancer
Mentor: Aurora Kerscher, PhD

1:30-1:44 PM Camille Williams, MD 2025 Student
Title: Corticotroph hyperplasia caused by NR3C1 germline variants in patients with ACTH-dependent hypercortisolism
Mentor: Ana Paula Abreu, MD, PhD

1:45-1:59 PM Taylor Drake, MD 2025 Student
Title: Stratifying high-risk patients, quantifying therapy efficacy, and detecting treatment/racial disparity in triple-negative breast cancer (TNBC) at Sentara-EVMS-VOA
Mentor: Amy Tang, PhD

2:00-2:14 PM Emily Pilc, MD 2025 Student
Title: Trochlear Dysplasia and Anterior Knee Pain after ACL Reconstruction: A Sex-Based Comparison
Mentor: Miho Tanaka, MD

2:15-2:29 PM Kanishk Sharma, MBBS Internal Medicine Fellow
Title: Impact of heart failure education on knowledge and comfort of healthcare in a Skilled Nursing Facility
Mentor: Marissa Galicia-Castillo, MD, MSEd, CMD, FACP, AGSF, FAAHPM

Short Break, Switch to Breakout Session Links

2:30-2:40 PM

Continued on next page

Poster Presentations

In person: Waitzer Hall, room 200 & 2nd floor lobby

2:40-3:30 PM	**Poster Session A**
3:30-3:40 PM	Short Break; Take Down A Posters, Display B Posters
3:40-4:30 PM	**Poster Session B**
4:30-4:45 PM	Short Break

Presentation of Poster Awards and Closing Remarks **Waitzer Hall, room 200**

4:45-5:00 PM

Awards from the Vice Dean for Research and Vice Dean for Academic Affairs
Eva Forgacs-Lonart, PhD, EVMS Research Advisory Committee Co-Chair
Paul Harrell, PhD, EVMS Research Advisory Committee Co-Chai

EVMS Biomedical Sciences Programs Poster Awards
David Taylor-Fishwick, PhD, Director,
EVMS Biomedical Sciences Graduate Programs

2022
KEYNOTE LECTURE

Discovering New Medicines for the Future

Milton L. Brown, MD, PhD, FNAI

Professor of Internal Medicine,
Vice Dean for Research,
Prudence and Louis Ryan Chair of Research
Eastern Virginia Medical School
Norfolk, VA

POSTER PARTICIPANTS

Biomedical Sciences

Masters Healthcare Analytics & MPH

Residents and Summer Scholars

Doctor of Medicine Students

Abstract Title: Impact of Social Isolation and Space Radiation on Stress Responsivity and Sleep

Investigator: Austin Adkins
Co-Investigator(s): Alea F. Boden; Justin D. Gotthold; Emily M. Hildinger; Ryan D. Harris; Laurie L. Wellman; Sleep Research Laboratory, Center for Integrative Neuroscience and Inflammatory Diseases; Richard A. Britten; Radiation Oncology, Center for Integrative Neuroscience and Inflammatory Diseases
Department(s): Sleep Research Laboratory, Center for Integrative Neuroscience and Inflammatory Diseases

Abstract

INTRODUCTION:
The long durations of the proposed Mars missions will expose astronauts to several physical and psychological stressors, including space radiation (SR), and periods of social isolation (SI). These stressors, along with mission demands, have the potential to impact sleep and may result in fragmented or reduced sleep. Indeed, poor sleep quality may occur more than sleep loss, though astronauts will likely experience both. Sleep problems have been reported by astronauts which occurred early and persisted throughout the mission. Sleep loss and poor sleep quality are linked to reduced neurocognitive and physical deficits in humans and animals. Poor sleep quality can also reduce the ability to cope with stressful experiences, as altered EEG oscillatory activity is involved dysfunctional cognition and behavior. Therefore, sleep loss poses a significant threat to mission success and crew health. In this study, we assessed freezing behavior, sleep duration, and sleep quality via electroencephalogram (EEG) and EEG power spectra activity during specific sleep states (NREM delta, <4 Hz, and REM theta, 4-7 Hz) of rats exposed to ground-based analogs of SI and SR and trained in conditioned fear (CF), a model of stress-related learning.

METHODS:
Male, outbred, Wistar strain rats (8-9 months old at time of study) were subjected to SI (visual barriers between cages, n=21) or individually housed (as a sham group, n=20). Separate groups of rats received SR (15 cGy GCRsim) treatment and were either individually housed (n=15) or subjected to SI (SI + SR; n=16). A sham group traveled with SR treated groups as a control to account for potential compounding effects of transit required for the experiment on the animals' sleep and behavior, and were either individually housed (n=5) or subjected to SI (n=3). At least 3 wks prior to testing, all rats were implanted with telemetry transmitters for recording EEG. For CF training, the rats were placed in a chamber and presented with 20 footshocks (ST: 0.8 mA; 0.5 s duration, 1.0 min interstimulus interval). They were assessed for fear memory recall to the context at one- (context (CTX)) and three-weeks (extinction (EXT)) following training. EEG recording occurred over a 20hr period at baseline (before training) and immediately after ST, CTX, and EXT, respectively. All CF training took place during the light period in the 4th h and sleep recording took place immediately after training.

RESULTS:
The rats were classified as either resilient (Res) or vulnerable (Vul) based on percent change in REM amounts for the first 4 h of sleep recording following ST compared to baseline (%Change = Total REM ST/Total REM Baseline x 100) with Vul rats having 50% or greater decrease in REM and Res rats having smaller decreases (£ 50%), no change, or increases in REM. During the light period (first 8 h of recording), baseline NREM amounts were lower in the SI Vul group compared to any other group. These differences persisted through CF, and both the Res and Vul SI animals displayed lower NREM by EXT. Despite this, delta power during NREM was highest in the SI groups following ST; this contributed to a higher number of NREM episodes, but the lowest duration of any group. There were no differences in baseline REM amounts for any group. Surprisingly, animals exposed to SR or SI + SR had higher total REM post-ST than any other group, and this persisted through EXT. These groups also had the highest number of REM episodes, but episode duration did not differ between groups. Despite having the highest amount of REM, theta power during REM after ST was lower in irradiated groups, and these groups exhibited increases in fragmented REM. Theta power was also decreased in the SI group, but these animals did not show signs of disrupted REM. Freezing behavior was increased in the irradiated groups compared to SI and Shams throughout CF.

CONCLUSIONS:
Exposure to SR may negatively impact the ability to cope with stressful experiences by impairing extinction learning (as indicated by increased fre ezing behavior during EXT). This may be related to poor REM quality in these groups, as REM is implicated in emotional and memory processing. Despite having lower NREM durations and lower REM theta power, extinction learning was not impaired in SI rats (as indicated by lower freezing behavior during EXT). This may be attributed to higher NREM delta power, or SI may have beneficial compensatory mechanisms that allow for REM quality to be maintained despite lower theta power.

Abstract Title: Imaging Considerations for Acute Stroke with Clinical Case Presentation

Investigator: Jason Agola
Co-Investigator(s): Garrison Glavich, MD, EVMS Radiology, Mitchell Wangsgard, MD, EVMS Radiology
Department(s): EVMS Radiology

Abstract

Introduction:
Acute stroke is a leading cause of death and disability in the U.S. (1). More than 700,000 people have a stroke every year with more than half of these individuals experience a reduction in mobility (1). It is estimated to cost the United States economy approximately 53 billion dollars a year (1). Major risk factors for stroke include prior stroke, hypertension, dyslipidemia, diabetes, smoking and obesity (1).

Case Information:
A geriatric male patient with history of seizures presented to the emergency department for concern of breakthrough seizures versus stroke. The patient endorsed slurred speech and mild altered mental status after possible seizure activity. A stroke alert was called with multiple imaging modalities carried out that did not show any acute large vessel occlusion in the head in the head but did show a large plaque at the left carotid. A second stroke alert for worsening symptoms with right sided motor deficits illustrated a new left MCA occlusion. Medical management was carried secondary to relative surgical contraindications and the patient's specific goals of care.

Discussion:
The first imaging modality when there is clinical suspicion of an acute stroke is usually a non-contrasted CT head (NCCT) (2). The main purpose of the NCCT is to ensure there is no intracranial hemorrhage that would be a contraindication to intervention (3). After the NCCT, generally if there is no hemorrhage detected, then CT angiography of the head and neck and CT perfusion are preformed to assess the usefulness of more advanced acute intervention (2). The most sensitive and specific test for acute stroke is a MRI head exam, although these are generally more time consuming than CT and there are commonly implanted medical devices that may be contraindications to MRI (2).

Conclusion:
Imaging in acute stroke is of paramount importance with regards to triaging those patients who would benefit from early treatment. As the U.S. population continues to age and stroke centers are becoming more common place, it is important for all clinicians to be familiar with the general imaging work up and treat algorithms that are present in acute stroke management.

Abstract Title: Using SIAH to risk stratify patients, quantify and guide immuno-oncology (IO) therapy (chemotherapy and pembrolizumab) in triple-negative breast cancer (TNBC)

Investigator: Jonathan Baker
Co-Investigator(s):
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Triple-negative breast cancer (TNBC) is the most aggressive subtype of breast cancer, with a high relapse rate and the worst survival. Immuno-oncology (IO) therapy is an exciting area of major breakthrough for TNBC. Improved pathologic complete response (pCR) rates (60-65%) were reported in high-risk, early-stage TNBC following chemo- plus IO-therapy in the neoadjuvant setting. Recently, the FDA approved an immune checkpoint blockade (ICB) therapy, pembrolizumab, for high-risk early-stage patients; and in PD-L1-positive, locally recurrent, unresectable, or metastatic TNBC. At the same time, unfortunately, the grade 3 or 4 treatment-related adverse events were significantly increased in response to the new IO-regimens. The challenge is: how to predict the treatment benefit of immuno-oncology (IO) therapy, while minimizing these adverse effects. Without a proper guide, pembrolizumab plus chemotherapy is often administered "blindly" in the neoadjuvant setting. Despite the benefit of this newly FDA-approved IO-therapy, 30-40% of high-risk early stage TNBC patients, and 60-70% of PD-L1-positive metastatic TNBC patients who receive the IO-therapy did not show any objective improvement. Thus, there is a pressing need to develop an accurate prognostic tool for better patient stratification and treatment optimization in TNBC. To address this unmet need, we propose to evaluate SIAH as a predictive biomarker to dovetail with PD-L1 status and pathologic response to optimize the use of IO-therapy for TNBC. We aim to demonstrate the clinical utility of SIAHON/OFF expression as a novel prognostic biomarker to risk stratify patients, predict the need for and/or efficacy of adjuvant and/or neoadjuvant immunotherapies.

Methods:
In this clinical study, we conducted SIAH and PD-L1 immunohistochemistry (IHC) staining using a newly constructed TNBC tumor microarray (TMA), utilizing tumor specimens collected from a large cohort of 400 TNBC tumors collected at the VCU Massey Cancer Center in collaboration with Dr. Harry Bear and his team. For immune biomarker staining, the whole tumor slides will be stained using neoadjuvant chemotherapy-treated TNBC residual tumors at the Sentara Cancer Network and VCU Massey Cancer Center to validate the TMA results and determine whether SIAH is an independent, prognostic biomarker in TNBC, capable of predicting early tumor relapse, cancer disparity, and patient survival.

Results:
Although still ongoing, we have observed an interesting, inverse relationship of SIAH and PD-L1 expression in a subset of ICB-naïve TNBC tumors. Our preliminary results suggest that SIAHHigh/ON in TNBC tumors may correlate with immuno-suppression, ICB-resistance, and/or the need for additional aggressive chemotherapies to control TNBC malignancy. Conversely, SIAHLow/OFF may indicate immuno-sensitivity, possible ICB-sensitivity, and good prognosis following surgery.

Conclusion:
Statistical analyses, independent IHC validation, and meticulous confirmation will be conducted to demonstrate the clinical utility of SIAHON/OFF expression as a novel prognostic biomarker to risk stratify TNBC patients, predict early tumor relapse, and quantify and predict chemo/IO-resistant in TNBC residual tumors to provide clinical benefit. Results thus far seem very promising.

Abstract Title: Extracellular Vesicles Are Potential Biomarkers For Social Determinants Of Health-Mediated Stress

Investigator: Matthew Bavuso
Co-Investigator(s): Noel Miller, Physiological Sciences\Biomedical Sciences MA
Department(s): Physiological Sciences

Abstract

INTRODUCTION:
Recent evidence supports psychosocial stressors to be social determinants of health (SDoH) and the existence of a connection to cardiometabolic diseases. There is less information available about the specifics of this connection with varying biochemical and pathogenic criterion commonly accepted to impact the development and progression of cardiovascular disease (CVD), particularly in at-risk groups. Recent investigations in the field have identified extracellular vesicles (EVs) as potential biomarkers for and/or contributors to CVD pathogenesis. This study aimed to identify any correlations between psychosocial factors and plasma EVs in a cohort of patients at risk for CVD. EV effects on coronary endothelial function were also determined.

METHODS:
EVs were isolated from heparinized plasma via size exclusion chromatography. EV numbers and size were determined through nanoparticle tracking analysis. Validated questionnaires were used to generate data pertaining to perceived chronic stress, social isolation, and loneliness. Human coronary endothelial cells (HCAECs) were treated with the isolated EVs for analysis of barrier function and migration via ECIS technology. Multivariable linear regression analysis, adjusted for BMI and arteriosclerotic CVD (ASCVD) risk scores, was used to determine any associations.

RESULTS:
There were no significant associations between psychosocial factors and isolated EV size or concentration (beta $p>0.05$). In adjusted models, there were significant negative correlations between perceived loneliness and EV-treated endothelial barrier function (beta = -0.44, $p=0.04$), but not with chronic stress (beta = -0.11, $p=0.6$) or social isolation (beta = -0.18, $p=0.4$).

CONCLUSION:
This data is suggestive of an association between perceived loneliness and EV-mediated endothelial dysfunction. These results provide demonstrative evidence that EVs have potential uses as biomarkers for SDoH-mediated stress and that EVs potentially link endothelial dysfunction and psychosocial stressors as SDoH.

Abstract Title: A subtype of brain pericytes contributes to decreased amyloid beta deposition in the brain of patients with Alzheimer's Disease

Investigator: Diana Bohannon
Co-Investigator(s): Daniell Long, MMCB; Woong-Ki Kim, MMCB
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION:
Alzheimer's disease (AD) is the most common form of dementia, and is characterized by β-amyloid (Aβ) plaque formation and vascular dysfunction. Recent studies have shown that cellular components of the blood-brain barrier (BBB), pericytes (PCs) in particular, may play a direct role in both Aβ buildup and changes in neurovascular function. Previously we identified a traditional smooth muscle actin (SMA)-negative subset of PCs, type-1 PC (PC1), and a disease-associated, SMA-positive PC subset, type-2 PC (PC2). In this study, we sought to determine whether they differentially interact with Aβ isoforms in AD.

MATERIALS AND METHODS:
Using IHC and IF we examined brain tissues from human AD patients and cognitively normal aged subjects for changes in BBB function, pericyte subsets, and known AD pathologies.

RESULTS:
Our initial findings demonstrated that patents with high percentage of PC2 exhibited less BBB breakdown, less dense Aβ42 plaques, and lower tissue Aβ42:Aβ40 ratios; all positive prognostic indicators in AD. In an attempt to identify the mechanism by which PC2 may reduce Aβ-related AD pathologies, we sought to identify the independent role of PC1 and PC2 on Aβ40 and Aβ42. Aβ42, but not Aβ40 was found to be internalized in PC1, but not PC2, as a part of the clearance process, leading to an increase in cleaved-caspase 3 apoptosis in the PC1 population of AD patient which correlated to PC loss. On the contrary, Aβ40 and Aβ42 builds up on the outside of PC2 where secreted proteolytic enzymes can degrade it without contributing to pericyte loss. This data suggests a long-term impact on Aβ processing and clearance for PC2, but not PC1 in the brains of AD patients.

CONCLUSIONS:
Collectively, our findings shed light on some of the discrepancies in the field concerning the role of pericytes in AD. By differentiating PCs into functionally distinct subtypes, we have been able to demonstrate clear differences between PC1 and PC2 in Aβ uptake and processing, which would likely convolute the data when combined into a single population. Further elucidating the mechanisms and triggers that activate Aβ clearance by PCs in a subset-specific manner may prove useful in reducing the build-up of excessive Aβ and toxic plaque formation without producing undesirable immune cell activation in the CNS of AD patients.

Abstract Title: Characterization of Lipid Droplet Associated Pro-fibrotic Macrophages in Sleep Fragmented Mice

Investigator: Lanay Clark
Co-Investigator(s): Ravin Fisher, Biomedical Science; Frank Lattanzio, Department of Physiological Sciences; Anca Dobrian, Department of Physiological Sciences
Department(s): Department of Physiological Sciences

Abstract

INTRODUCTION:
The growing incidence in obesity across multiple populations is driving non-alcoholic fatty liver disease to become the most common form of liver disease in the world. Nearly 25% of these individuals will develop non-alcoholic steatohepatitis (NASH) and may face some form of sleep fragmentation through airway obstruction. NASH is characterized by lipid droplet accumulation in the liver and progressive tissue fibrosis. The latter is a major concern due to lack of appropriate therapies to restore normal liver architecture and function. Our lab used a pre-clinical rodent model of NASH and examined effects of diet and sleep fragmentation on disease progression. Sleep fragmentation both in early and late stages of disease exacerbated liver fibrosis. The key cellular players involved in production of extracellular matrix are stellate cells and pro-fibrotic macrophages. Previous data from the lab showed that a population of macrophages surrounding the lipid droplets express abundant galectin-3 (fibrotic marker) and are significantly increased in mice subjected to sleep fragmentation. To further understand the phenotype of these lipid-associated macrophages (LAM) I tried to answer the question whether they are resident Kupfer cells or newly recruited circulating monocytes. To establish Kupfer cell phenotype I used Clec4 as a marker.

METHODS and RESULTS:
Co-expression of fibrotic and Kupfer cell markers was analyzed using immunofluorescence. I used the profibrotic phenotypic marker galectin 3 and Kupffer cell marker clec4. Primary anti-mouse antibodies were raised in rat and in goat, respectively. The two primary antibodies were incubated together overnight, at 4C, followed by 1.5hr incubation with the secondary antibodies in sequence that were and rabbit anti-goat and goat anti-rat respectively, with 6 washes in between the incubations. The result was modest co-expression of the markers in LAM and abundant expression of Clec4 in the parenchymal macrophages, as expected. This led to the conclusion that LAM may be primarily resident Kupfer cells in contrast to newly recruited circulating macrophages.

CONCLUSION:
Previous data used F4/80, a murine macrophage marker, and galectin 3 colocalization to characterize macrophage populations which yielded a baseline comparison for this study. This baseline population averaged at lower counts than the profibrotic lipid associated Kupffer cell counts and therefor definitive associations cannot be assessed without further information. Co-expression of galectin 3 and clec4 was highly prevalent for sleep fragmented mice and therefor original data found by the lab may be representative of Kupfer cells being the primary macrophage associating with lipid droplets.

Abstract Title: Role of Estrogen in Utero on Fetal Skeletal Muscle Development Important For Insulin Sensitivity and Glucose Homeostasis in Offspring

Investigator: Phillip Gauronskas
Co-Investigator(s): Gerald Pepe, Department of Physiological Sciences
Department(s): Department of Physiological Sciences

Abstract

INTRODUCTION:
Insulin resistance typically precedes and ultimately leads to insufficient insulin production and the onset of type II diabetes. Currently, in the US approximately 100 million people are either living with diabetes or prediabetes. Using their non-human primate baboon model and the aromatase inhibitor letrozole, Pepe and colleagues have shown that baboon offspring born to mothers deprived of estradiol (E2) during the second half of gestation exhibited insulin resistance and a deficit in first phase insulin release, which was not due to an impairment of fetal or offspring growth or an alteration in adipose sensitivity to insulin. We also showed that that the number of microvessels and the microvessel/skeletal muscle fiber ratio, which is important for delivery of insulin and glucose to myofibers, the size and amount of individual muscle fibers, as well as the distribution and ATP synthase content of mitochondria were significantly reduced in near term fetuses deprived of E2. Moreover, impaired microvessel/muscle fiber ratio was sustained in offspring. Importantly, all parameters in fetuses and offspring were restored to normal in animals treated with letrozole plus E2. Therefore, we proposed that the elevation in E2 during the second half of primate pregnancy promotes systemic micro-vascularization as well as growth of fetal muscle fibers essential for insulin sensitivity in adulthood. However, it remains to be determined whether the impairment of fetal skeletal muscle fiber growth and mitochondrial function in E2 deprived baboons is sustained in offspring. Accordingly, we have initiated studies to examine the latter.

METHODS:
Studies will be performed using samples of vastus lateralis skeletal muscle paraffin embedded or frozen (-80C) and originally obtained from post pubertal baboon offspring (n = 6/group) born to mothers untreated or treated in utero with letrozole ± E2. The specific activity of respiratory enzyme complexes and citrate synthase will be determined in enriched fractions of mitochondria. The distribution of mitochondria and detection of slow and fast myofibers will be determined by immunofluorescence and specific antibodies and procedures ongoing. The number and size of slow and fast fibers per fascicle and the area of the fascicle comprised of myofibers will be quantified by image analysis.

CONCLUSION:
We anticipate that impairment of fetal skeletal muscle mitochondria enzyme activity and myofiber development induced by estrogen deprivation in utero will be sustained in offspring. These studies coupled with our previous findings are clinically relevant since preterm birth, aromatase mutation, E2 receptor null mutation, and maternal-fetal exposure to endocrine disruptors, which curtail fetal exposure to the elevation in or action of E2, are associated with increased incidence of insulin resistance/type 2 diabetes in human offspring.

Abstract Title: To investigate the role of NFkB phosphorylation and activation in response to SIAH inhibition in impeding malignant tumor growth of oncogenic K-RAS-driven undruggable and incurable human cancer cell lines

Investigator: Ashleigh Hannah
Co-Investigator(s): Andrew Howell, B.S., Department of Microbiology and Molecular Cell Biology/Biomedical Sciences Research Graduate Program
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Seven-in-Absentia Homolog (SIAH), an evolutionary conserved RING-domain E3 ubiquitin ligase, is the most downstream signaling gatekeeper of EGFR/K-RAS signaling pathway. The RAS pathway activation is involved in cell proliferation, differentiation, and survival in normal development; The constitutive activation of the oncogenic EGFR/HER2/K-RAS pathway is a major driving force in promoting early tumor relapse, malignant tumor growth, local invasion, and systemic metastasis. Through investigation and coordinated drug development effort, a variety of targeted therapies against all the major signaling molecules in the EGFR/HER2/K-RAS signaling pathway has received FDA approval for clinical applications; however, the transient antitumor effect is often observed while the rapid emergence of drug resistance seemed to be unavoidable.

We discovered that SIAH function is indispensable for oncogenic RAS signaling in the deadliest human cancer types, i.e., pancreatic cancer, lung cancer, and colorectal cancer. We designed a potent SIAH inhibitor SIAH2PD, that interferes with SIAH dimerization, enzymatic activity, substrate binding, which in turn resulted in a complete eradication of oncogenic K-RAS-driven malignant tumor growth. The Tang lab has previously shown an amazing antitumor efficacy of this SIAH inhibitor, SIAH2PD, against oncogenic K-RAS-driven undruggable and incurable cancer cells (i.e., MiaPaCa, A549, MDA-MB-231, MDA-MB-468) in xenograft mouse models by abolishing tumorigenesis and metastasis in vivo. Even though tumor eradication was achieved, the molecular mechanism remained unclear and was cause for investigation into the specific mechanism of action following SIAH inhibition. By using Reverse Phase Protein Array (RPPA) and Principal Component Analysis (PCA) analyses, we found that phospho-NFkB p56 (Ser536) was upregulated in three cancer cell lines in response to SIAH inhibition. Phospho-NFkB p65 (Ser536) is an activated form of NFkB (i.e., Nuclear Factor kappa B) that can be phosphorylated by various kinases (i.e., GSK3B, TBK1, CDK6, PKCδ, etc.), many with known function in human cancer. The phosphorylated and activated NFkB plays a role in promoting inflammation through the production of inflammatory cytokines and increased proliferation signals that regulate the delicate balance of survival/proliferative/death genes/pathways and promote the vascularization and EMT invasive phenotype of tumor cells in a context-dependent manner. To validate these novel findings and delineate the roles of phospho-NFkB p56 (Ser536) and NFkB in KRAS-driven human cancer cells, Western Blot (WB), immunofluorescence staining (IF), fluorescence activated cell sorting (FACS) analysis will be conducted. In this study, we aim to delineate the role of NFkB p65 (Ser536) in synergizing or antagonizing with anti-SIAH therapy to eradicate stage IV malignant cancer cells in vitro.

Methods:
Several late-stage metastatic human cancer cell lines were used in this study, including MiaPaCa (PDAC), A549 (NSCLC), and MDA-MB-231 (TNBC). SIAH2PD, an inhibitor of SIAH, is expressed under the control of doxycycline (DOX)-inducible Tet-ON system in these SIAH-deficient human cell lines. Without DOX, no SIAH2PD inhibitor is induced, and these SIAH2-proficient human cell lines will be used as the controls. Altered NFkB and phospho-NFkB P65 (Ser536) expression will be measured and quantified by WB, IF, and FACS analyses.

Results:
By immunofluorescent (IF) staining, we have observed a significant increase in phospho-NFkB in three human cancer cells, including a TNBC cell line (MDA-MB-231), a PDAC cell line (MiaPaCa), and a NSCLC cell line (A549) in response to SIAH2PD inhibition, thus validating an increased phospho-NFkB p65 (Ser536) expression as depicted in the RPPA kinomic data.

Conclusion:
Phospho-NFkB p65 (Ser536) and NFkB identified via RPPA analysis will be authenticated and quantified in this investigational and validation study. The understanding of how SIAH inhibition is linked to NFkB phosphorylation and activation, inflammation, proliferation that are regulated by a multitude of pro-growth/anti-growth/anti-apoptotic/proapoptotic factors will be further investigated in this study.

Abstract Title: Infant associated CD206 single positive macrophages reappear in ART treated Adults

Investigator: Julian Hattler
Co-Investigator(s): Diana Bohannon, Microbiology and Molecular Cell Biology, PhD Biomedical Sciences; Marcelo Kuroda, Center for Immunology and Infectious Diseases, University of California Davis; Woong-Ki Kim, Microbiology and Molecular Cell Biology
Department(s): Microbiology and Molecular Cell Biology

Abstract

Introduction:
Perivascular macrophages (PVM's) have been well established as drivers of HIV/SIV neuropathogenesis and the primary brain viral reservoir. In adults, PVM's can be subdivided into CD163 single positive or CD163 CD206 double positive populations, however, recent work in infants has shown a third subset of CD206 single positive PVM's not observed in adults. In infected infants this subset is associated with ubiquitous expression of cell death pathway markers and likely plays a role in the differential SIV/HIV brain pathogenesis observed in infants. As such there is a great need to further investigate these CD206 single positive macrophages.

Methods:
5um thick sections from Rhesus Macaque frontal cortex formalin fixed paraffin embedded brain tissue from Uninfected (UI), and SIV infected with and without ART infants, less than 1 year of age, and UI, SIVnoE, and ART adults were analyzed through immunofluorescence staining. Human brain Buk 7 frontal cortex sections from UI, HIV infected ART treated without HIV associated neurocognitive deficits (HAND), and HIV infected ART treated with HAND were graciously provided by the National NeuroAIDS Tissue Consortium (NNTC) were analyzed through immunofluorescence staining. Using markers for CD163, CD206, and CSF1R percentage of macrophage subsets out of total macrophages and CSF1R MPI intensity was determined.

Results:
To better understand this unique subset of macrophages, CD163 and CD206 were probed through immunofluorescence, and the percentage of macrophages subsets determined across age, infection, and ART status. ART infants showed comparable levels of CD206 single positive macrophages to SIV infected infants however, surprisingly, CD206 single positive macrophages were also observed in ART treated adults, with little to no expression in UI or SIVnoE adults. To see if result was recapitulated in humans, UI, ART treated without HAND and ART treated with HAND frontal cortex tissue were examined for macrophages subtype percentages. Unlike macaques, low numbers of CD206 single positive macrophages were observed in UI humans, with ART treated patients with HAND showing a comparable percentage, however there was a significant increase in the percentage of CD206 single positive macrophages in ART treated without HAND compared to other groups.

To further investigate the high occurrence of cell death pathways in CD206 single positive macrophages, we stained with an antibody against CSF1R, a macrophage survival marker, and CD206 and CD163 to measure the MPI of CSF1R on the different macrophage subtypes. No difference was observed between CD163 single positive and double positive macrophages, however CD206 single positive macrophages showed significantly lower CSF1R expression.

Conclusion:
Recently discovered CD206 single positive macrophages were previously shown only in infants. Herein, we show this unique subset to reappear in ART treated macaque adults and ART without HAND human adults, indicating a potential role of this subset during ART treatment. ART response is varied between individuals, and we observed lower percentages of CD206 in HAND patients when compared to non-HAND patients. This CD206 single positive subset exhibited low expression of CSF1R which may indicate the vulnerability of this population and potentially result in the ubiquitous expression of cell death pathway markers previously observed in CD206 single positive macrophages in SIV infected infants.

Abstract Title: The use of Reverse Phase Protein Array (RPPA) to identify new tumor vulnerability and actionable drug targets against undruggable, incurable, and metastatic human cancer cell lines

Investigator: Andrew Howell
Co-Investigator(s): Julia Wulfkhule, Ph.D., Center for Applied Proteomics and Molecular Medicine, School of Systems Biology, George Mason University; Rosa Gallagher, Ph.D., Center for Applied Proteomics and Molecular Medicine, School of Systems Biology, George Mason University; Jonathan Baker, B.S., Department of Microbiology and Molecular Cell Biology; Ashleigh Hannah, B.S., Microbiology and Molecular Cell Biology; Emanuel Petricoin, Ph.D., Center for Applied Proteomics and Molecular Medicine, School of Systems Biology; Amy H. Tang, Ph.D. Department of Microbiology and Molecular Cell Biology
Department(s): Microbiology and Molecular Biology

Abstract

Introduction:
There will be 1,918,030 new cancer cases and 609,360 cancer-related deaths in the United States in 2022. Lung, pancreatic, colorectal, and breast carcinomas are the leading causes of cancer-related fatalities globally. These cancers are known to have EGFR/HER2/K-RAS pathway activation, tumor suppressorloss of function, and signaling network rewiring. The EGFR/HER2/K-RAS pathway is a major tumor driver whose hyperactivation is associated with malignant tumor growth, multidrug resistance, early tumor relapse, chemo-resistance, and metastasis. Despite more than 40 years of research, oncogenic K-RAS activation remains a largely undruggable target in clinical oncology. Seven-In-Absentia (SINA) homologues (SIAH) are evolutionarily conserved E3 ubiquitin ligases that play a critical gatekeeper role downstream of the EGFR/HER2/K-RAS pathway. We reported that SIAH is a tumor vulnerability ideally positioned to become a drug target for new anticancer therapy development. Our prior studies have shown that tumor growth was abolished in aggressive human tumor cell lines such as MiaPaCa, MDA-MB-231, MDA-MB-468, A459, and HeLa following SIAH inhibition; however, the underpinning molecular mechanisms that give rise to this anti-EGFR/K-RAS and anticancer phenotype remain unclear. Specific objectives: to delineate the molecular mechanism(s) of why anti-SIAH2PD targeted therapy is so effective in impeding and eradicating undruggable cancers, we conducted reverse-phase protein array (RPPA)-based kinomic analysis to delineate how major cancer signaling pathways and oncogenic K-RAS-dependent signaling networks are rewired and remodeled in response to SIAH2 inhibition. Ongoing studies aim to identify the molecular mechanism(s) and validate significantly dysregulated proteins/phosphoproteins identified from the RPPA-based kinomic analysis in the aborted tumors.

Methods:
300 proteins/phosphoproteins were quantitatively measured by the RPPA platform to identify new tumor vulnerabilities, actionable targets, and compensatory signaling network alterations in response to anti-SIAH targeted therapies in five cancer cell lines in triplicate. Doxycycline (DOX)-inducible Tet-ON MiaPaCa, MDA-MB-231, MDA-MB-468, HeLa, and A459 cell lines were generated from a single cell, and DOX-induced SIAH2PD expression was confirmed. Each of the cell lines was then subjected to one of four experimental conditions: Tet-ON control cells without DOX induction (group A), Tet-ON control cells with DOX induction (group B), Tet-ON-SIAH2PD cancer cells without DOX-induction (no SIAH2PD inhibitor) (group C), Tet-ON-SIAH2PD cancer cells with DOX-induction (SIAH2PD inhibitor) (group D). Reverse Phase Protein Array (RPPA), in conjunction with Principal Component Analysis (PCA), was conducted to quantify fold-changes of proteins/phosphoproteins whose expression was altered in response to SIAH inhibition. The ratios of D/C/B/A, D/C, D/B, C/A, and B/A were calculated using GAPDH normalized data. Prism was used to determine statistical significance of each protein in a pairwise comparison. Ongoing Western Blot and Immunofluorescence (IF) studies are being used to validate our key RPPA findings.

Results:
Supported by statistical analyses, we identified 6 unique proteins/phospho-proteins (NFκB, Caspase 7, PARP, Cofilin, PD-L1, and Collagens) that were significantly up-or down-regulated in response to SIAH inhibition. These proteins play a role in controlling and regulating cell growth, cell death, NFκB signaling, stress response, DNA damage, immune function, and cell attachment pathways. Thus, our data provide additional evidence supporting our tumor eradication phenotype observed in these malignant human cancer cell lines lacking functional SIAH. Western Blot and IF validation studies have yielded further supporting evidence to confirm our RPPA results. Finally, Cancer Landscape (CScape) pathway mapping will be utilized to categorize the synergistic feedforward, feedback, and compensatory signaling pathway activation/inactivation in response to SIAH blockade in these EGFR/K-RAS-driven human cell lines.

Conclusion:
Independent validation studies are being conducted to gain insight into pathway alterations and dynamic rewiring in order to uncover SIAH as a major tumor vulnerability in multiple malignant cancers. Our data supports the explanation as to why anti-SIAH targeted therapy works so effectively to shut down malignant tumor growth, as reported in the literature.

Abstract Title: Glycosylated RNA - A Potential Marker for Prostate Cancer

Investigator: Esther Jones
Co-Investigator(s): Spencer Moen, M.D., Department of Microbiology & Molecular Cell Biology; Aurora Esquela Kerscher, Ph.D., Department of Microbiology & Molecular Cell Biology
Department(s): Microbiology & Molecular Cell Biology

Abstract

Introduction:
In 2022, 34,500 men are estimated to succumb to complications that arise from prostate cancer (PCa). To combat this, clinicians encourage screenings and interventions to increase early detection and prolong survival. While this is beneficial for men who suffer from early-stage (localized) PCa (~97-99% 5-year survival rates), men who suffer from aggressive, metastatic (late-stage) PCa observe a considerably lower 5-year survival rate (~30%). This is largely attributed to a lack of effective prognostic biomarkers and treatments that can subdue the progression and effects of aggressive disease. Glycosylation, the addition of carbohydrates onto other biomolecules, is an intricate process that occurs as molecules move through the secretory pathway. Aberrant glycosylation contributes to the pathophysiology of various diseases. For example, increased sialylation, among other aberrant patterns, contributes to tumor growth and metastasis. As glycosylated RNAs (glycoRNAs) were recently discovered in animal cells using bio-orthogonal chemistry methods, we hypothesized that glycoRNAs are imperative for prostate homeostasis/function; thus, dysregulation of RNA glycosylation would correlate with increased malignancy, metastasis, and hormone insensitivity in cells. Findings from these studies could identify novel disease screening biomarkers for aggressive PCa.

Methods:
- A human prostate panel (RWPE-1, DU145, LNCaP, C4-2, PC3-N, PC3-ML) representing a spectrum of disease (varying in malignancy, hormone-response, and metastatic potential) was used for experimentation.
- Cells were treated with an azido-labeled sialic acid precursor (Ac4ManNAz) 48 hours before harvest to tag glycan moieties. Once harvested, RNA fractions (total, small (<200 nt), or large (>200 nt) RNA) were obtained
- RNA was subsequently digested (DNase I and Proteinase K) and purified by acid-phenol: chloroform extraction and LiCl precipitation.
- RNA samples were reacted with biotinylated DBCO to covalently label glycans and RNA was collected using column purification.
- For glycoRNA northern blot analysis, RNA samples were loaded onto denaturing formaldehyde 1% agarose gels and electrophoresed for gel imaging (SYBR gold). Separated RNA was transferred onto nitrocellulose membranes, crosslinked, probed with Streptavidin-IR800, and imaged.
- For endoglycosidase-based studies, Ac4ManNAz-treated samples were prepared as described above; however, isolated RNA was treated with PNGase F, O-glycosidase, or left untreated before protein digestion to remove N-linked or O-linked glycans from RNA before click reactions and northern blot analysis.
- For lectin-based studies, cells forwent Ac4ManNAz labeling and click reactions to prevent potential chemical artifacts. Purified RNA samples were probed with biotinylated lectins (WGA, ConA, or PNA) and Streptavidin-IR800 prior to northern blotting.

Results:
Northern blots containing small RNA fractions isolated from all Ac4ManNAz-treated prostate cell lines exhibited glycosylated RNA expression. Furthermore, a negative correlation was observed between fluorescence (indicating glycoRNA expression) and PCa aggression. Conversely, large RNA fractions and untreated samples did not display glycoRNA expression. RNA derived from untreated cells that were probed with biotinylated WGA (lectin) also displayed fluorescence, indicating the presence of N-linked sialyl moieties. PNGase F (an N-linked glycan-hydrolyzing enzyme) treatment of RWPE-1, DU-145, and LNCaP-derived RNA resulted in reduced fluorescence versus Ac4ManNAz-treated controls. Lastly, RWPE-1 and DU145 RNA samples observed sensitivity to O-glycosidase, an O-linked glycan-hydrolyzing enzyme.

Conclusions:
Small RNA fractions from Ac4ManNAz-treated cells were exclusively glycosylated. Moreover, RNA samples isolated from benign or indolent, hormone-sensitive PCa cells observed substantially higher glycoRNA expression levels versus aggressive, hormone-refractory PCa counterparts, indicating a potential downregulation of glycoRNA expression in aggressive disease. Secondly, lectin northerns of untreated RNA samples validated the presence of saccharide moieties on RNA species using click-independent methods. Lastly, glycoRNA sensitivity to PNGase F and O-glycosidase digestion suggested that multiple RNA species and/or pathways may be utilized for glycoRNA processing. Future studies aim to identify the species and associated glycans of prostate glycoRNAs.

Abstract Title: STAT4 deficiency in neutrophils improves advanced atherosclerotic plaque size and stability via impaired neutrophil development and activation

Investigator: Coles Keeter
Co-Investigator(s): Alina Moriarty-Shawler, Microbiology/Biomedical Sciences, PhD; Rachel Akers, Microbiology/Medical Masters Class of 2022; Shelby Ma, Microbiology/Biomedical Sciences, PhD; Jerry L. Nadler, Pharmacology/New York Medical College; Elena V. Galkina, Microbiology
Department(s): Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION:
Acute cardiovascular events and their complications derived from atherosclerosis remain the leading cause of mortality in the developed world. Chronic low-grade inflammation has been clearly identified as an indispensable contributor to the progression of atherosclerosis. Neutrophils are a key inflammatory driver during atheroprogression and plaque instability, yet key transcriptional regulators of neutrophil functions have been minimally characterized. Previous work by our group has established that the transcription factor STAT4 is critical for host defense in neutrophils. Therefore, this study aimed to investigate the contributory role of STAT4 in neutrophils during advanced atherosclerosis.

METHODS:
We have generated myeloid-specific *Stat4flox/floxLysMCreLdlr-/-,* neutrophil-specific *Stat4flox/floxS100A8CreLdlr-/-,* and control *Stat4flox/floxLdlr-/-* mice. All groups of mice were fed a diabetogenic diet with added cholesterol (DDC) to establish advanced atherosclerosis. Following 28 weeks of DDC feeding, aortic root plaque burden and stability were assessed histologically via Movat pentachrome staining. Blood hematology was assessed using a VetScan VS2 Hematology Analyzer. Nanostring gene expression analysis of isolated blood neutrophils from chow and DDC-fed *Stat4flox/floxLdlr-/-* and *Stat4flox/floxLysMCreLdlr-/-* mice was performed. Flow cytometry was utilized to analyze the bone marrow hematopoietic system. Live cell assays for mitochondrial superoxide species production, surface degranulation marker expression, and migratory adhesion marker expression were also analyzed by flow cytometry. Homing of neutrophils to atherosclerotic plaques was performed by adoptively transferring a 1:1 ratio of prelabeled *Stat4flox/floxLysMCreLdlr-/-* and *Stat4flox/floxLdlr-/-* blood cells into aged atherosclerotic *Apoe-/-* mice and detecting the migratory capacity of neutrophils to atherosclerotic plaques measured by flow cytometry.

RESULTS:
Stat4flox/floxLysMCreLdlr-/- and *Stat4flox/floxS100A8CreLdlr-/-* mice displayed similar reductions in aortic root plaque burden, decreased necrotic core size, and increased fibrotic cap thickness compared to control Stat4flox/floxLdlr-/- mice. Hematology analysis revealed decreased percentage and absolute counts of neutrophils, as well as decreased neutrophil/lymphocyte ratio in *Stat4flox/floxLysMCreLdlr-/-* mice compared to the control group. Analysis of the bone marrow hematopoietic system showed decreased abundance of granulocyte-monocyte progenitor cells, while frequency of hematopoietic stem cells, common myeloid progenitor cells, and myeloid-erythroid progenitor cells were unchanged. Nanostring analysis revealed decreased expression of several inflammatory genes including Nox-2, which is critical for reactive oxygen species production. This finding was corroborated via decreased mitochondrial superoxide production in *Stat4flox/floxLysMCreLdlr-/-* neutrophils. This decreased activation status was further characterized by attenuated surface expression of degranulation markers CD41 and CD63 and low expression of chemokine receptors CCR1 and CCR2. Importantly, competitive homing experiments demonstrated that *Stat4flox/floxLysMCreLdlr-/-* neutrophils have decreased migratory capacity to atherosclerotic plaques compared with control S*tat4flox/floxLdlr-/-* neutrophils.

CONCLUSION:
Our findings clearly highlight STAT4 as a novel transcriptional regulator involved in neutrophil development, activation, and migration in atherosclerosis. These data also indicate a pro-atherogenic role for neutrophil-derived STAT4 and how it contributes to multiple facets of plaque instability during advanced atherosclerosis in mice.

Abstract Title: Investigating HIV-1 TAT protein role in Atherogenesis

Investigator: Cassandra Kirk
Co-Investigator(s): Alina Moriarty MMCB/PhD Biomedical Sciences Program; Natalie Stahr MMCB/PhD Biomedical Sciences Program; Coles Keeter MMCB/PhD Biomedical Sciences Program; Shelby Ma MMCB/PhD Biomedical Sciences Program; Woong-Ki Kim MMCB; Ming-Lei Guo Pathology and Anatomy; Elena Galkina MMCB/PhD Biomedical Sciences Program
Department(s):

Abstract

INTRODUCTION:
With the recent development of antiretroviral therapy, HIV patients can live a long and normal lifespan. Recent evidence demonstrates an increased incidence of developing cardiovascular diseases (CVD) in aged HIV-infected patients. Epidemiological studies predict that about 78 % of HIV patients that live to 50 years or older will develop CVD. Atherosclerosis is the main pathology contributing to mortality and morbidity in CVD. HIV-infected individuals develop high rate of atherosclerosis. While traditional CVD risk factors likely play a role, data indicate that HIV-associated inflammation and immune activation are important mediators of CVD risk. The adaptive and innate immune responses play a complex cell-type specific role in atherosclerotic plaque burden. However, specific mechanisms of the implication of the immune system in HIV-accelerated atherosclerosis are unclear.

METHODS:
The transcription factor Trans-Activator of Transcription-TAT is strongly associated with HIV infection as it enhances the efficiency of viral transcription. TAT expression is neurotoxic and important for neuroAIDS pathogenesis. To understand the contributions of TAT protein in HIV-associated atherogenesis and the underlying molecular mechanisms of TAT-induced neuro and immunotoxicity in atherosclerosis, a doxycycline-inducible astrocyte-specific HIV-1 TAT transgenic mouse was used. This model provides an excellent tool to investigate how the expression of a HIV-associated protein impacts atherogenesis. An injection of recombinant adeno-associated virus vector (AAV) encoding a gain-of-function mutant PCSK9 into mice and feeding with high fat, high carbohydrate diet with added cholesterol (DDC) was used to promote atherosclerosis and associated insulin resistance. The experimental (TAT+RTTA+) and control (TAT-RTTA+) groups of males were injected with AAV-PCSK9 and fed DDC plus doxycycline diet (DDCdox) for 16 weeks. Insulin tolerance and glucose tolerance tests were performed on 13 to 14 weeks of DDC feeding. After 16 wks of DDCdox feeding, heart, colon, small intestine, aorta, carotids, omentum, brain, blood, spleen, and bone marrow were collected for further analysis. Hearts are being analyzed for plaque stability and development using MOVAT staining. Aortas were analyzed for plaque burden using Oil Red O stain. Cell suspension from spleen, bone marrow, blood, brain and enzymatically digested omentum and carotid arteries were counted and used in flow cytometry analysis (FACS) for immune profiling, hematopoiesis, and germinal center formation. Blood profiling and counts were performed using VS2 hematology analyzer

RESULTS:
Astrocyte-specific expression of TAT resulted in a moderate impaired blood glucose clearance levels within the DDCdox-fed AAV-PCSK9-TAT+RTTA+ mice in comparison with DDCdox-fed AAV-PCSK9-TAT-RTTA+ control mice. We found no cholesterol levels between DDCdox-fed AAV-PCSK9-DDCdox TAT+RTTA+ and control DDCdox-fed AAV-PCSK9-TAT-RTTA+ mice; however, overall circulating cholesterol levels were unexpectedly low. We detected a significant increase in the number and percent of peripheral blood neutrophils in DDCdox-fed AAV-PCSK9-TAT+RTTA+ mice in comparisons with age- and diet-matched DDCdox-fed AAV-PCSK9-TAT-RTTA+ control mice with the average of 15.1±2.3% and 6.9±1.2%, respectively ($p<0.012$). To test whether an increase in the neutrophil number is due to elevated production of neutrophil pre-cursors in the bone marrow, we are analyzing a hematopoiesis-based panel for the both groups by FACS. We also continue the analysis of collected tissues for immune cell composition and activation, formation of germinal centers to determine how TAT expression affects innate and adaptive responses in the DDCdox-fed AAV-PCSK9-TAT+RTTA+ mice.

CONCLUSION:
Our preliminary data suggest that TAT is involved in the regulation of peripheral blood neutrophil numbers and therefore can serve as a regulator of inflammation in HIV-associated atherosclerosis. Future analysis will provide insight into potential mechanisms of HIV TAT-dependent involvement in atherosclerosis development and progression.

Abstract Title: Cannabinoid-2 receptor activation reduces SARS-CoV-2-spike protein-induced excessive activation of neutrophils

Investigator: Janette Lockett
Co-Investigator(s):
Department(s): Physiological Sciences

Abstract

Introduction:
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the cause of the Coronavirus Disease 2019 (COVID-19) pandemic, has been the most serious threat to global public health. Although several vaccines are available, the effectiveness of the vaccine over longer periods remains uncertain. Acute lung injury (ALI) and its continuum acute respiratory distress syndrome (ARDS) is a common debilitating cause of respiratory failure in patients with COVID-19 which is characterized by uncontrolled inflammation due to a cytokine storm, progressive lung injury, and leads to high mortality and morbidities, especially among people with co-morbidities and the unvaccinated. It is therefore important to countermeasure the inflammation and cytokine storm in COVID-19 infection. Cannabinoid-2 receptor (CB2R) has anti-inflammatory properties, therefore we sought to test the effect of CB2R activation in regulating the SARS-CoV-2 Spike Protein Subunit S1 (S1SP)-induced ALI and inflammation in a mouse model. In our own studies, we have shown that pharmacological activation of CB2R reduced S1SP-induced increase in immune cell infiltration, neuropil population, and inflammatory cytokines. As an approach to depict the mechanism, we extended our studies to evaluate the role of CB2R in regulating the SISP-induced neutrophil activation and the formation of neutrophil extracellular traps (NETosis). We also examined the NLRP3 inflammasome signaling, a critical player in ALI development in mouse models.

Methods:
We used a mouse model of S1SP-induced lung injury. To activate CB2R, a selective synthetic agonist, HU308 (5 mg/kg) was intraperitoneally administered to K18-hACE2 transgenic mice that overexpress human ACE2. S1SP (0.6mg/kg body weight in 50µL) was intratracheally delivered into the lung. At 48h post S1SP exposure, mice were euthanized, and bronchoalveolar lavage fluid (BALF) and lungs were collected. The formation of neutrophil extracellular traps (NETs) was determined by examining the accumulation of extracellular histones, Citrulline-H3 and Histone-H2B, in the BALF by immunoblot. Immunofluorescence was used to examine the levels of Citrulline-H3 and Histone-H2B in lung tissue. In order to investigate the involvement of NLRP3 activation, we measured the protein levels of NLRP3, ASC, and Caspase-1 in the mice lung exposed to S1SP.

Results:
BALF Citrulline-H3 and Histone-H2B levels were found to be elevated after S1SP exposure. Mice that had received HU308 treatment had lower levels of BALF Citrulline-H3 and Histone-H2B as revealed by immunoblot analysis. These results were further confirmed by immunofluorescence as CB2R activation resulted in reduced expression of Citrulline-H3 and Histone-H2B in lung tissues. We did not observe significant changes in NLRP3, ASC, and Caspase-1 levels between PBS and S1SP-treated mice lungs as revealed by immunoblot analysis.

Conclusion:
Pharmacological activation of CB2R by the selective synthetic agonist, HU308, lessened the S1SP-induced lung inflammation by reducing excessive activation of neutrophils and the formation of neutrophil extracellular traps. Further studies involving pharmacological blockade of CB2R will help in understanding the specificity of the CB2R-mediated effect.

Abstract Title: Effects of Social Isolation and Space Radiation on Brain Morphology in Rats

Investigator: Zachary Luyo
Co-Investigator(s): Austin M. Adkins, Biomedical Sciences Ph.D. Candidate; Alea F. Boden, Pathology & Anatomy; Justin D. Gotthold, Pathology & Anatomy; Richard A. Britten, Center for Integrative Neuroscience and Inflammatory Diseases; Dr. Laurie L. Wellman, Pathology & Anatomy; Dr. Larry D. Sanford, Pathology & Anatomy
Department(s): Pathology/Anatomy

Abstract

Introduction:
Astronauts will experience periods of social isolation (SI) and exposure to space radiation (SR) during lengthy space expeditions such as the planned Mars mission. These stressors have the potential to produce deleterious effects on physical and mental health which can affect mission performance and reduce the ability to cope with stressful situations. Our lab has recently found that SI and SR have differential effects on sensorimotor performance, sleep, and freezing behavior in response to training in conditioned fear (CF). The basolateral amygdala (BLA), hippocampus (HPC), and medial prefrontal cortex (mPFC) are part of a three-way circuit, which can influence both sleep and the stress response. Both SI and SR have been shown to produce molecular and morphological changes in the brain. Identifying molecular and morphological changes in BLA, HPC, and mPFC by SI and SR may provide insights into the neural mechanisms behind these behavioral and physiological alterations, and potential avenues for mitigation. In this study, brains from rats exposed to variations of SI and SR and trained in a variety of behavioral tasks were histologically prepared for assessment of gross morphological changes in BLA, HPC, and mPFC.

Methods:
Male, outbred, Wistar strain rats (8-9 months old at time of study, n=6-10 per group) were subjected to SI (visual barriers between cages) or individually housed (as a sham group). Separate groups of rats received SR (15 cGy GCRsim) treatment and were either individually housed or subjected to SI (SI + SR). Following behavioral testing and CF, rats were euthanized via cardiac perfusion and had their brains removed. 30μm sagittal brain sections of each animal from each treatment group were obtained via cryotomy and assessed for morphological differences under a light microscope. Images were uploaded to ImageJ software for the measurement and calculation of total volume and shape of BLA, HPC, and mFPC and compared between each treatment group.

Results:
This is an ongoing study and data is actively being collected and analyzed. Based on preliminary data and previous research of others, we predict that we will find differences in regional volume between treatment groups, namely decreased volume in the BLA of the SR groups, as well as decreased volume in the BLA, mPFC, and HPC of the SI group. We also expect to find differences in the shape of the BLA and HPC in the SI group, specifically expansion of the BLA and HPC on the x-axis, but regression on the y-axis.

Conclusion:
Further work is necessary to verify these predictions. In the future, we plan to perform immunofluorescence (IF) staining to assess blood brain barrier (BBB) integrity and Nanostring to evaluate neuroinflammatory signaling between treatment groups. If our hypotheses are correct, data from these experiments may correlate our findings regarding changes in brain morphology, which could provide insight into how these morphological changes occur, and if SI, SR, or both expedite this process. This study will provide important insight into possible routes of mitigation against the adverse effects of SI and SR on behavior and overall cognitive health to ensure the integrity of crew health during space missions.

Abstract Title: CD45 dependent B cell receptor signaling regulates B cell functions in a subset dependent manner in atherosclerosis

Investigator: Shelby Ma
Co-Investigator(s): Sam Chan, Microbiology and Molecular Cell Biology\Biomedical Sciences; Alina Moriarty, Microbiology and Molecular Cell Biology\Biomedical Sciences; W. Coles Keeter, Microbiology and Molecular Cell Biology\Biomedical Sciences; Tayab Waseem, Microbiology and Molecular Cell Biology\Medical School; Philip Gauronskas, Microbiology and Molecular Cell Biology\Biomedical Sciences; Marion Mussbacher, Pharmacology and Toxicology\ Institute of Pharmaceutical Sciences,
Department(s): Molecular Cell Biology and Microbiology

Abstract

INTRODUCTION:
Cardiovascular disease due to atherosclerosis remains the leading cause of death worldwide, despite the use of treatments to reduce cholesterol. A chronic inflammatory environment is indispensable in the progression of atherosclerosis. The existence of antibodies against LDL, oxLDL, and ApoB suggests a spectrum of different antigens that can activate the immune system in atherosclerosis. B cells play a subset specific role in atherosclerosis. Marginal Zone (MZ) B cells are atheroprotective by suppressing proatherogenic T helper follicular cells. B1a and B1b secrete natural antibodies (Abs) that attenuate oxLDL uptake by macrophages. Innate response activator (IRA) B cells, which differentiate from B1 cells and Follicular (FO) B cells are proatherogenic by supporting proinflammatory Th1 response and neutrophil-associated inflammation. B cell receptor (BCR) signaling is important in B cell development, activation, differentiation, and functions, while important costimulatory molecules, like CD45, assist in the initial propagation of the BCR signal.CD45 is a protein tyrosine phosphatase that supports BCR signaling by dephosphorylating the inhibitory tyrosine of the src family kinases. Currently, it is not well understood how CD45 functions in different B cell subpopulations. Additionally, while the role of B cell subsets in atherosclerosis is well established, the role of BCR-associated signaling in B cell subsets in atherosclerosis are unclear.

METHODS:
We utilized a transgenic mouse model that express low levels of CD45 (CD45 L/L) and examined B cell subset specific activation. Flow cytometry was used to analyze Ca2+ flux responses and expression of B cell activation markers. Additionally, in vivo assay of IRA B cell generation through LPS-induced inflammation was performed. To test the effects of low expression of CD45 in CD45L/L B cells in atherosclerosis, we performed adoptive transfer of CD45L/L or WT B cells into B cell-deficient atherosclerotic prone mice *(uM-/-Apoe-/-)*. Following 23-28 weeks of high fat diet feeding, aorta plaque formation was assessed using Oil Red O staining.

RESULTS:
We demonstrated that reduced CD45 expression favors splenic MZ and B1 B cell differentiation under homeostatic conditions in vivo. Low CD45 expression also attenuated B cell activation in a subset dependent manner, with MZ B cells affected the greatest based on BCR-engaged Ca2+ efflux. Interestingly, while LPS-induced activation resulted in the generation of GM-CSF+ IRA B cells, the IRA differentiation through LPS-induced inflammation was inhibited with reduced CD45 expression compared to WT B cells. In atherosclerosis, CD45 L/L recipients had increased lesion formation accompanied by increased proatherogenic IRA B cells, despite an increase of atheroprotective MZ and decreased germinal center formation.

CONCLUSION:
Our results indicate that attenuation of BCR signaling through CD45 impacts B cell differentiation and activation in a subset specific manner. Attenuated MZ B cell activation expressing low CD45 levels suggests an atheroprotective role of BCR signaling n MZ B cells. This is corroborated with increased lesion formation in CD45 L/L B cell recipients. CD45 is also critically involved in B1a differentiation to IRA B cells. Overall, our data suggest that reduced BCR signaling through CD45 affects B cell differentiation and activation in a subset dependent manner and highlight a potential role of BCR-related signaling in regulation of immunity in atherosclerosis.

Abstract Title: Effect of Plasma Extracellular Vesicles on Cardio-Metabolic Status and Endothelial Dysfunction

Investigator: Noel Miller
Co-Investigator(s): Matthew Bavuso, Physiological Sciences/Biomedical Sciences; Allison Mathiesen, Physiological Sciences/Biomedical Sciences
Department(s):

Abstract

Introduction:
Circulating extracellular vesicles (EVs) indicate cellular stress, and are being considered as promising biomarkers for cardiovascular disease (CVD) and CVD contributors. Plasma EVs, representing parenchymal, vascular and immune cells secretomes, arrive to the endothelium from multiple vascular beds, enabling them to impact endothelial function. Metabolic diseases significantly increase the risk of CVD, and their mechanisms are not completely understood. EVs may link the two conditions. The goal of this study was to analyze associations between plasma EVs and biochemical and physiological parameters in a cohort of African American (AA) women with varying degrees of BMI and CVD risk, and to establish the effect of EVs on coronary endothelium function.

Methods:
A cohort of 24 AA women between 22-71 years of age with BMI values between 26-47 kg/m2 and ASCVD risk scores between 2.3-22.1 were included in this study. EVs were isolated from fasted heparinized plasma via size exclusion chromatography. EV size and amount were found using nanoparticle tracking analysis (Nanosight). Lipids, inflammatory cytokines, and metabolic panels were measured during phlebotomy. Human coronary endothelial cells (HCAECs) were treated with EVs derived from participants and endothelial function and migration were measured using electric cell-substrate impedance sensing (ECIS) technology. Associations were determined with multivariable linear regression analysis, adjusting for BMI and ASCVD risk.

Results:
Negative associations (beta=-0.712, $p<0.01$) among total triglycerides (TG), TG-rich lipoproteins (Lp), and EV size were found. EV concentration was found to be positively associated (beta= 0.51-0.61, $p<0.01$) with TG-rich Lp, LDL cholesterol and TNFa. There was also a positive association between reduced endothelial barrier function due to EVs with monocyte count (beta=0.42, $p<0.05$). There was a strong, negative correlation between the effect of EVs on increased endothelial migration and monocyte count (beta=-0.85, $p<0.001$), IL8 and CXCL10 (beta=-0.56-0.46, $p<0.05$).

Conclusion:
Altogether, this data shows that EV number and size shares a strong association with circulating lipids, while EV impact on endothelial dysfunction shares an association with inflammatory markers. This supports justification of EVs as potential indicators of endothelial dysfunction that associates with inflammatory and metabolic markers, after adjusting for BMI and ASCVD risk.

Abstract Title: A Mystery In the Making: Premature Death Of Males In A Model Of Atherosclerosis

Investigator: Alina Moriarty
Co-Investigator(s): Tayab Waseem, MD Program; W. Coles Keeter, Microbiology and Molecular Cell Biology; Larry Sanford, Pathology. and Anatomy; Elena Galkina, Microbiology and Molecular Cell Biology
Department(s):

Abstract

INTRODUCTION:
Atherosclerosis is a chronic inflammatory disease responsible for over 25% of annual global deaths. The progression of atherosclerosis extends across the lifespan and has been extensively linked to insufficient sleep. It is well known that adequate sleep is vital for overall health; however, today's fast-paced society often neglects the importance of sleep. Therefore, it is no surprise that poor sleep quality is strongly associated with increased risk of mortality due to a cardiovascular event. While the effects of gender have been studied in atherosclerosis, the impact of sexual dimorphism in Sleep Fragmented (SF)-associated atherogenesis is not known. Recently, we have shown that high fat diet (HFD) fed male Apolipoprotein E-deficient (Apoe-/-) mice on SF unexpectedly experienced premature death, with 80% of males not surviving past week 2 of SF, while 80% of females survived past week 8 under the same conditions. The goal of this study was to identify a potential cause of the premature death in HFD fed male *Apoe-/-* mice following sleep fragmentation.

METHODS:
Eight-ten-week-old male and female *Apoe-/-* and male *Ldlr-/-* mice were randomly assigned to a sleep fragmentation (SF), activity control (AC), or home cage (HC) groups. Mice in the SF and AC groups were housed in commercial sleep fragmentation chambers equipped with a mechanical sweeper. The bar in the SF group was active during the light period to fragment sleep. To account for the forced activity of stepping over the motorized bar, the bar in the AC group was active during the dark period. The mice were fed either a high fat (HFD) or a chow diet and subjected to the designated sleep paradigm for 2-8 weeks. Kaplan Meier Survival analysis were performed for each regiment. To test the effects of estrogen on survival, some HFD fed male Apoe-/- mice were supplemented with 17B-estradiol. Peripheral blood was collected to measure various biochemical markers, LPS, cfDNA, reactive oxygen species and immune populations in various tissues.

RESULTS:
Sleep fragmentation accelerated a development of atherosclerosis in HFD fed female Apoe-/- mice compared to activity and home cage controls age, sex and diet matched *Apoe-/-* females. Our results also revealed that sleep fragmentation in cooperation with absence of Apoe and estrogen induces a premature death in *Apoe-/-* male mice. Interestingly, HFD fed male *Ldlr-/-* mouse did not experience premature death when sleep fragmented, suggesting that not hyperlipidemia but APOE absence plays an essential function in the induction of death. Interestingly, male *Apoe-/-* mice fed a HFD did not experience SF-induced premature death when supplemented with17B-Estradiol. Furthermore, when compared to the other groups, HFD fed male *Apoe-/-* mice on SF had increased LPS levels, reactive oxygen species and cell free-DNA in their plasma. The analysis of circulating plasma proteins also suggested a multi-organ dysfunction of HFD fed Apoe-/- males compared to the other groups. Finally, the circulating blood of the HFD fed male *Apoe-/-* mice showed higher inflammatory CD11b+Ly6G+ cells with increased markers of degranulation (CD63).

CONCLUSION:
Our data suggests that a combination of known risk factors for chronic inflammation and atherosclerosis (male sex, ApoE genotype, and HFD) results in premature death in HFD fed *Apoe-/-* male when combined with inadequate sleep. Furthermore, our data suggests that this specific combination of co-factors might result in premature death due to a systemic increase in oxidative stress, possibly caused by leakage of LPS from the gut, which may be alleviated through the administration of 17B-Estradiol.

Abstract Title: Mouse Ovarian Follicles In Vitro - A Model to Study Ovulation

Investigator: Vanshika Patel
Co-Investigator(s):
Department(s): Physiological Sciences

Abstract

Introduction/Background:
Ovulation is a complex process, requiring interactions between oocytes and other follicular cells, together with paracrine, autocrine, and endocrine factors that regulate the maturation of ovarian follicles and, ultimately, release of a healthy oocyte. Follicle stimulating hormone (FSH) stimulates growth of small antral follicles to the preovulatory stage in vivo and in vitro. Ovulation in vivo is triggered by a surge of luteinizing hormone (LH), which stimulates epidermal growth factor (EGF) production by the follicle itself. Together, LH and EGF stimulate structural and functional changes within the follicle which result in ovulation. An in vitro model of this complex process will be a powerful tool to investigate the multiple structural and endocrine changes that together comprise ovulation.

Hypothesis:
FSH will lead to maturation of mouse antral follicles to the preovulatory stage in vitro. hCG+EGF will then induce ovulatory changes, such as follicle rupture, oocyte release, and luteinization.

Methods:
Mouse antral follicle culture: Mice were humanely euthanized, and both ovaries were aseptically removed. Early antral follicles (250-350 micrometer) were isolated and cleaned of interstitial tissue and small follicles. Isolated antral follicles were transferred to individual wells of a 96-well plate and cultured in media containing FSH for 4 days. After this period, the LH receptor ligand hCG and EGF were added to induce ovulation.

Follicle growth measurements: Follicles were photographed daily to monitor growth.

Ovulation assessment: 18 hr post hCG+EGF treatment, each follicle was photographed and assessed visually to determine if the cumulus oocyte complex was extruded from the follicle and if granulosa cells were differentiated into cuboidal luteinizing cells. Media was collected for quantitation of androstenedione (A4), progesterone (P4), and prostaglandin E2 (PGE2) by ELISA.

Results:
Mouse follicles did not increase in follicular diameter over the four-day culture period. No ovulations were observed in untreated (control) follicles as anticipated. The ovulation rate of hCG+EGF treated follicles was 15%, lower than the anticipated 80%.Treatment with hCG+EGF increased media A4 consistently in comparison to control follicles. P4 and PGE2 were increased in some experiments, but increased P4 and PGE2 were not consistently increased by hCG+EGF when compared to control follciles.

Conclusion:
Mouse follicles are not growing in vitro in response to FSH to their expected 40% increase in diameter. The antral follicles did respond to hCG+EGF with increased A4 production. P4 and PGE2 production in response to hCG+EGF remains inconsistent.

Future directions:
If successfully developed, this in vitro model can be used for insight of how novel paracrine mediators like neurotensin affect the process of ovulation. Translational applications for this model include understanding ovulation failure in women with diseases that damage the follicles and thus lead to infertility. This model may also a useful tool for developing novel, more effective methods of contraception.

Abstract Title: Neurotensin as a Novel Regulator of Vascular Permeability in the Ovarian Follicle.

Investigator: Andrew Pearson
Co-Investigator(s): Diane Duffy, Ph.D., Physiological Sciences
Department(s): Physiological Sciences

Abstract

Introduction:
Neurotensin (NTS) is a small neuropeptide which is produced in large quantities by the ovarian granulosa cells in response to the primary endocrine signal for ovulation, the luteinizing hormone (LH) surge. This phenomenon is conserved among mice, non-human primates (NHPs), and humans. This implicates NTS as a mediator of ovulation. The importance of NTS in ovulation is further implicated by the disruption of ovulation in neurotensin neutralized follicles of macaques. NTS neutralization also causes apparent disruption of follicular vasculature and extravasation of red blood cells.

Massive angiogenesis occurs during ovulation. New blood vessels grow into the previously avascular granulosa cell layer of the follicle. There is growing evidence that this angiogenesis is crucial for successful ovulation. Increased vascular permeability is a hallmark of angiogenesis and is controlled in large part by the adherens junctions of the vascular endothelial cells. Previously, we demonstrated that monkey ovarian microvascular endothelial cells (mOMECs) isolated from macaque follicle aspirates respond to NTS with a decrease in permeability using a trans-well permeability assay. We also showed that mOMECs are negative for the typical vascular endothelial adherens junction protein VE-cadherin (CDH5), both at the mRNA and protein levels. The specific hypothesis for this study is that NTS reduces permeability in ovarian microvascular endothelial cells via an increase in non-VE-cadherin-based AJs.

Methods:
Monkey ovarian microvascular endothelial cells (mOMECs) were enriched from follicle aspirates of cynomolgus macaques (Macaca fascicularis) via two rounds of CD31 magnetic bead isolation and endothelial cell selective culture conditions. To confirm our findings in the trans well permeability assay, we employed the biotinylated matrix in vitro vascular permeability imaging assay (Millipore). In this assay, glass 8-well chamber slides are coated with a biotinylated gel matrix. mOMECs were then seeded into the chamber slides and grown to confluence. mOMECs were then treated for 30, 60, or 120 minutes. Cells were treated with 5uM NTS, 1U/ml Thrombin, 10uM dibutyral cyclic AMP (Db cAMP), or left untreated. After treatment, fluorescein conjugated streptavidin was added to the well, which binds to the exposed areas of the biotinylated matrix in the gaps between cells. Cells were then PFA fixed and imaged. The area of green fluorescence was quantified as a measure of monolayer permeability.

Quantitative PCR measuring CDH2, CDH5, and CDH6 was performed on mOMEC cDNA. CDH2 protein expression in mOMECs was also determined using both immunofluorescent staining and western blot using an anti-CDH2 primary antibody.

Results:
In our biotinylated matrix permeability imaging assay, the 120-minute time point was found to be ideal for observing permeability changes with this assay. Thrombin, a known short-term up regulator of vascular permeability, was used as a positive control and increased permeability. Cyclic AMP is known to decrease vascular endothelial permeability; therefore, Db cAMP was used as a negative control and decreased permeability. 5uM neurotensin decreased mOMEC permeability in this assay.

Previously, CDH5 mRNA expression was not identified in mOMEC RNA-seq but N-cadherin (CDH2) and K-cadherin (CDH6) were. To confirm this expression, qPCR using primers targeting CDH2, CDH5, and CDH6 demonstrated the same expression pattern observed in our RNA-seq data of CDH2 ^{3} CDH6 >> CDH5. Immunofluorescent staining of CDH2 identified that mOMECs were CDH2 positive. CDH2 staining was localized to points of cell-cell contact between mOMECs, but not on plasma membranes where there were gaps between adjacent cells. Western blot analysis confirmed that mOMECs are CDH2 positive.

Conclusion:
Our biotinylated matrix permeability imaging assay data confirm our previous findings in the trans-well assay. Additionally, our characterization of mOMEC junctional proteins using multiple approaches indicates that CDH2 is the most highly expressed cadherin and localizes to points of contact between mOMECs.

These results indicate that NTS is indeed capable of regulating mOMEC permeability. We suspect that NTS may play a regulatory role in maintaining vascular integrity during the period of intense angiogenesis and accompanying increase in permeability.
Our results also show that mOMEC permeability is controlled by non-canonical cadherin proteins. In the absence of CDH5, adherens junction composition must include one or more other cadherin. CDH2 is present at the junctions of mOMECs and is therefore implicated as a mediator of mOMEC permeability. Further characterization of mOMEC junctions to identify other potentially involved cadherins, such as CDH6, is ongoing.

Abstract Title: Confirming Neuronal Differentiation of Human Embryonic Carcinoma Stem Cells

Investigator: Haley Pflanzer
Co-Investigator(s):
Department(s): Physiological Science

Abstract

Introduction:
The population of individuals living with a neurological disorder, such as Alzheimer's Disease, has increased significantly in the past five years and the number of diagnosed individuals continues to rise. NTERA-2 cl.D1, a pluripotent human testicular embryonic carcinoma cell line, has shown promise as an alternative cell source and suitable model for in vitro mechanistic studies of neurological diseases. NTERA-2 (NT2) cells possess phenotypes similar to those of committed CNS neuronal precursor cells and when exposed to all-trans retinoic acid, they have the ability to differentiate into post-mitotic neuronal-like (NT2N) cells.

This study investigates the differentiation of NT2 cells with Retinoic Acid (RA) exposure throughout the course of 8 weeks. Work focuses on assessing changes seen in morphological characteristics, gene expression, and protein expression of various markers used to confirm differentiation of NT2 cells into NT2N cells. Successful transfection of NT2N was also conducted to determine if this cell line will be a viable model for future tests involving the knockdown of various genes involved in the potential association between mitochondria dysfunction and Alzheimer's Disease.

Methods:
NT2 cells were grown in culture and growth curves were performed. At 90% confluency, cells were reseeded into T-75 flasks at low density and exposed to all-trans retinoic acid 2-3 times a week. After 4 weeks, cells were replated and continued to grow under normal media conditions for an additional 4 weeks. Cells were harvested at various time points (3, 5, 7, 14, 21, 28, 60 days) to investigate markers used to confirm differentiation.

Total RNA and protein were isolated from NT2 and NT2N cell pellets collected at indicated timepoints. Concentrations of isolated RNA were assessed by Nanodrop and used to generate cDNA reactions. qPCR was performed in triplicate to access differences in expression levels of Nestin, MAP2, Synapsin (Syn1), and β-actin genes in NT2 and NT2N cells. qPCR data was normalized to HPRT1. Protein was isolated using RIPA buffer with protease inhibitor cocktail and concentrations were determined by Micro Bicinchoninic Acid (BCA) protein assay. 30ug of protein was electrophorized on 4-12% Bis-Tris gels then wet transferred to PVDF membranes. Membranes were probed with the following antibodies: Nestin, MAP2, Synapsin 1, β-actin, HSP60, and GAPDH. Licor software programs, Image Studio and Empiria Studio, were used to measure and normalize band signal intensities to HSP60 (control gene) or total protein imaged from stained membrane.

Microscopy was used to investigate morphological changes of cells. Cells depicting successful differentiation were seeded into 6-well plates for transfection experiments. Experiments were done in duplicate using Origene siTRAN2.0 transfection reagent and TYE 563-labeled florescent transfection control siRNA. Each well received 1mL of fresh media and equal amounts of transfection buffer with varying concentrations (0.55-5.5nM) of florescent labeled control siRNA and varying amounts (1.2-2.4uL) of siTran 2.0 transfection reagent. Cells were incubated at 37°C for 12-18 hours. At 15 hours, media was replaced and cells were imaged using florescent microscopy.

Results:
NT2 cells began to morphologically change from small round cells into more elongated and branched cells following 10 days of RA treatment. As RA exposure time increased, cells began depicting a dense neuronal network with extensions of neurons suspended in the media and overlaying the monolayer of cells. Literature indicates that Nestin expression in NT2 cells decreases over time of differentiation while MAP2 and Syn1 are neuronal markers that become upregulated after several weeks of RA exposure. Data obtained from qPCR revealed that Nestin expression is downregulated more than 23-fold in NT2N cells while MAP2, Syn1, and β-actin expression is upregulated 5.9, 6.2, and 1.9-fold in NT2N cells. Western blot data also showed that Syn1 and β-actin protein expression is upregulated in NT2N cells. Florescent microscopy revealed successful transfection of NT2N cells in all experiments, with transfection efficiencies ranging from 73-90% indicated by TYE 563 expression; 90% transfection efficiency was achieved using 5 nM siRNA with 1.2 uL siTran 2.0 reagent.

Conclusions:
Based on changes in cell morphology, mRNA expression, and protein expression, differentiation of NT2 into NT2N cells was successful. Future work will include testing other protein and gene markers, as well as testing for MAP2 and Nestin though alternative approaches such as immunocytochemistry. Although transfection experiments were successful, cell viability studies and more differentiation work must be done before considering future knockdown experiments.

Abstract Title: Neurotensin stimulates theca steroidogenesis in the monkey ovarian follicle

Investigator: Megan Sage
Co-Investigator(s): Nehemiah S. Alvarez, Ph.D., Department of Physiological Sciences, Pavla Brachova, Ph.D., Department of Physiological Sciences, Diane M. Duffy, Ph.D., Department of Physiological Sciences
Department(s): Physiological Sciences

Abstract

INTRODUCTION:
Neurotensin (NTS), a 13-amino acid peptide, is produced within the ovarian follicle and is essential for ovulation to occur. Granulosa cells produce NTS in response to the ovulatory surge of luteinizing hormone (LH) and express NTS receptors. Theca cells surround the ovarian follicles and are responsible for producing androgens, which are converted by neighboring granulosa cells into estrogens. Theca steroidogenesis is known to be stimulated by LH or human chorionic gonadotropin (hCG) via LH-receptor (LHCGR) signaling, and by forskolin via receptor-independent activation of the protein kinase A (PKA) pathway. We hypothesize that NTS is a novel regulator of ovarian steroidogenesis and acts on theca cells to stimulate androgen production.

METHODS:
Ovaries were removed from adult, female cynomolgus macaques *(Macaca fascicularis)* after a modified ovarian stimulation protocol, and the theca layers were isolated from large antral follicles. Theca tissue was minced to uniform size and cultured for 24 hours in serum-free media with or without NTS, hCG, or forskolin. Media was then collected and analyzed for androstenedione (A4) and progesterone (P4) concentrations via ELISA or the ADVIA Centaur Immunoassay System, which were normalized to the DNA content of theca tissue. RNA was isolated from cultured theca tissue and analyzed for expression of mRNA characteristic of theca cells *(STAR, CYP17A1, VEGFA)* after reverse transcription and qPCR.

RESULTS:
NTS increased A4 concentration in media of cultured theca in a dose-dependent manner (0.13 ± 0.08 vs 0.38 ± 0.05 pg A4 per µg DNA, $p<0.05$). In contrast, media P4 concentration was unchanged in response to NTS at any dose. Treatment with hCG showed a dose-dependent increase in A4 (0.16 ± 0.09 vs 0.64 ± 0.25 pg A4 per µg DNA, $p<0.05$) and P4 (2.05 ± 0.62 vs 5.31 ± 1.94 ng P4 per µg DNA, $p<0.05$) compared with untreated cultures, while forskolin treatment also increased levels of A4 (0.16 ± 0.09 vs 0.64 ± 0.29 pg A4 per µg DNA, $p<0.05$) and P4 (2.05 ± 0.62 vs 9.76 ± 3.60 ng P4 per µg DNA, $p<0.05$) compared with untreated cultures. Theca-specific transcripts (STAR, CYP17A1, VEGFA) were present in all samples and confirmed theca identity of tissue.

CONCLUSION:
These results indicate that NTS stimulates steroidogenesis in theca cells. While hCG and forskolin increased both A4 and P4, NTS treatment showed a selective increase of A4 only. Given that both hCG/LHCGR signaling and forskolin promote PKA-mediated stimulation of steroidogenic enzymes, the contrasting A4-selectivity of NTS may be due to the use of a non-PKA mechanism of steroidogenic regulation. Future studies will continue to investigate the role of NTS in follicular steroidogenesis through its action on theca NTS receptors and its effect on steroidogenic machinery and cholesterol utilization.

Abstract Title: CSF1R Blockade in Prediabetic Rhesus Macaques

Investigator: Natalie Stahr
Co-Investigator(s): Amy Phou, Microbiology and Molecular Cell Biology; Julian Hattler, Microbiology and Molecular Cell Biology; David McGuire, Microbiology and Molecular Cell Biology; Woong-Ki Kim, Microbiology and Molecular Cell Biology
Department(s): Microbiology and Molecular Cell Biology

Abstract

Introduction:
Diabetes is a life-long disease that afflicts 37 million Americans. Although treatments to control blood glucose levels are largely effective, these patients can develop disabling retinopathy, neuropathy, nephropathy, heart disease, and stroke even with current treatments. Diabetes is increasingly being recognized as a chronic inflammatory disease, leading to investigation into the role of macrophages in driving this disease. Macrophage accumulation is documented in the pancreas of diabetics, as well as in insulin-sensitive tissues such as the liver, muscle, kidney and adipose tissue, correlating to the progression of diabetic complications. Additionally, colony stimulating factor 1 receptor (CSF1R), whose expression is restricted to myeloid cells, has been implicated in diabetes as a possible driver of diabetic complications. **It is unknown whether these dysregulated monocytes/macrophages cause disease and if their removal and endogenous replacement with fresh macrophages resolves disease.** Our long-term goal is to investigate and alleviate the underlying immunological causes of diabetic complications in insulin-sensitive tissues. We have recently performed a small-scale pilot study in which two animals were administered a high-fructose diet to induce pre-diabetic conditions (such as heightened fasting blood sugar and elevated total cholesterol levels). Following depletion of CSF1Rhi monocytes and macrophages, one animal exhibited a decrease in total cholesterol levels from 150mg/dL at the start of study to 118mg/dL 112 days after the initial treatment. In order to expand upon these findings, we are currently investigating the depletion of CSF1Rhi monocytes and macrophages in a larger cohort compared to an isotype control. Therefore, *we hypothesize that depletion of activated CSF1R+ tissue macrophages using a monoclonal antibody against CSF1R and replacement with freshly differentiated macrophages will alleviate inflammation in tissues and ameliorate diabetes-associated disease.*

Methods:
We have identified 6 aged Indian rhesus macaques with heightened fasting blood glucose as well as higher area-under-the-curve in an intravenous glucose tolerance test (IVGTT), indicating prediabetes. All animals had dextran and bromodeoxyuridine (BrDU) injected intravenously prior to the start of the study in order to ascertain turnover of long-lived macrophages in the insulin-sensitive tissues and determine current monocyte turnover in the blood, respectively. 3 animals were treated with an anti-CSF1R antibody (CSF1RR) administered i.v. (15 mg/kg) once every 2 weeks for 6 weeks. An isotype control was administered to the remaining 3 animals. Clinical parameters for the progression of diabetes such as blood pressure, plasma levels of cholesterol, and fasting blood glucose. An IVGTT as well as an intravenous insulin tolerance tests (IVITT) was performed prior to the first injection and will be performed after the third CSF1RR1 injection. Depletion of CSF1Rhi monocytes will be confirmed through frequent monitoring of immune cell subsets in the blood using flow cytometry.

Results:
Animals were divided into groups based on fasting blood glucose (average of 75mg/dL for each group), age (average of 20 years-old for each group), and weight (9.68kg and 7.74kg for the Control and CSF1RR groups respectively). The average total cholesterol level across the 6 animals was 152mg/dL. At this time, we have not seen a significant change in total blood cholesterol, fasting blood glucose, or blood pressure in either the control. Flow cytometry of the blood shows a decrease in the percentage of CD16+ monocytes in the animals following infusions of CSF1RR, but not in animals receiving the isotype control.

Conclusion:
Although at the time of this abstract there has been no appreciable difference in total blood cholesterol, fasting blood glucose, or blood pressure, we acknowledge that the decrease in cholesterol in the pilot study was not observed until day 46 of the study (following 3rd infusion) and that this study is currently only on day 30. Flow cytometry data demonstrates the successful depletion of CD16+ monocytes in the blood, which are known to express the higher levels of CSF1R compared to CD16- monocytes. Future reports of the study will include changes in monocyte turnover rate at end of study and tissue-macrophage subset turnover following completion of the study, as well as changes in plasma insulin, adiponectin, and inflammatory cytokine levels.

Abstract Title: A Global Analysis of Civil Unrest's Effect on HIV Prevalence in Adolescent Females

Investigator: Randi Alto
Co-Investigator(s): Mohan D. Pant, PhD, PStat / EVMS
Department(s): Department of Health Professions

Abstract

Introduction:
Despite only making up 10% of the human population, adolescent girls (ages 10- 19) account for 25% of all HIV infections. HIV is the leading cause of death in women of reproductive age. In addition to Sub-Saharan Africa, HIV transmission is relatively high in regions of civil unrest and regions accepting refugees from these war-torn areas. Globally, the effects of civil unrest have only exacerbated the already disproportionate effects of HIV on the female population. These hostile territories are characterized by forced population displacement, gender power differentials, lack of health infrastructure, unsafe living conditions, poverty, and scarcity of food.

Methods:
This is a retrospective analysis of civil unrest's effect on HIV prevalence in adolescent females, specifically within the 2010-2020 timeframe. For the purposes of this study, the Global Peace Index (GPI) 2022 dataset from the Institute for Economics & Peace is used in conjunction with UNICEF's 2021 Key HIV Epidemiology Indicators for Children and Adolescents dataset. Once GPI and HIV incidents rates are extracted, the data is cleaned and then uploaded into Tableau software. Tableau mapping visualizations are utilized to locate countries with the highest correlations between civil unrest and HIV incidence rates in adolescent females.

Results:
The correlation between HIV infections in adolescent females and civil unrest is highest in regions of Equatorial and Southern Africa. Yet, in regions such as the Middle East, with an elevated GPI score due to civil unrest, the rate of HIV incidence in the adolescent female population does not show a strong correlation with GPI.

Conclusion:
The findings of this study conclude the incidence of adolescent female HIV infection rates are location specific. These findings lead to the belief that civil unrest should be assessed with other variables such as a country's economic stability and healthcare infrastructure.

Abstract Title: The Syndemics of Sexual Health Disparities in Heterosexual Populations - A Systematic Review of Quantitative Studies of the Global Literature

Investigator: Brady Goggin
Co-Investigator(s): Shikha Trivedi, Medical Student; Esther Sarino, Library Services
Department(s): Community Health & Research - Pediatrics

Abstract

Introduction:
The theory of syndemics describes the clustering and synergistic interaction of disease driven by contextual and social factors, which worsen health outcomes for a population. The theory has been applied primarily to study sexual minority populations, less is known about the patterns and mechanisms of syndemic sexual health disparities in heterosexual populations.

Methods:
We comprehensively searched four major databases (including PubMed, PsycInfo, CINAHL, Web of Science) and identified 222 studies in English literature which addressed sexual health outcomes and syndemics in heterosexual populations. Each study was independently screened, and data were extracted by two graduate students, and results were reviewed and verified by a senior researcher for accuracy and consistency Forty-four studies which involved quantitative analyses of empirical data from heterosexual populations were reviewed Descriptive statistics were used to present the characteristics and measurements of sexual health syndemics. Content analysis was conducted to summarize the analytical approaches of the studies.

Results:
The vast majority of the 44 studies were cross-sectional (65.5%), community-based (72.7%/32), and from high-income countries (68%/30). Regarding study populations, 45.5% (20) included only women, 27.3% (9) included only men, 34.1% (15) included both women and men, 27.3% (12) focused on adolescents/youth, and 15.9% (7) focused on migrants/ immigrants. Regarding sexual health outcomes, 56.8% (25) of studies reported HIV status, and 43.2% (19) reported other STIs (e.g. chlamydia, gonorrhea, syphilis; herpes, Hepatitis, and HPV). More than half of the studies reported drug/substance use (54.4%/24), 47.7% (21) reported alcohol use, and 6.8% (3) reported tobacco/cigarette use. More than half (52.3%/23) included depression, and 34.1% (15) included stress/anxiety. Over half (56.8%/25) of the studies included childhood adversity (including childhood physical, sexual abuse, and parental separation). About one-third (29.5%/15) reported poverty and 15.9% (7) reported incarceration. While regression models have been used to examine the associations, few studies have addressed the synergies and dynamics of sexual health disparities in heterosexual populations.

Conclusion:
Existing research on the syndemics of sexual health in the heterosexual population is limited by its geographic scope and methodology approach. And more advanced analytical framework is needed to capture the mechanisms of sexual health disparities in heterosexual populations.

Abstract Title: Could Adverse Childhood Experiences be the Root Cause of Adult Behavioral and Emotional Problems of US Veterans?

Investigator: Toni Lee McCreash
Co-Investigator(s): Mohan D. Pant, PhD.
Department(s): Department of Healthcare Analytics/School of Health Professions

Abstract

Introduction:
The International Classification of Diseases 11th edition (ICD-11) was adopted in 2019, effective January 1, 2022. The ICD-11 manual identifies Complex Post-Traumatic Stress Disorder (CPTSD) separately from PTSD as its own diagnosis. CPTSD involves three areas described as disturbances in self-organization (DSO) such as emotional dysregulation, negative self-concept, and relationship disturbances. Dr. Judith Herman from Harvard University in 1988 described patients who experienced long-term trauma as having clusters of symptoms categorized as impacting cognition, behavior, somatization, and emotion. Studies have shown that trauma can affect the amygdala, prefrontal cortex, and hippocampus that regulate emotion, reasoning, and memory. Improving physical and mental well-being is of utmost importance for the current and future generations as trauma is also a transgenerational phenomenon.

Methods:
This will be a retrospective, secondary, observational case series study designed to analyze data from a de-identified group of United States veterans who responded affirmatively to a series of trauma-related questions in a longitudinal study conducted from 2016 to 2019. The US veterans at the time were transitioning from active military service to civilian life. The dataset, containing 9,566 observations, was collected across six interview waves. The dataset used Adverse Childhood Experiences (ACEs) survey questions as well as questions related to behavioral, physical, financial, social, relational, and other aspects of participants' lives. This dataset has generalizability because ACEs are applicable to the population at large and affect adult behavior whether in the military or not. The US military dataset was used because of the quality of the dataset and the visibility that this population receives. Chi-squared tests were conducted against variables of interest, mainly ACE variables associated with depression, anxiety, anger, stress, sleep, problem-solving management/resiliency, and PTSD.

Results:
Preliminary results indicate a strong association of ACEs with anger, depression, anxiety, and stress. For example, physical neglect and anger had statistically significant association between each other χ^2 (df=4,n=5875)=153.71, p<.0001 , emotional neglect and anger had statistically significant association between each other, χ^2 (df=4,n=5875)=255.08, p<.0001, physical abuse and anger had statistically association between each other, χ^2 (df=4,n=5876)=189.09, p<.0001, emotional abuse and anger had statistically association between each other, χ^2 (df=4,n=5875)=253.24, p<.0001, sexual abuse and anger had statistically association between each other, χ^2 (df=4,n=5875)=79.288, p<.0001, domestic violence and anger had statistically association between each other, χ^2 (df=4,n=5874)=123.05, p<.0001, and family history of mental illness or alcohol abuse and anger had statistically association between each other, χ^2 (df=4,n=5874)=183.72, p<.0001 for the fifth wave of data collection.

Conclusions:
ACEs are most likely behind adult behavioral and emotional issues affecting all aspects of life. Protocols should be designed to ensure proper support is provided children in schools and adults in the workplace.

Abstract Title: Analysis of Disease-free Survival Events of Adjunctive Chemotherapy versus Radiotherapy in Relation to Initial Duke's Staging at Diagnosis in Colorectal Cancer Patients

Investigator: Keerthana Velayudham
Co-Investigator(s): Mohan D. Pant, PhD / Healthcare Analytics
Department(s): Healthcare Analytics

Abstract

Introduction:
Colorectal cancer (CRC) is the third most diagnosed cancer and the second leading cause of cancer-related deaths in the United States. The standard of treatment for most colon cancers is to perform local excision or resection. The location and staging of the cancer are important factors in treatment approaches and physicians often consider the risk profile of the patients. Often, the use of chemotherapy and radiation is considered in some rectal cancers. It has become common to incorporate both forms of therapy, known as "chemoradiotherapy," for some stage II and III rectal cancers with the hope of reducing reoccurrence rates. While the use of adjuvant chemotherapy in stage III (lymph node positive) colon cancer is fully established as a standard treatment, there is still some controversy because only a limited number of randomized clinical trials have been conducted to evaluate the efficacy of adjuvant treatments in other stages of cancer and uncertainty of how to best combine therapies in order to prolong survival among metastatic colorectal cancer patients. Both forms of neoadjuvant therapies have their own significant side effects as radiation can cause radiation proctitis, cystitis, and bone marrow insult. The objective of this study is to investigate how radiation, chemotherapy, and duke's stage influence the recurrence of the disease using the CRC dataset from the Queen's University Belfast Cancer Research.

Methods:
The small subset of the patients at the Queen's University Belfast Cancer Research (QUBCR) center were retrospectively studied. This colorectal cancer dataset was found on Kaggle website and we identified four variables of interest which are the disease-free survival event, patients who received adjunctive radiotherapy, patients who received adjunctive chemotherapy, and duke's stage. We assessed the 62 patients to see the influence of adjunctive radiotherapy, adjunctive chemotherapy, and duke's stage on the disease-free survival (DFS) event. Radiotherapy, chemotherapy, and survival events were dichotomized (no radiotherapy vs radiotherapy, no chemotherapy vs chemotherapy, and no disease-free survival vs disease-free survival). Associations between radiotherapy, chemotherapy, duke's stage, and disease-free survival were determined by using logistic regression.

Results:
A logistic regression was performed with the response variable as the DFS event and all the other variables in the dataset as the predictor variables to see what potential associations might exist. The only significant predictor from the logistic regression model was adjunctive radiotherapy. Radiotherapy had the lowest odds ratio (OR) of 0.18 (95% confidence interval (CI): 0.03-0.79; p-value = 0.03), with the second lowest OR belonging to Duke's Stage D of 0.33 (95% CI: 0.03-2.71; p-value = 0.31). Adjunctive Chemotherapy had an OR of 0.9 (95% CI: 0.21-3.95; p-value = 0.9).

Conclusion:
The use of Adjunctive Radiotherapy may lead to lower reoccurrence rates of CRC relative to the use of chemotherapy. Multiple factors might contribute to this finding. While the results were not significantly linked to a particular Duke's stage at diagnosis, there was still an apparent benefit from adjunctive radiation in the disease-free reoccurrence events. This study had a relatively small sample size of 62 patients in which there could have a variety of interactions among the patients. It is not clear as to the length and occurrences of each type of therapy. In addition, the dataset does not provide details of other potential co-morbidities, diet, and lifestyle influences. It is not clear what specific cocktail of chemotherapy was utilized and it is more than likely that it was not the same exact formula. Perhaps, future studies could perform a more controlled study with larger sample sizes and more controlled treatments to assess the relative risk of CRC reoccurrence based on the available treatment choices used in treating CRC at different stages.

Abstract Title: A misnomer worth paying attention to

Investigator: Sarah Al Allawi
Co-Investigator(s):
Department(s): Internal Medicine

Abstract

Introduction:
Lupus pernio (LP) is a distinct variant of cutaneous sarcoidosis. The term is a misnomer as it is neither associated with systemic lupus erythematosus, lupus vulgaris (cutaneous tuberculosis) for which it has been mistaken, nor pernio (Chilblains), a rare inflammatory skin condition typically affecting acral skin in response to cold, damp conditions. LP typically presents with violaceous or erythematous, indurated, infiltrative plaques primarily distributed on the central face, often with nasal alae involvement. It is more common in African Americans and females between 45 and 65.

Case description:
A 51-year-old African American male with known pulmonary sarcoidosis who had been recently tapered of long-term steroids developed a worsening facial rash. He presented with bilateral violaceous macular cutaneous lesions affecting his right alar rim, nasal tip, and cheeks consistent with LP. He was referred to dermatology with biopsies revealing non-caseating granulomatous inflammation suggestive of sarcoid. He went on to have nasal, laryngeal, and tracheal complications from sarcoid.

Initial treatment of his LP with triamcinolone injections and topical ointment resulted in minimal improvement; this was followed by a series of therapies involving hydroxychloroquine and adalimumab with an inadequate response. Eventually, he was started on serial infliximab infusions with significant improvement.

Discussion:
Sarcoidosis is a multisystem, noncaseating granulomatous disorder. The skin is the second most common organ affected after the pulmonary system. LP is a type of cutaneous sarcoidosis typically manifesting as blue/ red to violet, smooth, shiny nodules and plaques primarily distributed on the central face and, less frequently, the ears, lips, hands, and feet. The presence of lupus pernio appears to be associated with an increased risk for extracutaneous disease, particularly higher risk for upper respiratory tract disease.
LP is very resistant to treatment compared to other forms of cutaneous sarcoidosis. Without treatment, the lesions progressively infiltrate and indurate, eroding the underlying cartilage and bone, causing considerable destruction and disfigurement.

Treatment usually follows a therapeutic ladder determined based on the extent of cutaneous disease and additional organ involvement. Topical or Intralesional steroid injections are among the first lines of therapy. Topical calcineurin inhibitors like tacrolimus are sometimes used in conjunction with steroids. Systemic glucocorticoid therapy is only considered in patients with rapidly progressive skin lesions or those with disfiguration. Antimalarials, methotrexate, and tetracycline derivatives are often used as glucocorticoids sparing agents. Tumor necrosis factor-alpha inhibitors (e.g., Infliximab or adalimumab) are indicated in resistant cases.

Surgical excision of the lesions is not recommended as there is a high risk of recurrence in the surgical scars. Reconstructive surgery can be considered to improve cosmetic appearance in patients with severely disfiguring nasal lesions.

Conclusion:
Lupus pernio carries an important association with upper respiratory tract disease in sarcoidosis.

Abstract Title: Expect the Unexpected: RV Perforation During Lead Extraction

Investigator: Ayeman Basith
Co-Investigator(s): Kanishk Sharma, Internal Medicine, Glennan Center for Geriatrics and Gerontology
Department(s): Internal Medicine

Abstract

INTRODUCTION:
The most common indications for pacemaker lead removal are infection, venous occlusion, recall, lead malfunction, or mechanical lead failure.1,2

Large series of patients who have undergone cardiac pacemaker lead extraction have reported high success rates (95 to 99 percent) and low complication rates (<1 percent). However, significant complications do occur, including cardiac tamponade, vessel laceration, traumatic tricuspid regurgitation (TR), and death.3-5 We present a rare case of a 76-year-old female who had cardiac tamponade due to RV free wall perforation during a pacemaker lead removal.

CASE:
A 76-year-old female with a history of Mobitz type II 2nd degree AV block s/p dual-chamber pacemaker placement in 2012, CREST syndrome, CAD s/p stent, and breast cancer was admitted to the hospital due to concern of pacemaker site infection in the right subclavicular region. She had undergone pulse generator replacement three months prior. The wound initially healed, but the scab fell off, exposing the pacemaker. She denied complaints of fever, chest pain, shortness of breath or palpitations. The skin exam showed a small opening without erythema or drainage. Her vital signs, complete blood count, basic metabolic panel, chest X-ray and EKG were unremarkable.

Cardiothoracic surgery discussed extraction of the entire system and re-implantation on the left side. During the procedure, the RA lead was removed without any complications. While removing the right ventricular lead patient became hemo-dynamically unstable. An emergent intra-operative echocardiogram showed a pericardial effusion. A pericardial window showed active venous bleeding, and the patient's vitals rapidly improved with drainage. Upon further opening the pericardium, a right ventricular free wall perforation was identified and repaired with 4-0 prolene repair stitch. A left subpectoral dual chamber pacemaker was placed, and the patient was monitored overnight in the cardiac ICU. Repeat echo at post-operative day 6 showed a new reduced EF of 35% (from 60% in March 2019) with no effusion. The patient was started on carvedilol 3.125 twice a day and discharged with close cardiology follow-up.

DISCUSSION:
Incidence of cardiac perforation during ex-plantation of an implanted lead is less than 1%.6 Extraction of leads is technically challenging, primarily due to the fibrous connections between the leads and the vascular wall and endocardial surface.7Other risk factors for a complication during lead removal include Female sex, steroid use, anticoagulant use, age greater than 75 years, body mass index (BMI) less than 25, chronic lung disease, and history of coronary intervention.8 Clinical presentation may vary clinically from chest pain, dyspnea to cardiac arrest secondary to tamponade.9 Transthoracic echocardiogram and CT scan remain leading modalities of diagnosis. When performed by experienced operators, mortality is usually less than 1 percent of patients, with significant complications seen in 2 to 4 percent.10-13 Due to rarity of incidence, management guidelines remain unclear. Cardiotomy with surgical removal remains an effective tool in patients with failed transcutaneous approaches, respiratory compromise, or hemodynamic instability like in our case.

CONCLUSION:
1. All patients should undergo pre-procedural evaluation, which includes a complete history and physical exam, electrocardiogram (ECG), chest radiograph, and assessment of device function and pacemaker dependency.
2. Factors that increase the likelihood of adhesion formation between endovascular structures and cardiovascular implantable leads include, lead placement for more than two years and ICD leads
3. Due to the risk of endovascular injury, lead extraction procedures should be performed with cardiothoracic surgical backup available.

Abstract Title: mtDNA Mutation Detection in Alzheimer's Brains and Functional Analysis of Differentiated NT2 cells

Investigator: Destyni Hubbard
Co-Investigator(s): Frank Castora, PhD, physiology department
Department(s): Physiology

Abstract

Introduction:
Alzheimer's disease (AD) is the most prevalent type of dementia, which causes memory and other cognitive functions to deteriorate. It is established that mitochondrial dysfunction significantly contributes to the pathogenesis of neurodegenerative diseases. Deficits in oxidative capability, more specifically, cytochrome c oxidase (CO) activity, have been seen in AD brains. Dr. Castora's lab previously identified a single T9861C point mutation in mtDNA that codes for subunit 3 of respiratory complex 4 (RC4) in brains with AD. To further examine the relationship between mitochondrial malfunction and AD, a study of mitochondrial gene expression was undertaken in our lab. Nine mitochondrial genes were identified as genes of interest (GOIs) by RT2PCR array and qPCR analysis. Our lab is beginning siRNA knockdown experiments to evaluate the effect of this treatment on mitochondria and the markers of AD. Analysis of the genes will be conducted using the Ntera-2 cell line that acts as a neuronal cell model for neurodegenerative disease.

Methods:
1. Test for the presence of the T9861C mutation in newly acquired control and AD brains using PCR amplification/ HaeIII digestion and allele-specific PCR (AS-PCR).
2. Begin preparation for siRNA transfection by differentiating NT2 cells with retinoic acid and investigating optimal transfection conditions with varying concentrations of transfection agent and siRNA. Success of the differentiation will be determined by analyzing nestin mRNA levels using qPCR. If time permits, siRNA-mediated knockdowns of the genes of interest will be conducted to evaluate their function in AD etiology. Results: After AS-PCR, several brain samples required further mutation testing. They were examined using PCR and Hae III digestion. This second analysis showed that none of the new samples possessed the T9861C mutation. qPCR of nestin mRNA within retinoic acid-treated NT2 cells confirmed that differentiation into neuronal-like cells was accomplished. Adequate concentrations of siRNA and transfection agent were identified for optimal conditions for the uptake of siRNA by these cells.

Conclusion:
Based on our data, there were no new samples containing the T9861C mutation. Successful differentiation of NT2 cells provide a cell line that imitates neurons genotype and phenotype. This cell line will be used for siRNA transfection where GOI's will be silenced to observe how they affect mitochondrial dysfunction. This study is being carried out to learn more about the causes of AD and potentially develop a therapy that focuses on mitochondrial health.

Abstract Title: Spine strangler: A case of spinal epidural lipomatosis in a young male

Investigator: Anum Javaid
Co-Investigator(s): Kanishk Sharma, Internal Medicine
Department(s): Internal Medicine

Abstract

Introduction:
Spinal stenosis is the narrowing of intervertebral foramina most commonly caused by degenerative changes in the vertebral bodies. Other common causes include achondroplasia, ankylosing spondylitis, or Paget disease. We report a case of a 32-year-old male who presented with difficulty walking and was found to have a rare culprit, spinal epidural lipomatosis (SEL).

Case Information:
A 32-year-old obese male presented with an eight-month history of progressive bilateral leg weakness and back pain, with acute worsening in the past two weeks. He also had associated bilateral lower extremity pain, weakness, numbness, and multiple mechanical falls in the past six months. On physical exam, he was afebrile and normotensive with BMI of 38. He was A/A/O x 4, with neurologic exam significant for muscle strength 2/5 in left leg, 3/5 in right leg, and 5/5 in bilateral upper extremities. He had diminished sensation below L3 in both legs, +4 bilateral patellar reflex with clonus, and upgoing bilateral plantar reflexes. Labs showed normal levels of cholesterol, triglycerides, hbA1C, and TSH. MRI thoracic and lumbar spine revealed spinal cord stenosis with cord compression and myelopathy at T5-T6 due to left central disc extrusion, thickening of ligamentum flavum, and diffuse dorsal epidural lipomatosis. Neurosurgery was consulted, and he underwent urgent T5-T6 decompressive laminectomy with partial T4-T7 laminectomies for evacuation of epidural lipomatosis. At the time of discharge to a rehabilitation facility, his weakness improved in lower extremities with 4/5 muscle strength bilaterally.

Discussion:
Spinal epidural lipomatosis is seen in 2.5% of population and is caused by excessive adipose tissue in the epidural space. The exogenous steroid group represents 55.3% cases, while obesity-associated disease represents 24.5%. In our patient, obesity may be a driving factor for SEL. SEL is most common in patients taking exogenous steroids, such as post-transplant patients. SEL is also seen in people with type 2 diabetes mellitus, increased production of endogenous steroids, HIV on protease inhibitor therapy, Scheuermann's disease, and those on androgen antagonist therapy.

Management of SEL depends on the presentation. With acute neurologic deficits, the first-line treatment is urgent surgical decompression. Conservative management of inciting features is recommended if there is a slowly progressive disease. It includes cessation of steroids and treatment of endocrinopathies. Weight reduction has been shown to significantly reduce SEL in obese patients, with one report recommending at least 15 kgs of weight loss to help control symptoms. If conservative therapy is not successful, decompressive surgery such as laminectomy with or without removal of fatty tissue can be considered. Removing as much fatty tissue as possible avoids post-surgical complications. Unfortunately, mortality rate within one year after surgical decompression is as high as 22%.

Conclusion:
Spinal epidural lipomatosis can cause progressive bilateral leg weakness due to spinal stenosis.

Abstract Title: Teaching patient preparation prior to radioiodine therapy.

Investigator: Fiora McRae
Co-Investigator(s): Richard Lussier DO, UVA, Department of Radiology; Sarah Shaves MD FACR, EVMS, Department of Radiology; Lester Johnson MD PhD FACR, EVMS, Department of Radiology
Department(s): Radiology

Abstract

Introduction:
Prior to radioiodine as definitive treatment of hyperthyroidism, patient screening and education are critical for good patient care. Discussion of risks and benefits, alternatives and expected outcomes is a part of standard informed consent. As radioiodine administration is not a common procedure, we recognized the need for a teaching tool for ensuring radiology residency trainees have the necessary experience to adequately prepare patients for the intervention.

Methods:
We developed a three-step approach to resident preparation for Iodine-131 (I131) therapies. First, a didactic teaching conference was created to discuss proper patient screening prior to consideration for I131 therapy and detailed review of techniques and cautions specific to radioiodine administration as well as expected and potential uncommon outcomes. Prior understanding of details of the procedure was assessed with a pre-test before the presentation and a post-test following the didactics.

We then created a simulation using standardized patients (SP) to prepare the residents for a real-life interaction. The simulation was created in conjunction with members of the Sentara Center for Simulation and Immersive Learning with discussion and training of the SP by a senior resident, supervised by a faculty radiologist, using the materials from the didactics lecture. Each resident then had a standardized interaction eliciting appropriate information as they screened the SP for a simulated I131 therapy followed by obtaining informed consent. Verbal feedback on patient interactions was then provided immediately by the trained SPs followed by written feedback on recorded content by a faculty radiologist.

Results:
Fifteen residents across all four years of radiology residency participated in the didactic teaching conference, pre- and post-test assessment, and the SP interaction. Average results of the pre- and post-test assessment were calculated for each class year. First-year residents scored an average of 64%, second-year residents scored an average of 65%, third-year residents scored an average of 48%, and fourth-year residents scored an average of 75% on the pre-test assessment. Following the didactic teaching conference, first-year residents scored an average of 96%, second- and third-year residents scored an average of 98%, and fourth-year residents scored an average of 97% on the post-test assessment. The average percent correct across all four years of the radiology residency program increased 54% from an average of 63% on the pre-test to 97% on the post-test assessment. Feedback from SPs indicated most residents showed excellent empathy and good pacing of the interviews. Review of simulated patient interactions demonstrated an overall appropriate level of understanding of important screening information and risks and benefits of I131 therapy. Omission of some details of the procedure was identified despite the preparation.

Conclusion:
Development of a standardized approach to educating radiology residents prior to performing I131 therapies with repetition improves resident knowledge. Omission of some details of the procedure was identified despite the preparation, indicating that a checklist might be a useful tool for a radiology resident obtaining informed consent.

Abstract Title: Does Neurotensin Influence Granulosa Cells via STAT3?

Investigator: Jessica Miller
Co-Investigator(s):
Department(s): Physiology

Abstract

INTRODUCTION:
Neurotensin (NTS) is a neuropeptide that serves a range of paracrine and endocrine functions within the brain, gastrointestinal track and cardiovascular system. It is mediated by the G-coupled receptors, neurotensin receptor 1(NTSR1) and neurotensin receptor 2 (NTSR2), and by a type I transmembrane protein, sortilin (SORT1). These receptors and their functions have mainly been studied in the central nervous system, but we recently identified them in the ovary. After the luteinizing hormone (LH) surge, the endocrine trigger for ovulation, NTS expression increases in granulosa cells (GC) which is essential for the ovulation of a mature follicle. The purpose of the present study is to identify which signal transduction pathway(s) are activated by NTS in granulosa cells of ovulatory follicles.

METHODS:
Granulosa-luteal cells were collected from In Vitro Fertilization (IVF) patients and cultured for about seven days to allow cells to return to their pre-ovulatory state, as demonstrated in previous studies. Once GC have returned to a pre-ovulatory state they again become responsive to stimuli such as human chronic gonadotropin (hCG), which is used to mimic the LH surge in vitro. After this culture period, GCs were exposed to NTS (0.5-50 μM) or hCG (20 IU/ml) for 1-4 hours. GC proteins were separated on gels, and western blots were performed using antibodies for the signal transducer and activator of transcription 3 (STAT3), and phosphorylated STAT3 (P-STAT3). Densitometry was performed, and the ratio of P-STAT3/STAT3 was determined. To determine if P-STAT translocated to the cell's nucleus, GC plated on chamber slides were also treated with NTS or hCG, then fixed. Immunohistochemistry was performed using a STAT3 or P-STAT3 antibody. Cells were photographed through a microscope.

RESULTS:
In cultured human GCs, the ratio of P-STAT3 to total STAT3 increased over time of exposure to NTS, with maximal P-STAT3/STAT3 achieved after 4 hours. Treatment with NTS at higher doses (5-50 μM) resulted in STAT3 immunolocalization in the nucleus of GC; STAT3 was not prominent in the nucleus of control GCs nor GCs treated with 0.5 μM NTS. Granulosa cells treated with hCG also resulted in STAT3 localization in the nucleus. Similarly, immunolocalization of P-STAT3 was primarily nuclear and was more eminent after treatment with 50 μM NTS and hCG.

CONCLUSION:
Neurotensin increases the phosphorylation of STAT3. Increased STAT3 phosphorylation and nuclear location after NTS treatment supports the hypothesis that at least one of the NTS receptors utilizes STAT3 for signal transduction. STAT3 is a common transcription activator that plays a crucial role in intracellular signaling. Further investigation of how NTS drives phosphorylation of STAT3 and possible genes being regulated are currently being performed. Future studies will use NTS receptor selective antagonists to determine which NTS receptor(s) are responsible for STAT3 phosphorylation. Understanding the signal transduction of NTS within GCs and identifying the receptors involved will expand our knowledge of ovulation and may improve future treatments for infertility or identify novel targets for contraception.

Abstract Title: COVID-19 Mediated Electrical Storm Managed with Milrinone

Investigator: Spencer Moen
Co-Investigator(s): Marina Johnston MD, EVMS Pulmonary and Critical Care; Philip Gentlesk, MD, Sentara Cardiology Specialists; Rishik Vashisht, MD, Sentara Pulmonary, Critical Care, and Sleep Specialists
Department(s): Sentara Pulmonary, Critical Care, and Sleep Specialists

Abstract

Introduction:
SARS-CoV-2 infection (COVID-19) can lead to an inflammatory response affecting multiple organs. Ventricular arrhythmias, including ventricular tachycardia (VT) and ventricular fibrillation (VF), have been reported in nonvaccinated otherwise healthy individuals. Our case reports resolution of refractory VF with use of low dose milrinone infusion. An inotropic agent usually used in heart failure patients, milrinone also possesses proven anti-inflammatory effects, which may have allowed it to succeed where the traditional agents failed.

Case Report:
A previously healthy 22-year-old male who was fully vaccinated against SARS-CoV-2 infection (COVID-19) presented to an outside hospital after falling at home. Patient was found to be in VF and required multiple defibrillations at home and en route to the hospital. Additionally, he received 5 minutes of CPR and amiodarone before reaching the emergency department (ED). In the ED, patient had refractory VF requiring repeated defibrillations and intubation.

Initial laboratory workup was significant for SARS-CoV-2 positive PCR and subsequent inflammatory markers were only mildly elevated. Mild hypokalemia and hypomagnesemia were both corrected. Urine drug screen and remaining lab workup was unrevealing.

Amiodarone was replaced with lidocaine bolus and continuous infusion without improvement. While on the continuous lidocaine infusion, he received additional amiodarone and metoprolol boluses, vasopressors, and 22 more defibrillations despite ongoing treatment. Milrinone bolus was given and continuous infusion at 0.25 mcg/kg/min was started as empiric salvage therapy for the electrical storm. Sinus rhythm was achieved, and no further VF arrhythmias were noted. Patient was taken to the cardiac catheterization lab for emergent coronary angiography which did not show significant coronary disease.

On hospital day 10, cardiac magnetic resonance imaging was done, which showed an EF of 50% and no signs of an infiltrative process, myocarditis, or ischemic changes. A dual chamber ICD was placed prior to discharge. Comprehensive screening for genetic mutations predisposing to arrhythmias was done as outpatient and was negative.

Discussion:
SARS-CoV-2 induced cytokine storm is well documented and is associated with high levels of inflammatory cytokines including IL-6, TNF-α, and IL-1β. These changes lead to a combination long QT syndrome (LQTS) and sustained prolongation of action potential duration (APD). The inflammation mediated APD prolongation may escape the standard therapeutics of intravenous (IV) amiodarone and lidocaine in VF.

Milrinone is a phosphodiesterase 3 (PDE-3) inhibitor that increases cyclic monophosphate (cAMP). Traditionally considered an inotropic agent, milrinone has dose dependent anti-arrhythmic activity. Elevated cAMP levels augment inward L-type Ca current and reduce transient outward K current potentially creating an antiarrhythmic effect. Additionally, cAMP can lead to direct cytokine suppression, including IL-6, TNF-α, and IL-1β.

After multiple failed doses of IV amiodarone and lidocaine, our patient's refractory VF shortly terminated after milrinone administration without further recurrence. We posit that the above discussed pathways of the milrinone directly counteracted the effects of cytokines associated with his COVID-19 infection. While temporal correlation with milrinone use and resolution of refractory VF cannot be ruled out, previous studies on its anti-inflammatory properties are highly supportive of the therapeutic effects observed.

Conclusion:
To our knowledge, this is the first reported case of refractory VF due to an acute SARS-CoV-2 infection in a previously healthy patient with appropriate vaccine response. This case illustrates that there may be a potential therapeutic role for milrinone use in cytokine-induced inflammatory cardiac channelopathy refractory VT that do not resolve with traditional therapies.

Abstract Title: Copperhead Snake Bite and Antivenom Treatment

Investigator: Spencer Moen
Co-Investigator(s): Alexander Gogoli MD, Internal Medicine
Department(s): EVMS Internal Medicine

Abstract

Case Information:
A 46 year old male presented after a snake bite to his left hand that occurred the day prior while he was working in his garden. He was able to identify it as a copperhead and noted a single puncture bite. On the initial physical exam, his left hand exhibited diffuse edema and minor erythema that extend up the forearm and slightly past the elbow. Per Poison Control recommendations, he received six units of Crofab antivenom (2 vials every 6 hours for three total doses). Unfortunately, the swelling continued to progress up to his shoulder, making flexion of the left elbow limited due to edema and pain. He was instructed to keep the majority of his arm below the level of his heart to limit the spread of poison further up the extremity, towards the greater vessels, due to potential myotoxic and myocardial suppressive side effects. There was initial concern for coagulopathy given an elevated D-Dimer, but since his CPK, fibrinogen, platelets, and prothrombin time were within normal limits, additional doses of Crofab were not given, nor was he started on full anticoagulation. 48 hours post envenomation, the patients swelling regressed down to his hand, wrist and mid-forearm. He was discharged home with medications for pain and was given the number for Poison Control for further follow up.

Discussion:
Almost 5000 venomous snake bites are reported yearly, 50 percent of which are Copperhead bites. Copperhead snakes, also known as Crotalinae, belong to the Viperidae family. Their venom is a complex mixture of toxic compounds including phospholipase A2 (PLA2), phosphodiesterases, hyaluronidases, peptidases, and metalloproteinases, capable of producing quite a variety of effects post envenomation. Locally, enzymatic action on the extracellular matrix, the vascular endothelium, and the basement membrane causes tissue swelling, redness, and pain, which can progress to the point of tissue necrosis and autoamputation. Hematologically the venom can cause low platelets, low fibrinogen, and elevated prothrombin time. Cardiovascularly the venom can cause increased capillary permeability, vasodilation, bleeding, and direct myocardial depression.

For minor bites, defined as minimal localized swelling and now abnormalities, treatment is supportive care. For moderate and severe envenomations, defined as marked/progressive swelling as well as systemic findings, antivenom is recommended. Antivenom works by having the fragment antigen binding (Fab) portion of digested IgG antibodies bind to and neutralize the venom. FabAV/Crofab was made available to the US in 2007 and until 2019 was the antivenom of choice for rattlesnake, cottonmouth, and copperhead envenomations. Fab2AV/Anavip was released originally for rattlesnake envenomation, but in 2021 became approved for Copperhead and Cottonmouth venom as well. Its Fab had longer half-lives which resulted in reduced risk of subacute coagulopathy and bleeding following treatment of envenomation.

Conclusion:
Since our patient presented with markedly increased swelling and elevated D-Dimer, he was deemed to be at risk for at least moderate envenomation, and was given antivenom. 48hrs post envenomation and 24hrs post antivenom, swelling had regressed, range of motion was restored, and pain was under control. As evident with our patient, and with recent research, Fab2AV/Anavip works well to halt and reduce tissue destruction, decreases time to return to work, reduces post-envenomation coagulopathy, and reduces long term disability.

Abstract Title: A Delicate Balance: Management of Primary Hyperparathyroidism and Congestive Heart Failure

Investigator: Nikita Mohan
Co-Investigator(s):
Department(s): EVMS Endocrinology

Abstract

Introduction:
Primary hyperparathyroidism is a condition where excessive parathyroid hormone production, usually due to a parathyroid adenoma, leads to increased calcium levels. Commonly these cases are asymptomatic and detected incidentally on routine labs. They can be managed conservatively with sufficient fluid intake, regular calcium and creatinine, and bone density monitoring. Patients should avoid dehydration by maintaining sufficient fluid intake, avoiding diuretics, bed rest, and a high-calcium diet. Congestive heart failure patients on diuretics with primary hyperparathyroidism require a delicate balance of volume status to prevent exacerbation of either condition. Here we present a case of an elderly woman with repeated hospitalizations due to dehydration and fatigue.

Case Information:
An 82-year-old elderly female with a past medical history of congestive diastolic heart failure (Ejection Fraction 40%), primary hyperparathyroidism (diagnosed 17 years ago), sick sinus syndrome with a pacemaker, persistent atrial fibrillation on warfarin, and pre-diabetes presented to the emergency room with complaints of worsening bilateral lower limb swelling since a few months. She denied any symptoms of shortness of breath, abdominal pain, nausea, vomiting, orthopnea, paroxysmal nocturnal dyspnea, syncope, chest pain, or urinary or bowel complaints. At home, she was taking Losartan 50 mg daily, Furosemide 20 mg daily, Carvedilol 12.5 mg twice daily, and warfarin. Vital signs were stable, and a physical exam was significant for bilateral lower extremity pitting edema. Chest x-ray showed cardiomegaly with mild pulmonary vascular congestion. Pertinent labs included NT pro-BNP 2190, Calcium 11.3, PTH 143, Vit D, 25 hydroxy 48.6. The patient was started on IV diuretics and her home goal-directed medical therapy (GDMT) for heart failure exacerbation. A repeat echocardiogram (ECHO) showed EF of 39%, grade III diastolic dysfunction, severe pulmonary hypertension, and severe mitral and tricuspid regurgitation. As the patient's hypercalcemia was less than 1 mg/dl above the upper limit of normal, she was managed conservatively, advised to maintain hydration at home, and resume Vitamin D 1000U daily. The following modifications were made to her GDMT: Furosemide 30 mg, Spironolactone 12.5mg, and Dapagliflozin 10 mg daily.

The patient returned to the emergency room three weeks later with symptoms of fatigue, decreased appetite, and decreased fluid intake. Vital signs were stable, and the physical exam was remarkable for dry oral mucous membranes. Labs were significant for Calcium 13.4, Potassium 5.7, Creatinine 1.7 (baseline 1.0), PTH 204, and Vitamin D 54.1. Repeat ECHO showed EF 15%. She was started on gentle IV fluids 0.9% NS due to congestive heart failure. Patient's hypercalcemia and acute kidney injury improved with hydration. She was started on Cinacalcet 30 mg daily due to concern for QTc prolongation. At the time of discharge, the following modifications were made for better volume status control - Losartan was discontinued, Carvedilol changed to 6.25mg twice a day, Furosemide 20 mg daily, and continued spironolactone and dapagliflozin.

The patient had a follow-up appointment with Endocrinology post-discharge; however, she ended up in the emergency room a week later with similar complaints of fatigue, dehydration, and decreased PO intake. Relevant labs included Calcium 13.3, Sodium 131, and urinalysis suggestive of urinary tract infection. The patient received IV fluid boluses and oral antibiotics. She was discharged home from the emergency room with home health.

Discussion:
This case highlights the challenges involved in managing patients with primary hyperparathyroidism and heart failure with reduced ejection fraction. Especially in elderly patients, the two conditions require a delicate balance to maintain a euvolemic status. This patient's primary hyperparathyroidism was well controlled for more than fifteen years on just adequate PO intake (did not meet surgical criteria). However, her heart failure worsened, resulting in a higher requirement for diuretics, worsening her hypercalcemia. Medical management for primary hyperparathyroidism includes IV fluids, bisphosphonates, and calcimimetics. Even though parathyroidectomy is a well-established treatment modality, she would not be a suitable candidate due to her age, comorbidities, and overall clinical picture.

Conclusion:
Primary hyperparathyroidism and congestive heart failure require a delicate balance in treating both conditions to avoid aggravating the other.

Abstract Title: A Misleading Case of Ground Glass Opacities

Investigator: Dipan Oza
Co-Investigator(s):
Department(s): Pulmonary and Critical Care

Abstract

INTRODUCTION:
In the pandemic era, strong history of exposure and nonspecific diagnostic testing can easily anchor a clinician on the diagnosis of Covid-19. Clinicians must be cognizant that while the omnipresent "ground-glass opacities" may suggest a diagnosis of Covid-19, the specificity remains low and the differential should remain broad. This case highlights the importance of careful history taking and gathering of key medical information based on discerned observation of common laboratory values.

CASE INFORMATION:
A 40-year-old male presented to the hospital for worsening fatigue, dyspnea on exertion, and pre-syncopal episodes with exertion for 2 weeks. Four weeks prior to presentation, he was exposed to several family members that tested positive for Covid-19. The patient quarantined with them for the subsequent two weeks. He noted the pre-syncopal symptoms upon returning to work in shipping and packing for a storage company, where he had been working for several years. After two additional weeks of worsening fatigue and dyspnea on exertion, he presented to the emergency department (ED) and was admitted for acute hypoxemic respiratory failure requiring supplemental oxygen.

Patient has no significant medical or surgical history, takes no medications, and denies any significant family history. He lives with his partner and their four children. He denied smoking cigarettes, vaping, or recreational drug use. He drinks alcohol socially one to two times per month. He is unvaccinated for Covid-19.

In the ED, physical exam was significant for tachypnea at rest, persistently dry cough, high flow nasal oxygen (HFNO) by Vapotherm of 30L and 40% FiO2, and pleuritic chest pain. The patient tested negative for Covid-19 by nasopharyngeal RT-PCR. Previously, the patient tested negative on the day his family members were diagnosed and just before returning to work, approximately two weeks prior to presentation. Patient was admitted for presumed Covid-19 pneumonia due to his unvaccinated status and close contact with multiple Covid-19 positive family members. Despite being started on high dose steroids, patient developed increasing dyspnea and HFNO requirements, prompting pulmonology consultation.

Discussion/Clinical Findings
In the ED, the patient's partner tested positive for COVID-19, but he was negative. Previously, the patient tested negative on the day his children were diagnosed and a few days before returning to work. Patient was admitted for presumed COVID-19 due to his unvaccinated status and close contact with multiple COVID-19 positive family members. Initial laboratory data were significant for C-reactive protein (CRP) of 17.4 mg/dL (0.0-0.5 mg/dL), Ferritin of 873 ng/mL (10-291 ng/mL), WBC of 10,300 K/µL with an absolute lymphocyte count of 1.7 K/µL, Hemoglobin of 12.0 g/dL, platelets of 171K/UL, total protein of 8.5 g/dL, albumin of 2.8 g/dL, and NT-proBNP of 62 pg/mL. Chest x-ray (CXR) showed diffuse bilateral reticular infiltrates and diffuse ground glass opacities on chest CT. Patient was started on steroids for presumed COVID-19 infection and empirically treated for community acquired pneumonia. Pulmonary consult service was requested one week after admission due to increasing high-flow nasal cannula requirements despite increasing steroids and completing antibiotics.

Physical exam was significant for tachypnea at rest, persistently dry cough, HFNC of 30L and 40% FiO2, and pleuritic chest pain. Additionally, patient revealed weight loss of approximately 40 lbs pounds since his initial exposure. Repeat labs showed no significant leukocytosis or electrolyte abnormalities. CRP and Ferritin initially improved but rebounded from 4 to 10 mg/dL and 620 to 693 ng/mL, respectively, between days 4 and 8. Repeat COVID PCRs were negative on days 2 and 4 of admission, anti-spike and anti-nucleocapsid antibodies were negative on days 2 and 8 of admission. Given worsening clinical status, imaging findings, and an initial globulin gap of 5.7 g/dL, additional labs, including HIV, were ordered. HIV returned positive with absolute CD4 count of 17 cmm (1%). Lactate dehydrogenase was elevated to 702 U/L. Empiric treatment for Pneumocystis jirovecii pneumonia (PJP), later confirmed by bronchoalveolar lavage, was started with Trimethoprim-sulfamethoxazole and continuation of steroids. His symptoms quickly improved, and he was discharged on room air one week later.

Conclusion:
While an abundantly common finding during the Covid-19 pandemic, the differential diagnosis of ground glass opacities on a Chest CT is broad. Disease progression and symptom onset after exposure to Covid-19 can provide clues to help build the differential diagnosis and avoid anchoring on a Covid-19 diagnosis.

Abstract Title: Investigating the efficacy of pHLIP-mediated delivery of antimirs against miR-888 and miR-891a to PCa cells

Investigator: Katherine Routon
Co-Investigator(s):
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION:
Prostate cancer (PCa) is the second leading cause of male cancer-related deaths in the United States. 20% of men diagnosed with PCa will later progress to advanced, metastatic disease of which there is only a 30% 5-year survival rate. Thus, better therapeutic options are needed to increase patient survivorship. MicroRNAs (miRNAs) are abnormally expressed in tumors and fluids from PCa patients. These miRNAs are found to act as tumor suppressor genes and oncogenes to influence tumor formation and disease progression. We recently identified the miR-888 cluster of seven miRNA genes (including miR-888 and miR-891a) as increased in human metastatic PCa cells and prostatic fluids from high-grade PCa patients compared to low-grade and non-cancer patients. Treatment of non-aggressive human PCa cell lines to overexpress miR-888 or miR-891a increased cell proliferation, invasion, and migration. Conversely, inhibiting these miRNAs by using synthetic antisense miRNA oligonucleotide antimirs reversed these phenotypes, highlighting their clinical potential. pH low insertion peptide (pHLIP) is a promising therapeutic that targets acidic tumor microenvironments and has already proven its specificity in detecting tumors in breast cancer imaging. It is hypothesized that pHLIP reagents conjugated to antimir-888 or antimiR-891a oligonucleotides will allow specific delivery to human PCa tumor cells and effectively reduce miR-888 and miR-891a expression resulting in a block in cancer progression. This will be the first study of its kind to study the effectiveness of pHLIP therapeutics in the context of prostate disease.

METHODS:
pHLIP delivery was optimized using fluorescently labeled empty pHLIP (pHLIP-Cy5) in cultured LNCaP cells grown in media at pH 7.4 or pH 6.0. LNCaP and PC3-ML were then treated with pHLIP antimir-888 or pHLIP antimir-891a at 2uM and 4uM at a pH 6.0. Harvested cells were isolated for RNA (Ambion miRvana kit) and qRT-PCR was used to determine if miRNA expression was suppressed and rescued miRNA target (SMAD4, TIMP2, RBL1) levels.

RESULTS:
Delivery optimization determined that the empty pHLIP-Cy5 reagent at a concentration of 4 μM preferentially entered prostate cancer cells when cultured in media at pH 6.0 compared to pH 7.4 by 3 hours. Treatment of PC3-ML cells with 4 μM of pHLIP-antimiR-888 or pHLIP-antimiR-891a for 3 hours in media at pH 6.0 exhibited significant reduction in miR-888 and miR-891a levels relative to cells treated with scrambled negative control pHLIP-NC67 reagent. However, further validation is needed to determine if pHLIP-antimir suppression of miR-888 and/or miR-891a will also rescue and elevate the miR-888 and 891a downstream targets (ex, prostate tumor suppressors SMAD4, RBL1, and TIMP2) using qRT-PCR and western blot analysis.

CONCLUSION:
pHLIP is a promising novel reagent in PCa and this study showed efficient pHLIP-Cy5 localization in cultured PCa cells at a pH 6.0, mimicking the acidic tumor microenvironment. Delivery of pHLIP conjugated to antimiR-888 or antimiR-891a effectively reduced miRNA expression. Further studies need to be done to determine if these pHLIP antimiRNA reagents against miR-888 cluster member can block tumor growth and metastasis using mouse models. These new therapeutics hold promise to increase patient survival and allow new modalities for PCa treatment.

Abstract Title: An accidental cure: Five-year follow-up of metastatic basal cell carcinoma treated with nivolumab

Investigator: Kanishk Sharma
Co-Investigator(s):
Department(s): Hematology and Oncology, Virginia Oncology Associates

Abstract

Introduction:
Less than 0.1 percent of cutaneous basal cell carcinomas will metastasize, so data for treatment of metastatic basal cell carcinoma (mBCC) is limited. FDA-approved therapies for mBCC include the hedgehog pathway inhibitors (HHI) vismodegib and sonidegib and the recently-approved PD-1 inhibitor cemiplimab. A single case of complete remission of mBCC after immune checkpoint inhibitor(ICI) has been reported, but no long-term results are available. We describe a case of an exceptional responder with mBCC with a complete response to nivolumab (an ICI), who has remained in long-term remission off all therapy.

Case information:
A fifty-seven-year-old white male with a history of multiple localized basal cell carcinomas resected from the sternum, shoulder, and upper back developed right flank pain. On X-rays, lytic bone lesions were found on the right tenth and eleventh ribs. Monoclonal protein studies were negative. CT-guided core biopsy of a rib lesion showed metastatic squamous cell carcinoma. PET scan showed additional bone lesions over the lateral right fifth rib, T1 vertebra, and right sacrum. He began carboplatin and paclitaxel for presumed metastatic non-small cell lung cancer (NSCLC). However, treatment was stopped after cycle #5 due to hospital admission for vomiting and diarrhea. Nivolumab was started as second-line therapy for presumed NSCLC. After eight months, a PET scan showed no hypermetabolic lesions, consistent with a complete response to nivolumab.

A new oncologist reviewed the case and sent the original biopsy sample for genomic testing to verify tissue of origin, which showed a 96% probability that the cancer was mBCC. Nivolumab was continued due to excellent response. After three years of therapy, repeat CT chest/abdomen/pelvis remained negative for malignancy. The patient developed significant diarrhea, and colonoscopy biopsy showed collagenous colitis attributed to nivolumab. Five and a half years after presentation, and two years since stopping Nivolumab, repeat scans remain negative for active disease off all treatment.

Discussion:
At this patient's presentation, ICI was not used to treat patients with mBCC. A few case studies showed mBCC responding to ICI, but this case demonstrates long-term remission that persisted off therapy. PD-ligand-1 (PD-L1) expressed by cancer cells can bind the programmed cell death-1 (PD-1) receptor on T-cells, leading to T-cell inhibition. Basal cell carcinomas bear the highest tumor mutational burden of any human cancer, creating tumor neoantigens recognized by T cells and making tumors more sensitive to ICI. In 2020, pembrolizumab (an ICI) was FDA-approved for treating advanced tumors of any histology with high TMB. The tumor mutational burden for our patient is unknown.

In February 2021, Cemiplimab was approved based on the EMPOWER-BCC 1 trial results, which included only 28 patients with mBCC, showing 21% partial response but no complete responses. Patients maintained their response for at least nine months.

Conclusion:
Our case report shows that ICI can be highly effective against mBCC and raises consideration of a class effect. This report supports ICI therapy as second-line treatment in mBCC or when a patient is intolerant or resistant to HHI treatment.

Abstract Title: Impact of heart failure education on knowledge and comfort of healthcare Staff in a Skilled Nursing Facility

Investigator: Kanishk Sharma
Co-Investigator(s): Dr. Ismail El-Moudden, Healthcare Analytics, and Delivery Science Institute
Department(s): Glennan Center for Geriatrics and Gerontology

Abstract

Introduction:
Approximately 20% of hospital discharges for heart failure(HF) in the United States result in an admission to a skilled nursing facility (SNF). Patients discharged to a SNF with HF are usually older, frailer, and have more significant comorbidities with higher mortality risks than those who go home after hospitalization. 30-day re-hospitalization rates for HF from SNF range from 24% to 43%. A study suggested that Medicare spent $3.39 billion on potentially avoidable SNF hospitalizations.

This project aimed to assess SNF staff's comfort and knowledge in treating HF patients before and after intervention with HF education.

Methods:
Communication between authors and SNF staff was established. A pre-designed and pretested questionnaire analyzed healthcare staff's knowledge regarding HF. The questionnaire also includes demographics like role (CNA, LPN, RN, BSN), age, gender, experience in nursing, and time at SNF. Pretests were conducted in February 2021. The intervention included authors providing HF educational sessions to the SNF staff in March 2021. During the sessions, a pre-recorded video about HF education was played. A one-page summary of AMDA Clinical Program Guidelines for HF was also provided. A post-test was conducted three months after the educational sessions in June 2021 to assess knowledge retention by SNF staff.

All statistical analyses were performed in collaboration with the EVMS Healthcare Analytics and Delivery Science Institute (HADSI) using SAS version 9.4 (SAS Institute, Cary, NC). Descriptive statistics mean or median (interquartile), min, max, standard error, or frequency have been utilized to summarize the data. Kruskal-Wallis One-Way ANOVA on Ranks was conducted to assess the median difference of the scores in comfortable levels before and after the intervention.

Results:
The total number of participants reduced from 73 to 26 in the post-test. The post-test analysis showed that minimum scores went from 40% to 55%. The interquartile range reduced to 10% from 15%. Only 73.97% of participants were very comfortable during the pretest. In comparison, 92.3% felt very comfortable caring for HF patients in the post-test. Most pretest participants were LPNs(46.6%), followed by CNAs(38.36%). Post-test participants consisted of 42.3% LPNs and 57.6% CNAs. Most participants were females in the pretest (94.4%) and post-test (100%). Kruskal-Wallis One-Way ANOVA on Ranks showed a statistically significant difference (P= 0.02689) between participants who were "somewhat comfortable" and "very comfortable" during the post-test.

Conclusion:
Our study showed that a short educational intervention for healthcare staff improved their knowledge and confidence in caring for patients with HF, which can also improve patient outcomes. This type of intervention can easily be standardized across SNFs, helping nurses better prepare and improve the quality and amount of information and care they provide patients.

Further studies need to be conducted to evaluate the impact of HF education on patient outcomes at SNFs. The drawback of this quality improvement intervention included losing participation during the post-test due to the COVID pandemic. The dropout rate was high due to staff turnover and multiple restrictions on meetings at the SNF. Patient outcomes were not collected as part of this QI project but would have been helpful indicators to track. This study shows that if implemented well, an easy educational intervention may help improve the confidence and knowledge of health care workers at SNFs.

Abstract Title: One diagnosis does not rule out another

Investigator: Yuliia Varava
Co-Investigator(s): Samuel Stephenson, M4, Internal Medicine EVMS; Sami Tahhan, professor MD, Internal Medicine; Tyler Nguyen, PGY-1, MD, Internal Medicine; Julie Yi, PGY-1, MD, Internal Medicine
Department(s): Internal Medicine

Abstract

Introduction:
Thromboangiitis obliterans, also known as Buerger disease, is a cannabis and tobacco-induced non-atherosclerotic inflammatory disease typically involving both small and medium sized vessels of the extremities. The disease can lead to multiple manifestations including superficial thrombophlebitis, cold sensitivity/ Raynaud phenomenon, digital ischemia, organ ischemia and arthralgias.

Case description:
A 35-year old cannabis using male, who started tobacco smoking 4 months prior, presented to the emergency department in the summer with a two-week history of severe bilateral finger pain, numbness, and tingling which worsened with cold exposure and improved with rewarming. The pain occurred in random 30 minute episodes in which his fingers would change from black to white and was severe enough to completely immobilize him.

Physical exam showed ulcerations on digits 2, 4, and 5 bilaterally. Vascular studies confirmed critical small vessel disease in these digits but with sparing of his radial and ulnar arteries.

Further workup ruled out autoimmune causes including SLE, Rheumatoid Arthritis, Sjogren's, mixed Connective Tissue Disease, Scleroderma, hypercoagulable disorders, cryoglobulinemia and embolic sources.

We started the patient on amlodipine, sildenafil, and topical nitrates. By hospital day five, he had improved enough to be discharged on the above regimen along with gabapentin and hydrocodone for breakthrough episodes, and the recommendation to never smoke again.

The patient was ultimately diagnosed with Buerger's disease due to fitting clinical diagnostic criteria: age less than 50 years old, recent history of tobacco use, distal extremity ischemia (objectively noted on vascular testing) and exclusion of other potential explanations. We thought that he had secondary cold insensitivity / Raynaud phenomenon which occurs in more than 40 percent of patients with Thromboangiitis Obliterans.

Discussion:
This case is unique in that both the presentation of Buerger's disease and Raynaud's were unusual.
He presented with upper extremity digital ulcers only whereas in Buerger disease lower extremity ulcers occurred in 46 percent, upper extremity ulcers in 28 percent, and ulcers in both upper and lower extremities in 26 percent in one series.

The patient presented with only small vessel involvement of the digits whereas we think of Buerger disease as a condition typically involving both small and medium size vessels.

He presented with a clinical picture of Raynaud's disease during a sweltering summer month and he had involvement of digits 2, 4, and 5 whereas primary Raynaud's phenomenon often spares the little finger and rarely has ulcerations at initial presentation. Nevertheless, his presentation fits Raynaud phenomenon secondary to Thromboangiitis Obliterans.

This case highlights that vasculopathies can present with variable and atypical presentations. It is important to consider atypical presentations and the relationship between two disease processes to avoid anchoring on just one diagnosis.

Conclusion:
Thromboangiitis obliterans can lead to secondary Raynaud phenomenon.

Abstract Title: A foot wound in a well-controlled diabetic patient with a history of Guillain-Barré Syndrome

Investigator: Yuliia Varava
Co-Investigator(s): David Armas, Internal Medicine, Observer; Jennifer Ryal, MD; Julie Yi, PGY-1, Internal Medicine; Tyler Nguyen, PGY-1 Internal Medicine 5.Samuel Stephenson, M4, Internal Medicine
Department(s): Internal Medicine

Abstract

INTRODUCTION:
Guillain-Barré syndrome (GBS) is a rare but serious post-infectious immune-mediated neuropathy. Although GBS has a favorable outcome in >80% of patients, some individuals have long-term complications and functional disability.

CASE INFORMATION:
A 48-year-old male with history of insulin independent type 2 diabetes, GBS, STEMI, tobacco use, and hypertension presented with left-sided foot lesion. On physical exam, he had a fluctuant nodule on the left lateral and plantar aspects of the 5th metatarsal head with hyperkeratotic tissue and circumferential erythema. There was no sensation to light touch, proprioception or pain on the lower extremities bilaterally. Patient appeared unbothered by the foot lesion but upon further questioning recalled that it has gotten more erythematous over the last two days. Past medical history is significant for GBS secondary to gastroenteritis diagnosed in August 2018. Patient was treated with IVIG at that time, but continued to experience chronic unsteady gait and bilateral lower extremity weakness and paresthesia despite treatment. Patient`s labs were notable for HA1c of 5.7% and blood glucose in the 130s. Podiatry was consulted and did a debridement with a local wound care and no plans for fu rther surgical intervention. Patient was started on doxycycline for 7 days due to penicillin allergy for his foot wound.

DISCUSSION:
Residual neuropathy persists long after the acute attack of GBS in 50% of patients. Existing studies emphasize residual motor dysfunction, and residual sensory changes following GBS are infrequently discussed. Our patient with long-term lower extremity sensory deficits secondary to GBS developed a foot infection resembling a neuropathic foot ulcer, despite his diabetes being well controlled. This case highlights the importance of multidisciplinary follow-up of patients with chronic neurologic deficits secondary to GBS, including early recognition of neuropathic foot ulcers.

CONCLUSION:
GBS can lead to the neuropathic foot ulcers and appropriate long term follow up including self foot inspection is needed for its prevention.

Abstract Title: It is Never a Spider Bite

Investigator: Alejandra Vargas
Co-Investigator(s): Alexandra Mari/Infectious Disease; Jairo Norena/internal medicine; Alynna Knaub/internal medicine
Department(s): Sentara Pulmonary, Critical Care, & Sleep Specialists

Abstract

Introduction:
Nonspecific symptoms and exam findings can delay diagnosis and appropriate treatment. We present a patient who initially presented to the emergency department for concern of spider bite-related symptoms. Additional history, physical findings, and laboratory data evaluations led to invasive meningococcal disease (IMD) diagnosis. Although rarely encountered in clinical practice, thanks to routine vaccination, a clinician must remain astute to this diagnosis. An unrecognized case carries severe ramifications for the patient and healthcare workers (HCWs), who may require post-exposure prophylaxis.

Case:
A 30-year-old African American male with a past medical history of alcohol use disorder presented to the emergency department with confusion and severe myalgias several days after sustaining a reported spider bite. The patient was toxic-appearing, diaphoretic, tachycardic, tachypneic, hypoxic, with mottled lower extremities that were cool to touch. Initial labs revealed leukocytosis, thrombocytopenia, acute renal and liver failure, rhabdomyolysis, coagulopathy, and lactic acidosis. Cardiac enzymes were significant for troponin elevation. Empiric antibiotics with bacterial meningitis dosing were started with Vancomycin and Ceftriaxone. Computed tomography of the head was unremarkable; however, chest/abdomen/pelvis images showed bilateral parenchymal opacities, right pleural effusion, and bilateral perinephric stranding. An echocardiogram was significant for a left ventricular ejection fraction of 30% with global hypokinesis.

Overnight, the patient developed worsening nuchal rigidity, diffuse muscle weakness, and progressive bilateral lower extremity retiform purpuric rash with areas of temperature dissociation. He was admitted to the intensive care unit for shock. Due to acute delirium, he required intubation, which revealed an erythematous posterior oropharynx. Cerebrospinal fluid (CSF) from lumbar puncture was notable for severe pleocytosis. PCR of CSF, as well as blood and urine cultures, confirmed Neisseria meningitidis. HCWs exposed to patient's oral secretions received post-exposure prophylaxis.

The suspected spider bite was ultimately determined to be the initial manifestation of purpura fulminans (PF). The patient steadily improved with antibiotics and supportive care. However, after five days, he developed bilateral lower extremity paralysis. Magnetic resonance images of the thoracic and lumbar spines were negative for epidural abscesses, but pelvic images demonstrated myositis in the gluteus maximus and quadratus femoris. Also, the left gluteus had hemorrhagic myonecrosis with subcutaneous cellulitis. After intense physical therapy, the patient recovered some strength in his lower extremities and was discharged to a skilled nursing facility.

Discussion:
Invasive meningococcal disease carries a mortality rate exceeding 10%. Though meningitis is the most common manifestation of meningococcus, its vast and often vague presentations can lead to fatal delays in diagnosis. As many as 12% of cases feature both meningitis and bacteremia syndromes. Some of the atypical findings in our patient included PF, cardiomyopathy, and subsequent myositis despite antibiotic treatment.

As an angioinvasive organism, meningococcus has the potential to rapidly disseminate to all organs including the skin. In patients with IMD, PF mainly occurs in children and adolescents with a prevalence of 5-25% and a mortality rate of 20-70%. Myocarditis is a lesser-known complication of IMD and may be an underrepresented cause of mortality, likely due to the need for invasive biopsies for definitive diagnosis. Our clinical diagnosis is based on the presentation, troponin elevation, and cardiomyopathy. Musculoskeletal sequelae are rare, especially myositis leading to myonecrosis and concurrent cellulitis. While epidural abscesses are of concern, the need to evaluate for myonecrosis as the etiology of neuromuscular deficits is not as well appreciated nor often considered.

Conclusion:
This case highlights the classic findings of meningococcus including meningitis, purpura fulminans, and multiple organ dysfunction, as well as rare features including cardiomyopathy, myositis, and myonecrosis.
This case highlights the classic findings of meningococcus including meningitis, purpura fulminans, and multiple organ dysfunction, as well as rare features including cardiomyopathy, myositis, and myonecrosis. In addition, our case serves as a reminder of the potential for the increasing incidence of diseases once more obscure, due to changes in vaccine acceptance, and the importance of physicians being vigilant in differential diagnosis so that prompt treatment can be initiated.

Abstract Title: When Blood is Thicker than Blood

Investigator: Alejandra Vargas
Co-Investigator(s): Jairo Norena, Internal Medicine
Department(s): Critical Care Medicine, Internal Medicine, Pulmonary Medicine

Abstract

Introduction:
Hyperviscosity syndrome (HVS) refers to a collection of symptoms resulting from decreased blood flow due to either an abnormal shape of the red blood cells (RBCs) or a pathologic increase in serum proteins, white blood cells (WBCs), or platelets. This oncological emergency can cause multiple organ damage if not treated immediately. We present a challenging case of hyperviscosity syndrome due to hyperleukocytosis complicated by metabolic acidosis and non-ST-elevation myocardial infarction (NSTEMI).

Case:
A 61-year-old female with a history of myeloproliferative disease presented to the emergency department with a 4-day history of generalized abdominal pain, vomiting, acute onset of lightheadedness, tunnel vision, and chest discomfort on deep inspiration. Physical exam revealed epigastric distention and tenderness. Laboratory parameters showed WBCs of 140.7 K/uL, hemoglobin (Hgb) of 7.6 g/dL, platelets of 23 K/uL, and normal levels of troponin, D-dimer, fibrinogen, uric acid, calcium, phosphorus, potassium, and lactic acid. In addition to empiric infection coverage with vancomycin and piperacillin/tazobactam, hydroxyurea was given for hyperleukocytosis, allopurinol was given for tumor lysis syndrome prevention, and one unit of platelets was transfused. A bone marrow biopsy was suggested in consultation with Heme/Oncology, but the patient declined.

On the third day of admission, the patient developed hypotension, near syncope, shortness of breath, headache, and worsening chest pain, requiring admission to the intensive care unit for vasopressors and leukapheresis. An electrocardiogram showed ST depression in V4 - V5; laboratory results showed Hgb of 5.3 g/dL, WBCs of 231 k/uL, platelets of 34 k/uL, troponin of 217 ng/L, lactic acid of 12 mmol/L, and metabolic acidosis. The patient's clinical status rapidly deteriorated, leading to obtundation and agonal breathing necessitating emergent intubation. Due to concerns about anemia-induced NSTEMI and possible hemorrhagic stroke, the patient received a unit of red blood cells and a unit of platelets. Leukapheresis was initiated shortly after.

Unfortunately, despite leukapheresis, repeat labs revealed worsening multiorgan failure with increases of WBC to 368.6 k/uL, creatinine to 2.1 mg/dL, alanine aminotransferase to 619 U/L, aspartate aminotransferase to 817 U/L, alkaline phosphatase to 137 U/L, phosphorus to 9.8 mg/dL, and lactic acid to 21.7 mmol/L. Her Hgb and calcium decreased to 4.3 g/dL and 6.9 mg/dL, respectively, and her pH was persistently around 6.80. Ultimately, hyperviscosity syndrome lead to the patient's demise.

Discussion:
Hyperviscosity syndrome is characterized by a reduced flow of whole blood in the postcapillary venule system, which may result from the deformity of red blood cells (sickle cell disease and spherocytosis) or pathological elevations of blood components, either cellular (red blood cells, white blood cells, platelets) or acellular (serum proteins).

A high level of clinical suspicion is required to diagnose HVS based on the history and physical examination. The classic triad of HVS symptoms includes mucosal bleeding, visual changes, and neurological problems. HVS can lead to ischemia and thrombosis of the cerebral, pulmonary, cardiac, and renal circulations, ultimately leading to multiorgan failure if left untreated. Plasmapheresis is considered the mainstay of treatment until induction chemotherapy can be administered safely. The challenge in treatment arises with consideration of transfusion of blood products in the setting of anemia and thrombocytopenia. Clinicians should resist the urge to transfuse due to the usual threshold values and only transfuse if there is a second clinical indication, such as anemia-induced NSTEMI, as blood products typically increase viscosity and worsen symptoms.

Conclusion:
Thromboembolic events, myocardial infarctions, and life-threatening microvascular obstruction that result in multiple organ failure can all be prevented when hyperviscosity syndrome is treated promptly. The treatment consists of supportive therapy, plasma exchange, and chemotherapy. The present report emphasizes the importance of starting plasmapheresis as soon as possible to avoid fatal complications.

Abstract Title: Acute Aortic Injury: Signs and Symptoms and subsequent grading

Investigator: Todd Yeates
Co-Investigator(s): Thomas Michael Pender, Radiology
Department(s): Radiology

Abstract
Acute aortic injury is an unfortunately common outcome in trauma with a significant risk of mortality.

Herein we discuss the case of a 36 year old male, found down following a pedestrian versus motor vehicle incident, evaluated with a noncontrast CT and later CTA of the chest showing a grade III thoracic aortic injury. In this case, the outcome was thankfully improved by detection of the injury through associated peri-aortic findings on a noncontrast CT scan of the chest, though this is not always possible.

Herein we detail the significance of blunt trauma aortic injury, subsequent grading of these injuries, and their clinical significance.

Abstract Title: Patient Characteristics and Response to Biologic Therapy in Moderate to Severe Difficult to Control Pediatric Asthma

Investigator: Sarah Abernathy
Co-Investigator(s): Phillip Mendez, DO, MPH, Department of Pediatrics; Lindsey Moore, DO, Dept of Pediatrics Division of Allergy and Immunology; Maripaz Morales, MD, Dept of Pediatrics Division of Allergy and Immunology
Department(s): Division of Pediatric Allergy and Immunology

Abstract

Background:
A subset of patients with moderate to severe asthma remain poorly controlled despite maximizing the standard treatment of high-dose inhaled steroids with or without long-acting beta-agonists. Biologic therapies (Omalizumab, Mepolizumab, and Dupilumab) offer a new opportunity as add-on asthma controllers and have been approved for use in patients 6-12 years and older who are refractory to standard treatment. However, studies on their real-world application and outcomes among the pediatric population are lacking. This study aims to assess the characteristics of our pediatric population that needed biologic therapy, their response to prescribed biologics, and reasons for discontinued therapy.

Methods:
A retrospective chart review of patients placed on biologic therapy at the Allergy, Asthma, & Immunology (AAI) Clinic at CHKD was performed. Patient records were reviewed for demographics, spirometry measures (FEV1), quality of life measures, and number of ED visits and asthma exacerbations from one year prior to the start of therapy to approximately one year following. These measures were compared using two-sided statistical analyses and performed using SPSS.26 data software.

Results:
54 patients with moderate or severe asthma were reviewed. Most patients had severe asthma (85%) and the mean age was 11 years (SD 3.11). 74.1% of patients were Black or African American, 24.1% were White, and 1.9% were unreported. There was an increasing trend in the quality of life measures in the 12 months post-therapy ($p=0.024$ in moderate asthmatics, $p=<0.001$ in severe asthmatics). There was no significant change reported in spirometry measures. The number of asthma exacerbations and ED visits decreased significantly in the 12 months post-therapy, ($p=0.002$; $p=0.003$, respectively). Of the 54 patients, 10 discontinued therapy, 6 of which failed to respond to therapy and 1 experienced an adverse reaction.

Conclusion:
The results demonstrate the benefit of biologic therapy in moderate to severe pediatric asthmatics as reflected by the improvement in quality of life measures, and fewer ED visits/asthma exacerbations experienced in the 12 months post-therapy. Limitations to this study include inconsistent patient follow-ups at the AAI, limitations during COVID, and patient compliance. Future research may include comparing outcomes between the different biologic therapies available.

Abstract Title: Impact of Telemedicine on Care of Patients Living with HIV in the Hampton Roads Area

Investigator: Kripa Ahuja
Co-Investigator(s): Margaret Baumgarten MD, EVMS Family Medicine; Fang Fang PhD, HADSI
Department(s): Internal Medicine

Abstract

Introduction:
Since March 2020, telemedicine visits have been increasingly important to limit the spread of the COVID pandemic. Some individuals with HIV have significant barriers to care that may prevent a full spectrum of care with telemedicine visits. They may lack effective equipment, privacy, or transportation for laboratory tests and medication pick-up. According to the AIDSVu website, 7,331 individuals were living with HIV in the Hampton Roads area of Virginia as of 2019.1 Similar to national data, a majority of people with HIV in the Hampton Roads area are faced with healthcare disparities. Black and Hispanic/Latinx individuals were more likely to be diagnosed with HIV, despite representing a smaller proportion of the general population. In addition, Black and Hispanic/Latinx populations were less likely to achieve viral load suppression and more likely to be diagnosed at a late stage of HIV than white populations.2 Compared to the general US population, individuals living in Hampton Roads had a lower median household income and a higher percentage living in poverty1. The impact of these healthcare disparities on access to telemedicine visits is less clear.

Methods:
We performed a needs assessment to further understand the necessities that the HIV population in the Hampton Roads area requires. The assessment included a literature review of telemedicine's impacts on various aspects of medical care, including compliance and adherence to prescriptions, laboratory testing, and follow-up appointments.

Results:
From our needs assessment, we were able to (1) Determine inclusion and exclusion criteria for our study population, (2) Determine relevant data points to be collected from our study population.

Conclusion/Future Directions:
Though the COVID pandemic is not at its height, the shift to telemedicine remains ever-present and continues to change the course of future medicine. The HIV population in the Hampton Roads area is an underserved population at risk of receiving inadequate care, especially with virtual medicine. More large-scale studies are needed to fully understand the changing landscape of telemedicine and the impact that telemedicine has on vulnerable populations.

Abstract Title: Unanticipated Platelet Function Fluctuations Occur During the First 8 Hours after Neurointerventional Procedures in Patients Receiving Dual Anti-Platelet Therapy

Investigator: Travis Allen
Co-Investigator(s): David Loy, MD, PhD, Dept. of Radiology and Medical Imaging / Bon Secours St. Mary's Hospital; Matthew Austin, MD, Dept of Radiology and Medical Imaging / Bon Secours St. Mary's Hospital
Department(s): Neurointerventional Radiology - UVA/Bon Secours Mercy

Abstract

Introduction:
Antiplatelet agents are administered before and after neuroendovascular surgery to minimize implant-associated thromboembolic events. Dual antiplatelet therapy (DAPT) uses aspirin plus P2Y12 receptor inhibitors: clopidogrel, ticagrelor, or prasugrel. Effects are quantified in P2Y12 reactivity units (PRU) and aspirin reactivity units (ARU) by the point -of-care assay, Accumetrics VerifyNow. We hypothesized that intraoperative events such as anesthesia may affect platelet inhibition, increasing the risk of unanticipated ischemic events in the early postoperative period.

Methods:
This retrospective study was approved by the institutional review board. 50 patients who underwent VerifyNow testing preoperatively and within 12 hours postoperatively after placement of cervical or intracranial stents at a single institution (January 1, 2018 - May 25, 2021) were included. PRU values > 194 and ARU values> 550 were considered subtherapeutic. Anesthetic agents, clopidogrel responsiveness, platelet count, liver function, procedure type and length, NIH stroke scale scores, and demographics were compared to perioperative platelet inhibition values.

Results:
Our results indicate that P2Y12 inhibition is likely affected by intraoperative events. Approximately 25% of patients exhibited marginal (170-193) or subtherapeutic (>194) PRU values during the first 8 hours following neuroendovascular procedures. The greatest variation occurred in the ticagrelor group (PRU median change 84) and was more likely to occur with reduced doses of both ticagrelor and clopidogrel. A single prasugrel patient (clopidogrel non-responder) exhibited the greatest absolute change (156 to 316). ARU variations were less pronounced, suggesting that perioperative aspirin-mediated platelet inhibition is more resilient.

Conclusion:
In conclusion, patients undergoing elective neuroendovascular procedures may be at risk for thromboembolic ischemic complications during the first 8 hours postoperatively due to shifts in P2Y12-mediated platelet inhibition. ARU values were less affected, supporting the use of DAPT as an ongoing clinical standard of care.

Abstract Title: Disparities in COVID-19 Vaccine Uptake among Filipino Americans in Eastern Virginia: Findings from a Mixed Method Study

Investigator: Jaime Luis Almirante
Co-Investigator(s): Cynthia C. Romero, M.D., Director of the M. Foscue Brock Institute for Community and Global Health; Marc Franco T. Nepomuceno, M.S.; Hongyun "Tracy" Fu, Ph.D., Department of Pediatrics: Community Health and Research
Department(s): Department of Pediatrics: Community Health and Research

Abstract

Introduction:
Although it is widely acknowledged that COVID-19 vaccine uptake is crucial in reducing the strain on healthcare systems and increasing herd immunity, results from a range of studies revealed high levels of vaccine hesitancy in the United States, particularly among racial and ethnic minorities. However, little is known about the patterns and factors related to the uptake of the COVID-19 vaccine in Filipino Americans (FAs) in the Eastern Virginia region, despite this region being home to around 30,000 FAs (the largest Filipino American community in the United States). This study filled the gap in literature by utilizing a mixed method study that was conducted in April/August 2022 in Hampton Roads and the Eastern Shore of Virginia.

Methods:
The study integrated an online quantitative survey and in-depth interviews with Filipino key informants who were recruited from a range of social media channels and in-person events via the existing AAPI networks in Eastern Virginia, following three sampling criteria: 1) being decedents of Asian and Pacific Islanders; 2) ages 18-85 years, and 3) residents of Hampton Roads and the Eastern Shore. Survey data from a subsample of FAs (N=281) was analyzed using descriptive statistics and multivariable logistic regression. Key informants (N=25) were recruited via snowball sampling for virtual semi-structured interviews (30-45 minutes) via Zoom. Guided by the grounded theory and the Creswell method, semantic analysis was conducted to identify key themes.

Results:
The vast majority (93%, 262/281) of FAs received at least one COVID-19 test, among which 16% (41/262) ever tested positive. More than half (66%, 184/281) were fully vaccinated, among which 74% ever received a booster shot (137/184). The odds of receiving a vaccine were lower among females (AOR: 0.07, 95% CI: 0.02-0.22), who received Medicare (AOR: 0.10, 95% CI: 0.04-0.25) and Medicaid (AOR: 0.24, 95% CI: 0.11-0.55); and were higher among those with a college degree (AOR: 3.60, 95% CI: 1.25-10.40). Results of the in-depth interviews indicated that key barriers to vaccine uptake included concerns over the side effects and a lack of confidence about the effectiveness of COVID vaccines.

Conclusions:
Findings revealed significant disparities in COVID-19 vaccine uptake across sub-groups of FAs, highlighting the need to target the female and the socioeconomically disadvantaged FAs in Eastern Virginia.

Abstract Title: A Case Series of 20 Patients with Comorbid Hidradenitis Suppurativa (HS) and Human Immunodeficiency Virus (HIV): a retrospective single-institution chart review

Investigator: Sarah Alnaif
Co-Investigator(s): Ryan Saal, BS, School of Medicine; Joshua Edwards, MPH, Community-Engaged Learning; Catherine Derber, MD, Department of Infection Disease
Department(s): Department of Dermatology

Abstract

Introduction:
Among patients with human immunodeficiency virus (HIV), there is a higher incidence and later age of onset of hidradenitis suppurativa (HS) compared to patients without HIV. However, the relationship between HS severity and HIV control has not been formally established.

Methods:
A retrospective chart review was performed of patients with co-morbid HIV and HS who were actively managed for both chronic diseases at a single institution between 01/01/2010 and 11/01/2021. The following data were gathered from the relevant medical visits: demographic variables, Hurley Stage, dermatologic exam, subjective assessment of HS flaring, CD4+ count, percent CD4+ lymphocytes, and viral load.

Results:
A total of 20 patients were identified with comorbid HS and HIV with at least three clinical visits within the healthcare system for these two conditions. The average age of first visit of 35.3 ± 9.08 years. Among this cohort, a majority of patients were diagnosed with HIV first, with an average time between diagnoses of 10.20 ± 7.59 years. There was a female predominance (75%), as well as Black/African American race (85%). The average BMI noted across all encounters was 31.92. The most noted comorbid conditions were depression, hypertension, obesity, hyperlipidemia, acne, generalized anxiety disorder, anemia, diabetes mellitus, and polycystic ovary syndrome. In the dermatology encounters, patients' HS was described primarily as Hurley stage II HS (61.9%), followed by stage I (26.2%) and stage III (10.7%). In 69% of the dermatology encounters, patients' HS were noted as flared, indicating a more acute state of disease. The sites of HS involvement were the upper extremities (60.5%), lower extremities (35.8%), trunk (19.8%), neck (8.6%), and head (4.9%). The average viral load, CD4+ count, and percent CD4+ lymphocytes across the study period were 20,421.6, 801.91, and 35.31%, respectively. There was a wide range in the use of treatments for both diseases.

Conclusion:
There have been rare instances of a descriptive analysis examining patients treated for both HS and HIV. However, the relationship between HS severity and HIV control remains unclear. In both HS and HIV, there are elements of common pathogenesis, including elevation of IL-1, IL-6, IL-8, IL-10, and TNF-a. Further, comorbidities common to HIV often correlate with HS severity (e.g., metabolic syndrome). This study aims to further describe and categorize patients with comorbid HS and HIV. Initial analysis suggests there was not a statistical relationship identified between common markers of HIV control and severity HS Hurley Stages, but further analysis is merited to elucidate this relationship.

Abstract Title: CQI Finding methods to improve health programs to increase recruitment of men

Investigator: Harshit Amin
Co-Investigator(s): Mady Wright, EVMS MS2\Summer; Scholars; Amy Paulson, EVMS Department of Community Health/Summer Scholars; Dr. Margaret Baumgarten, Ghent Family Medicine\Summer Scholars
Department(s): EVMS Department of Community Health

Abstract

Introduction:
There is a paradox in men's health, with men being a population who are less likely to seek ways to improve their health while also being more likely to face negative health outcomes. This CQI project focuses on find how health programs in the Norfolk and Portsmouth regions can be best reprogrammed to recruit and retain male participation.

Methods:
Key informant interviews were conducted with adult male (n=117) patients from EVMS Ghent and Portsmouth Family Medicine both in person and over the phone from a larger database of patients (n=1739) with chronic conditions over the past 6 months. The data was stored in Qualtrics and Redcap, which was then further analyzed using excel and SPSS.

Results:
Overall, 117 patients were surveyed in total, with 40 recruited in person from Portsmouth Family Medicine, 9 in person from Ghent Family Medicine, and 68 informants from over the phone. Of these patients, 91.22% of participants were self-reported as healthy or better, although 91% of the participants in the phone surveys were listed as having chronic conditions. In addition, around 51% of participants expressed interest in different men's health programs with only 37% stating they would be likely to enroll in these programs. Relating to marketing materials, men stated a small preference for testimonials (40), but statistics (28) and before/after pictures (32) also being important. Key themes of barriers related to enrollment include fear of healthcare and physicians, rigid gender roles and expectations to be strong and provide, and finally a resistance to change and a dislike for being told what to do with regards to their health.

Conclusion:
With most key informant interviews coming from a database of individuals with chronic conditions, over 91% informants of them self-reporting as healthy implies a potential disconnect between the patient's actual health and how they may perceive it. This disconnect can potentially be improved through changes in patient-physician communication and male health education. The next step in the PDSA cycle for this CQI involves acting to design new health programs which can incorporate male participant preferences being mindful of barriers they may face.

Abstract Title: A Quality Improvement Project titled: Are we providing purposeful practice? - An analysis of formative weekly quizzes for specific themes identified in summative post exam reviews (AY 2021-2022)

Investigator: Elsie Amoako-Kissi
Co-Investigator(s): Dr. Mily Kannarkat: EVMS Department of Internal Medicine
Department(s): EVMS Department of Internal Medicine

Abstract

Introduction:
A committee reviews exam performance by EVMS MD students on individual multiple-choice questions. Student feedback and poor item performance (questions for which <50% of students answered correctly, and which have a discrimination index less than 0.10) is reviewed together by the committee. During these post exam review processes, certain types of questions were consistently flagged for review by this committee. These types of questions include:

1. Questions including 'most likely' (and its equivalents)
2. Questions including a clinical vignette (description of a patient scenario)
3. Questions including a graph, table or picture
4. Questions of higher order format (requiring more than a recall of facts)

United States Medical Licensing Examinations (USMLE) and EVMS module exams are utilized as summative assessments and are tied to EVMS MD Program Outcomes related to medical knowledge. These types of questions are routinely utilized on these exams to assess for higher level understanding and integration of knowledge. Therefore, it is important to provide formative opportunities for purposeful practice and self-assessment on these types of questions.

Methods:
Location
All parts of the project were conducted online using Zoom video conferencing and Microsoft Excel Spreadsheets.

Data collection
All multiple-choice questions (483 total) from 21 mandatory and 3 optional weekly quizzes administered to the MD class of 2025 during their M1 year (AY 2021-22) were collated into a pdf. Access to these same quizzes in Blackboard was also available for comparison. A master spreadsheet (data table) was then developed with columns corresponding to the 4 types of questions identified in post exam review. A definition and specific inclusion criteria for each of the columns was agreed upon. Each question was reviewed at a minimum of 3 times to ensure consistent categorization and classification. Based on the definitions, questions that met the inclusion criteria were entered into the corresponding column.

Results:
All weekly quizzes administered in the first year of medical school for AY21-22 contained a majority of first order questions. Zero percent of the total number of questions in the Human Structure module and only twelve percent of the total number of questions in the Skin, Muscle and Bone module required interpretation of a graph, table, or image. In every module, weekly quizzes included both questions containing a clinical vignette and questions including "most likely" (or its equivalent) in the lead in of the multiple-choice question stem. However, these questions did not necessarily require interpretation of details from the clinical vignette or stem in order to answer the question correctly.

Conclusion:
Analysis of these weekly quizzes demonstrated a potential gap between opportunities for formative practice and summative assessment of the specific types of questions that have been identified in the post exam review. Use of first order questions, primarily fact-recall questions, do not challenge students to strive for a high level of understanding and integration of knowledge. Interestingly, there were disproportionately low number of questions that required interpretation of an image, table, or graph even when module content could lend itself well to the inclusion and expectation of interpreting images. Additionally, although there was inclusion of the "most likely" phrase in the lead-in of questions included on weekly quizzes, these questions did not consistently require prioritization of information to answer the question correctly. Moving forward, this feedback will be provided to faculty and educational leadership in order to explore opportunities to increase formal practice on these types of questions.

Abstract Title: A Quality Improvement Project titled: Are we providing purposeful practice? - An analysis of formative weekly quizzes for specific themes identified in summative post exam reviews (AY 2021-2022)

Investigator: Elsie Amoako-Kissi
Co-Investigator(s): Dr. Mily Kannarkat, EVMS Office of Medical Education/ Department of Internal Medicine
Department(s): EVMS Office of Medical Education/ Department of Internal Medicine

Abstract

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Abstract Title: Investigation of ferroptotic mechanism of IL-13 induced changes in cell differentiation patterns of human airway epithelial cells in air liquid interface, as a model of asthmatic airway remodeling.

Investigator: Mary Anand
Co-Investigator(s): Jinming Zhao, Environmental and Occupational Health, Graduate School of Public Health, University of Pittsburgh. University of Pittsburgh Asthma and Environmental Lung Health Institute. Sally Wenzel, Environmental and Occupational Health, Graduate School of Public Health, University of Pittsburgh. University of Pittsburgh Asthma and Environmental Lung Health Institute. Kazuhiro Yamada, Department of Respiratory Medicine, Osaka Metropolitan University Graduate School of Medicine, Japan. John Trudeau, Department of Environmental and Occupational Health, Graduate School of Public Health, University of Pittsburgh.
Department(s): Environmental and Occupational Health, Graduate School of Public Health, Asthma and Environmental Lung Health Institute, University of Pittsburgh

Abstract

Introduction:
Asthma is a chronic airway disease characterized by bronchodilator responsive airway obstruction. In most asthma patients, excessive Type-2 inflammation involving IL-13 is prominent. Uncontrolled asthma is associated with epithelial remodeling consisting of goblet cell hyperplasia and decreased relative numbers of ciliated epithelial cells. This impairs mucociliary clearance and worsens airway obstruction. The mechanisms of remodeling are not fully understood, but a recently identified form of programmed cell death called ferroptosis may be integral. Ferroptosis is triggered by peroxidation of polyunsaturated fatty acids, conjugated to phosphatidylethanolamine by the 15 lipoxygenase (15LO1) enzyme. Ferroptosis is believed to be excessive in asthma with Type-2 inflammation as 15LO1 is highly expressed in the airway epithelial cells of these patients. Ferrostatin-1 (Fer-1) is an antioxidant inhibitor of ferroptosis. Basal cells are progenitors of goblet cells and ciliated cells, and are identified by cytokeratin 5 (KRT5). In chronic rhinosinusitis, a condition strongly associated with Type-2 inflammation, our lab recently reported high KRT5 and 15LO1 in nasal airway epithelial cells, suggesting a link between human airway epithelial cell (HAEC) differentiation and ferroptosis. SAM pointed domain-centering ETS transcription factor (SPDEF) identifies goblet cells, while acetylated a-tubulin is a marker of ciliated epithelial cells. We hypothesized that IL-13 impacts HAEC differentiation through activation of ferroptotic pathways, and Fer-1 counteracts the effects of IL-13. Specifically, we hypothesized that IL-13 stimulation of HAECs would increase 15LO1, KRT5 and SPDEF and decrease acetylated a-tubulin and these effects would be counteracted by Fer-1. We hypothesized early (less well) differentiated HAECs would be more impacted by IL-13 and Fer-1 than more mature, well differentiated HAECs.

Methods:
HAECs were collected from bronchoscopic brushings of a healthy volunteer. The study was approved by the University of Pittsburgh Institutional Review Board and the participants gave informed consent. HAECs were cultured in air-liquid interface (ALI). HAECs were subjected to three conditions: IL-13 (10 ng/mL), IL-13 (10 ng/mL) + Fer-1 (1 μM), and No treatment (NT). Early differentiated HAECs were subjected to treatment conditions on day 0 of ALI culture and were treated every 48 hours until harvest on day 8 of ALI. Mature differentiated HAECs were subjected to treatment conditions beginning on day 15 of ALI culture and were treated every 48 hours until time-course harvests on treatment days 0, 1, 3, 7, 10, and 13 (treatment day 13 harvested cells had 28 total days in ALI). At harvest, HAECs were lysed, proteins separated by gel electrophoresis and 15LO1, KRT5, SPDEF, and acetylated a-tubulin proteins analyzed by Western blot, indexed to GAPDH.

Results:
In early differentiation HAECs, IL-13 increased 15LO1 (~500% > NT), and SPDEF (~100% > NT), whereas it decreased KRT5 (~50% < NT) and acetylated a-tubulin (~25% < NT). In all cases, Fer-1 partially or fully prevented the effects of IL-13, yielding expression levels similar to NT. In more fully differentiated HAECs, IL-13 increased 15LO1 (mean ~400% > NT) at all time points. SPDEF was not measurable at treatment days 0, 1, and 3 but at treatment days 7, 10, and 13 SPDEF was increased by IL-13 (mean ~10% > NT). IL-13 decreased KRT5 (mean ~100% < NT) and acetylated a-tubulin (mean ~100% <NT) at all time points. Fer-1 did not prevent the effects of IL-13 on 15LO1 or SPDEF but it partially prevented the effects of IL-13 on KRT5 and acetylated a-tubulin.

Conclusion:
In contrast to our hypothesis, IL-13 decreases KRT5 expression, suggesting loss of basal cells. Despite this, goblet cells (represented by SPDEF) increased, suggesting that the increase in goblet cell differentiation may explain the loss of basal cells. IL-13 skews the HAECs towards differentiation of goblet cells and away from ciliated cells (represented by acetylated a-tubulin). In early differentiated HAECs, inhibition of ferroptosis prevents these changes but in more mature cells, the Fer-1 effect is modest or absent. The association of ferroptosis and IL-13 induced changes in HAEC differentiation requires additional study.

Abstract Title: Impact of Statin Usage and Intensity on Patient Reported Outcome Measures Following Arthroscopic Rotator Cuff Repair Surgery

Investigator: Serge Andreou
Co-Investigator(s): Carlo Del Donno, MD Class of 2025 Amanda Firoved, Jordan-Young Institute Research Coordinator Justin Griffin, MD Jordan-Young Institute Assistant Professor
Department(s): Jordan-Young Institute (Orthopedic Surgery)

Abstract

INTRODUCTION:
Statins are very commonly prescribed for treatment of dyslipidemias and prevention of atherosclerotic cardiovascular disease. Type and dosage of statin classifies them into low, moderate and high intensity based on their lipid-lowering effects. While Statins are generally safe and efficacious drugs, they have been known to have effects on soft tissue such as muscle toxicity which tend to scale with dose and intensity of statins. Studies following Rotator Cuff Repairs (RCR's) have shown either no effect or even a positive effect of Statins on postoperative markers of success, most notably revision surgery rates. Only one low-powered study to date has been performed to evaluate the effect of statin usage on Patient Recorded Outcome Measures (PROMs), in which no difference was found. It is theorized that the antifibrotic effects of statins that lead to tendinopathy may actually protect muscles from common complications such as atrophy, fibrosis, and fatty infiltration following RCR. This study aims to investigate if postoperative functional outcomes following RCR with statin use is improved as compared to RCR without statin use. Additionally, the purpose is to identify if the strength of statin is a factor associated with improved postoperative functional outcomes.

METHODS:
The study was a retrospective survey study (# 20-07-EX-0134). Participants included in this study, N=324, underwent arthroscopic rotator cuff repair by Dr. Bonner or Dr. Griffin between January 1, 2015 and December 31, 2019. Potential participants were contacted via email and/or through the mail. The potential participants were provided informed consent. Once consent was signed, the participants completed PROMs (Visual Analog Scale for Pain (VAS), Simple Shoulder Test (SST), EQ-5D-5L, and American Society of Shoulder and Elbow Surgeons Score (ASES). Surgical information and medical history including Statin relevance were collected via chart review.

Patients were divided into four groups: presence of Statin Usage and dyslipidemia (Group 1), statin usage with normal range lipids (Group 2), no statin usage with dyslipidemia (Group 3) and no statin usage and normal range lipids (Group 4). There were 81 that qualified for Group 1, 45 in Group 2, 127 in Group 3 and 71 in Group 4. In the second analysis, patients from Groups 1 & 3 were subdivided into further groups: usage of low intensity statin (Group 1a), usage of moderate intensity statin (Group 2a) and usage of High Intensity Statin (Group 3a). PROMs and health variables were compared and statistically analyzed to determine any significant difference between the groups. PROMS outcomes, Age, sex, comorbidities, and tear sizes were used as the dependent variables. Multivariant analysis of variance (MANOVA) via SPSS Statistics for Windows, Version 27.0 (SPSS Inc, Chicago, Ill., USA) was utilized for all statistical analysis.

RESULTS:
For the first analysis comparing groups 1-4, Pillar's trace showed no significant difference between groups (V=.035, F (5,15)= .745, p =.739). For the second analysis comparing groups 1-3, Pillar's trace also showed no significant difference between groups (V=.058, F (5,10)= .715, p =.710). Means of dependent variables and p values can be seen for the first analysis in table 1 and can be seen for the second analysis in table 2.

CONCLUSION:
Neither statin usage nor intensity were shown to significantly impact patient reported outcome measures following arthroscopic rotator cuff repair regardless of presence or absence of dyslipidemia. All groups did extremely well regarding their post-operative scores. Statin usage following arthroscopic rotator cuff repair does not affect patient reported outcome measures, further research is necessary to evaluate the benefits of perioperative statin therapy for all patients undergoing arthroscopic rotator cuff repair.

Abstract Title: Methotrexate-induced Acute Leukoencephalopathy in Adult Chronic Myeloid Leukemia. From physiopathology to medical recommendations perspective.

Investigator: Fatima Arif
Co-Investigator(s): Randa Eldosougi, MD Class of 2026
Department(s): Department of Pathology and Anatomy

Abstract

Introduction:
Methotrexate (MTX) is a disease-modifying antirheumatic drug where it exerts anti-inflammatory effects at lower doses as compared to its anti-proliferative chemotherapy effects used in patients with hematologic malignancies. Intrathecal MTX in pediatric, adolescent, and adult can present with adverse side effects such as symptoms of focal neurological deficits (FNDs), confusion, and even seizures. MTX-induced Leukoencephalopathy (LE) can be acute and reversible or lead to irreversible chronic long-term FNDs due severe extensive neural damage. We discuss a case of a patient with underlying chronic myeloid leukemia who developed acute neurological symptoms post intrathecal MTX administration. It is important to consider a systematic medical imaging (magnetic resonance imaging, MRI) in patients with leukemia's to monitor MTX-related acute neurotoxicity vs. recurrence of malignancy

Case Report:
A 60-year-old female with a past medical history of chronic myeloid leukemia (CML) presenting with acute lymphoid blast crisis of CML under treatment with dasatinib. The patient was hospitalized and received intrathecal MTX infusion without immediate complications and underwent a second dose of intrathecal MTX with dexamethasone the following day. Nine days after, the patient had an episode of headaches (8/ 10), which failed to subside with over-the-counter analgesics. The headaches were associated with intermittent episodes of arterial hypertension, non-fluent speech, and bradypsychia. The patient was afebrile during these episodes.

On physical examination, the patient was awake, oriented, with isochoric and reactive

pupils, no diplopia, and with conserved overall cranial nerve function. Language was preserved with no motor or sensory deficits. Coordination was preserved and no meningeal signs.

A head computed tomography and cerebral spinal fluid (CSF) sample from a lumbar puncture were normal. The initial differential diagnosis was posterior reversible encephalopathy syndrome (PRES). An MRI with gadolinium revealed confluent enhancing fluid-attenuated inversion recovery hyperintensity in the frontal, left parieto-occipital regions, and semioval centers. There was no evidence of restricted diffusion, midline shift or mass effect. The transient LE findings lead to progressive multifocal leukoencephalopathy (PML) as a probable diagnosis. Repeat CSF analysis was normal and JC virus PCR was negative. MTX-induced LE was the final diagnosis and MTX therapy was suspended. A follow-up MRI of the brain showed a decrease in hyperintense lesions.

Discussion:
Acute MTX-induced neurotoxicity is theorized to be due to its effects of decreasing adenosine breakdown, causing adenosine-induced vasodilation, and subacute, chronic toxicity due to increasing cerebrospinal fluid levels of homocysteine. Homocysteine is metabolized into homocysteine acid and cysteine sulfonic acid which causes seizures and excitotoxic neuronal cell death, causing direct toxicity to the vascular endothelium. Intrathecal administration of MTX is associated with the highest risk of acute LE versus high-dose intravenous (IV) administration. IV MTX mediated LE is dose-dependent with the development of acute LE in 3-15% of cases with a recurrence rate of 10-56% with continued therapy.

MTX-induced LE on neuroimaging shows hyperintensity signals in the periventricular white matter, specifically in the centrum semiovale. Periventricular neurons adjacent to germinal matrix layers in the head and tail of the caudate nucleus, as well as neuronal groups in the medial and lateral septum, the cingulate, frontal, and parietal neocortices, thalamus, and hippocampus are consistently vulnerable to hypoxic/ischemic degeneration and damage due to excitotoxic action of N-methyl aspartate (NMA). This is partly due to the elevated number of NMDA receptors seen in these areas, rendering these neuronal cell populations sensitive to excitotoxicity.
Currently, there is no widely established protocol in place to ensure that patients receiving intrathecal or IV MTX are monitored through magnetic resonance imaging. Imaging is usually ordered in response to new neurologic symptoms, however, continued monitoring starting at the time of treatment is imperative to prevent irreversible neurologic deficits in patients who may present asymptomatic, or with nonspecific symptoms.

Abstract Title: Epidemiology of Track and Field and Running-Related Injuries Presenting to the Emergency Department from 2012 to 2021

Investigator: Fatima Arif
Co-Investigator(s): Mohan Pant, PhD, Associate Professor, Master of Public Health Program; Haad Arif, University of California Riverside/Class of 2025
Department(s): Eisenhower Desert Orthopedic Center, Rancho Mirage, CA

Abstract

Background:
Track and Field and Running-related injuries comprise 0.84 per 1000 injuries amongst high school athletes alone. This current study aims to update trends pertaining to track and field and running-related injuries across all age groups with new COVID-19 era data as well as identify any new epidemiological patterns not previously described.

Purpose:
To investigate the epidemiology of track & field and running-related injuries presenting to U.S Emergency Departments from 2012 to 2021 by injury type and patient demographics.

Study Design:
Descriptive epidemiology study.

Methods:
A retrospective analysis was conducted utilizing the publicly available National Electronic Injury Surveillance System (NEISS) database for patients presenting to U.S Emergency Departments with injuries relating to track and field and running from January 2012 through December 2021. Sample weights were used to produce nationwide estimates of injury burden based on 8,400 actual cases. Extracted data included age, sex, race, date, injury characteristic (diagnosis, body region injured, location of injury occurrence), and disposition. Cases were stratified by sex, age, and injury type to determine any epidemiological patterns.

Results:
A total of 8,400 individuals with track and field and running-related injuries presented to NEISS EDs from 1 January 2012 to 31 December 2021. Most injuries occurred in women (n = 4400, 52.4%), in individuals between 15 and 17 years of age (n = 4000, 47.6%) (see Figure 1) and of Caucasian race (n = 3134, 37.3%). Most injuries occurred in patients aged between 15 - 17 years (n = 2804, 33.3%), followed by 12 - 14 years (n = 2743, 32.6%), and over 30 years (n = 976, 11.6%). The most common specified diagnoses were strain/sprain (n = 2786, 33.2%), fracture (n = 1132, 13.5%) and contusion (n = 562, 6.7%). The location of injury was most commonly at sporting events (n = 3718, 44.3%), school (n = 3071, 36.6 %), and in the public (n = 417, 5.0%). Patients under 14 years of age were more likely to sustain injuries at school while those over 14 years old were more likely to sustain injuries at sporting events. Individuals 30 years old and older made up the largest proportion of injuries sustained at public events. Most patients were examined or treated in the ED prior to being released (n = 7916, 94.2%). Monthly injury trends displayed a bimodal pattern, spiking initially in April (n = 1726, 20.5%) and then again in September (774, 9.21%).

Conclusion:
Track and field injuries, as well as running injuries, seem to be increasing in the past 10 years, especially amongst 15 - 17 year olds. The majority of these injuries involved strain/sprains and occured predominantly in Caucasian females. With the COVID-19 pandemic, there was a marked decrease in Emergency Room admissions for Track and Field/ Running injuries. Findings from this study would suggest a strong age as well as gender component to injuries. These findings can play a role in injury prevention and ensuring appropriate precaution is taken for athletes of all ages.

Abstract Title: Rugby in the COVID-19 Era: A Comparison of Trends in Rugby-Related ED Visits

Investigator: Fatima Arif
Co-Investigator(s): Haad Arif, University of California Riverside SOM/ Class 2025
Department(s): Trauma and Acute Care Surgery, Riverside Community Hospital, Riverside, CA

Abstract

Background:
Rugby is the ninth most popular sport in the world and is growing at a considerable rate amongst players of all ages and genders. As with any high-impact contact sport, there is a substantial risk for injury, especially given the lack of protective gear in rugby. To date, injury studies have investigated rugby-related injuries at either a specific level of gameplay, within a specific age group, or for a particular injury. This current study aims to evaluate how COVID-19 impacted patterns of ED visits presenting for rugby-related injuries.

Methods:
The NEISS database was examined for rugby injuries in the United States from January 2012 through December 2021 to produce nationwide estimates of injury burden. Evaluated data included age, sex, race, date of initial ED visit, injury characteristic (diagnosis, body region injured, location of injury occurrence), and ED discharge disposition. Cases were stratified by sex, age, and injury type to monitor for epidemiological patterns.

Results:
A total of 2,896 individuals with rugby-related injuries presented to NEISS EDs from 1 January 2012 to 31 December 2021. The majority of injuries occurred among males (73.9%), Caucasians (45.3%), and in the 15-19 year-old age range (44.9%). Injuries most commonly affected the upper body, specifically the head (23.1%), face (13.8%), and shoulder (12.4%) with fractures and sprains comprising 22.3% and 18.5% of ED diagnoses. A significant portion of injuries occurred in March, April, or May (38.5%). From 2012 to 2021, annual rugby-related ED visits (RRV) decreased by 48.38%, with 401 visits in 2012 compared to 207 visits in 2021. During the study period, the least amount of injuries occurred during 2020 with 68 visits, a 76.55% decrease from the average overall yearly visits of 290.

Conclusion:
While interest in rugby is increasing, annual rugby injuries are declining; perhaps due to a rise in concussion protocol awareness and emphasis on safe tackling practices. COVID-19 effectively halted all organized rugby participation in 2020, but as lockdown restrictions lifted in 2021, monthly injury patterns resumed similar trends as in the pre-COVID-19 era. Unlike other sports such as American football, which saw an increase in injuries following 2020, due to factors including canceled practices and incomplete preseason preparation, rugby followed its prior downward trajectory of annual RRV. This study's findings suggest that while rugby injuries drastically decreased due to a lack of participation during the initial COVID-19 lockdown, COVID-19 has not had a lasting impact on altering annual RRV.

Abstract Title: Visualization of the Entire Portal and Hepatic Venous systems in a Single Acquisition with Ferumoxytol-Enhanced MRA

Investigator: Krishan Arora
Co-Investigator(s): Amir Imanzadeh, MD, Department of Radiology, UCLA David Geffen School of Medicine; Arash Bedayat, MD, Department of Radiology, UCLA David Geffen School of Medicine
Department(s): Department of Radiology, Division of Cardiovascular Imaging, David Geffen School of Medicine at UCLA

Abstract

Introduction:
With dynamic contrast enhancement as is typical with MR and CT, appropriate time windows to capture portal and hepatic venous filling are very different. Multiphase imaging with both CT and MR is therefore necessary and is frequently suboptimal for at least one territory. High-quality imaging, especially of the smaller
terminal vessels, improves the diagnosis of portal hypertension, portal and hepatic venous thromboses, porto-systemic shunts, and vascular malformations (AVMs). Ferumoxytol is an iron-based nanoparticle with an intravascular half-life of 14-15 hours, which should avoid the challenges of multiple-phase imaging. We aimed to assess the visualization, diagnostic confidence,
and presence of artifact in the portal and hepatic venous systems in patients who underwent ferumoxytol-enhanced steady-state MRA (FE-MRA).

Methods:
We conducted an IRB-approved and HIPAA-compliant study of 20 consecutive patients (mean age = 62.5 years) who underwent breath-held 3D MRA of the abdomen during the steady state distribution of ferumoxytol, 4 mg /kg. One radiologist blinded to all clinical data scored the images. Overall image quality, visualization of the hepatic venous system and visualization of the portal system were each scored with a 5-point modified Likert image quality scale. Secondary and tertiary vessels were emphasized in scoring. A 5 represented high, uniform contrast and sharp vessel boundaries, and a 1 was non-diagnostic. Confidence in diagnosing vessel patency, stenosis, or occlusions was scored with a 3-point modified Likert image quality scale (3 = high confidence including smaller vessels, 1 = low confidence). Artifact due to motion, stents, devices, or embolization coils was scored with a 5-point modified Likert image quality scale (1 = none, 5 = severe).

Results
Image quality scores were excellent (4.5 ± 0.7) and visualization scores for the hepatic and portal systems were 4.6 ± 0.5 and 4.6 ± 1.3 respectively. Confidence in diagnosis of vessel patency, stenoses or occlusions was high (2.9 ± 0.3) and included smaller vessels (fig 1). Scores for artifact due to motion or hardware devices was low (1.5 ± 0.6).

Conclusion
The entire portal and hepatic venous systems can be evaluated in a single breath-held 3D acquisition during the steady state distribution of ferumoxytol. Smaller, terminal vessels were routinely seen on FE-MRA, due to its pharmacokinetic properties. Future work will require comparison with gadolinium-based contrast agents. Because of its kinetics and relaxivity, ferumoxytol holds promise to become the new standard for imaging visceral venous anatomy.

Abstract Title: Comparative analysis of STI diagnoses in Eastern Virginia during the COVID-19 pandemic

Investigator: Saritha Attanagoda
Co-Investigator(s): Saritha Attanagoda, MD 2023; Elizabeth Li, MD 2023
Department(s): Community Engaged Learning

Abstract

Introduction:
During the COVID-19 pandemic, changes in patient care services were made to facilitate social distancing and increase resources for COVID-19 related care. While these changes were necessary, they also affected other areas of healthcare including the detection and management of sexually transmitted infections (STIs). In the first 40 weeks of 2020, there was an 18.2% decrease in the number of reported chlamydia cases compared to the prior year. However, there was no significant difference in the number of gonorrhea diagnoses for the same time period. This was observed in ages 14-49, a group that is known to have the highest rates of STI cases in the U.S.

Methods:
We used publicly available census data from the Virginia Department of Health to obtain STI cases in the Eastern Region of Virginia, which has some of the highest rates of STIs in the state. We looked at data from 2018 through 2021 to account for the timeline of the COVID-19 pandemic. The Eastern Region includes, but not limited to, Norfolk, Chesapeake, Virginia Beach, Portsmouth, Suffolk, and Williamsburg counties. These incidences were further broken down by age ranges 15-39, 40-59, and 60+ within the Eastern Region of Virginia to observe potential differences in the number of STI cases between different age groups.

Results:
The rate of chlamydia diagnoses in 2018, 2019, 2020, and 2021 were 806.8, 879.8, 772.3, and 773.6 per 100,00 people respectively. The rate of gonorrhea diagnoses for the same years were 251, 293.7, 338.6, and 302.4 per 100,00 respectively. The rates of new HIV diagnoses were considerably smaller with 13.7, 16.7, 12.2, and 13 per 100,00 people for 2018, 2019, 2020, and 2021 respectively.

The number of new cases of gonorrhea, chlamydia, and HIV between 2018 and 2021 were then obtained for three age groups: 15-39, 40-59, and 60+. In the 15-39 age group, the number of cases of chlamydia for 2018, 2019, 2020, and 2021 were 14372, 15682, 13812, and 13836 respectively. In this age group, the total number of gonorrhea cases were 4262, 5010, 5704, and 5100 in the same years respectively. Finally, in the 15-39 age group, the number of new HIV cases were 172, 219, 170, and 181 in 2018, 2019, 2020, and 2021 respectively.

Conclusions:
This data shows fewer chlamydia diagnoses during the pandemic while gonorrhea and HIV cases remained consistent pre- and during COVID-19.
In the subgroup analysis with age groups, the number of gonorrhea and HIV cases in the 40-59 and 60+ age groups remained relatively similar pre- and during the pandemic. However, the data is suggestive of a decreasing number of chlamydia cases within the 15-39 year old age group during 2020, the height of the pandemic. This could be attributed to decreased rates of STI testing in the Eastern region during the pandemic, but decreased rate of transmission is also a possible consideration.

Abstract Title: A Case of Delusions in a Patient Receiving Cabergoline for a Prolactinoma: Pathophysiology and Proposed Treatment with Aripiprazole

Investigator: Saritha Attanagoda
Co-Investigator(s): Charles Springer, MD 2023; Charles D. Miks, MD 2023; Gina Vivino, MD 2023; Robert Rodgers, MD 2023
Department(s): Psychiatry and Behavioral Sciences

Abstract

Introduction
Cabergoline is a dopamine-2 receptor agonist used as a first-line treatment of pituitary prolactinomas. We describe the case of a 32-year-old woman with a pituitary prolactinoma who was treated with cabergoline for one year, during which time she developed delusions. We also discuss the use of aripiprazole to mitigate her psychotic symptoms while maintaining the efficacy of cabergoline treatment.

Case Information
The patient was a 32-year-old female with no past psychiatric disorders who presented to our clinic for the gradual onset of paranoid and persecutory delusions occurring over the prior eighteen months. As a result, the patient became increasingly socially isolated. At the time of her first clinic visit, the patient was no longer able to work outside of her home. Our patient also reported symptoms of anxiety and sleep impairment. She denied any other psychiatric symptoms. Vital signs and physical exam were within normal limits. The mental status exam was significant for impaired judgment and insight.

Our patient's medical history was significant for a prolactin-secreting microadenoma for approximately 14 months prior to her arrival at our clinic. She initially presented to her endocrinologist with galactorrhea and worsening headaches of one year's duration. A magnetic resonance image (MRI) of the head showed a 2.4 mm hypodense focus consistent with a prolactinoma. She subsequently started cabergoline 0.5 mg thrice weekly. A follow-up MRI showed a stable microadenoma and the patient reported her symptoms had resolved.

Discussion
Cabergoline has emerged as an efficacious non-surgical treatment for pituitary prolactinomas because it has high binding affinity to dopamine-2 receptors, resulting in long-lasting inhibition of prolactin secretion from lactotrophs in the anterior pituitary gland.1,2,3 Chang et. al. in 2007 reported two cases in which 0.5 mg cabergoline induced a worsening of psychotic symptoms in patients previously diagnosed with schizophrenia.7 Furthermore, Davie in 2007 and Pérez-Esparza et. al. in 2017 both describe cases of previously nonpsychotic patients who started cabergoline for a pituitary prolactinoma and developed psychiatric symptoms such as gambling, paranoid delusions, major depression, and auditory hallucinations.8,9 The likely mechanism by which cabergoline induces psychotic features is thought to involve dopamine-2 receptor binding, and strong evidence suggests that dopamine is involved in the final common pathway responsible for positive symptoms of psychosis.3

As indicated above, psychotic exacerbations have occurred in patients shortly after receiving 0.5 mg starting doses of cabergoline.7 Our patient was initiated on 0.5 mg cabergoline thrice weekly. The recommended dosage for initiating therapy with cabergoline is 0.25 mg twice a week.13 It is possible that our patient was started on a higher dose than necessary, which increased the likelihood of psychosis.

In managing our patient, we ultimately decided to initiate treatment with aripiprazole. Aripiprazole is a third-generation antipsychotic that acts as a partial agonist at dopamine-2 receptors, as well as a partial agonist at 5-HT1A serotonin receptors and an antagonist at 5-HT2A serotonin receptors. Its partial agonism at dopamine-2 receptors allows for dopamine stabilization; aripiprazole blocks dopaminergic transmission at high dopamine concentrations but stimulates dopaminergic transmission at low dopamine concentrations. In the setting of a prolactinoma and cabergoline therapy, aripiprazole could potentially mitigate the hyperdopaminergic effects of cabergoline in the mesolimbic pathway associated with psychotic symptoms, while preserving dopaminergic inhibition of prolactin via the tuberoinfundibular pathway.14

We thus propose the consideration of aripiprazole as an adjunctive medication for the treatment of psychiatric side effects of cabergoline. This treatment plan allowed for the continued treatment of this patient's prolactinoma while simultaneously resolving her medication-induced delusional disorder.

Conclusion
Our patient is a 32-year-old woman who developed delusions while being treated for a pituitary prolactinoma with cabergoline for one year. For such patients, we propose the adjunctive use of aripiprazole to treat psychiatric symptoms while continuing standard prolactinoma treatment.

Abstract Title: Awareness and counseling among dermatologists of the association between hydrochlorothiazide and increased rates of non-melanoma skin cancer development: barriers and opportunities

Investigator: Jason Bard
Co-Investigator(s): Heather A. Kornmehl, DermSurgery Associates, Bellaire, Texas
Department(s): Dermatology

Abstract

Introduction:
Hydrochlorothiazide (HCTZ) is one of the most commonly prescribed anti-hypertensive agents. However, thiazides are known to cause phototoxic and photoallergic reactions in the presence of both UVA and UVB light. Numerous studies have linked cumulative HCTZ use and the development of non-melanoma skin cancers (NMSCs). In August 2020, the U.S. Food and Drug Administration (FDA) approved changes to the HCTZ drug label to indicate that the medication can increase the risk of NMSC. It also now counsels patients to partake in sun-protective behaviors and undergo regular total body skin exams. Despite this update, it is unknown what proportion of dermatologists are aware of this association and how often screening and counseling are performed.

Methods:
An observational, cross-sectional survey study was administered using REDCap, a secure web application, from November 2021 to January 2022. Eligible participants were dermatology residents and board-certified dermatologists associated with a dermatology training program. The survey was distributed through the Association of Professors of Dermatology listserv, which reaches American dermatology residency program directors and other academic dermatologists. The survey contained 13 questions including information on demographics, awareness of the medication risk, counseling frequency and barriers to counseling. The estimated completion time was around five minutes. Survey data was kept confidential and anonymous. Chi-square testing was utilized to compare proportions between resident and attending respondents.

Results:
A total of 83 respondents completed the questionnaire (37 dermatology residents and 46 attendings). 71.1% of respondents stated they were aware of the association between HCTZ use and NMSC development prior to the survey. Only 28.9% of respondents were aware of the FDA's changes to the HCTZ drug label. A greater proportion of attending respondents (84.8%) than resident respondents (54.1%) were aware of the association between HCTZ use and increased risk of NMSC ($\chi 2 = 7.98$, $p=0.0047$). Similarly, 45.7% of attendings yet only 8.1% of residents were aware of the FDA label change ($\chi 2 = 12.1$, $p=0.0005$). When asked how often one checks if a patient is taking HCTZ while screening for skin cancer and how often counseling is performed, 61.4% of participants selected "never" or "rarely." More resident respondents (n=31, 83.8%) selected one of these responses than did attending respondents (n=20, 43.5%) ($\chi 2 = 10.59$, $p=0.0011$). The most reported barrier to counseling by dermatologists was the lack of specific guidelines regarding skin cancer screening recommendations for patients taking HCTZ. Other commonly reported barriers to counseling by respondents included lack of knowledge of the risk association and lack of time in clinic.

Conclusion:
The well-established link between cumulative HCTZ use and the risk for the development of cutaneous malignancy has been recently highlighted by the FDA. Concerted efforts should be made in residency training and continuing medical education to ensure that trainees and established dermatologists are aware of this association. Even when aware of this association, dermatologists report many barriers to counseling of patients with regards to this association. Specialty-specific efforts should be made to implement clear guidelines on best screening practices and optimized counseling strategies for patients taking HCTZ.

Abstract Title: Improving Pediatric Care for Spanish-Speaking Patients at Student-Run Free Clinic

Investigator: Mackenzie Barker
Co-Investigator(s):
Department(s): Community Engaged Learning

Abstract

Introduction:
Student-run free clinics fill an important gap for uninsured patients, especially in minority communities with large barriers to accessing healthcare. However, the students who staff these clinics may lack the experience necessary to provide high-quality care. Pediatric visits may prove particularly difficult because students typically have no pediatric exposure until the third year. It is important that free clinics provide high quality care if they are to improve, rather than contribute to, health disparities. This project focuses on a strategy to assist student clinicians in achieving this high quality of care.

Methods:
To assess the needs of the Esperanza pediatrics clinic, student clinicians were asked via anonymous survey to report on their pediatric encounters. In response to the needs assessment, a comprehensive pediatrics resource binder was created that contains well child check templates, developmental milestone checklists, parent education handouts, vaccine schedules, and other useful items. To ensure easy access to the resources, front desk staff pre-filled charts with the appropriate resources according to patient age and preferred language. Student clinicians were surveyed again after introduction of the resources to determine what percentage of students used them and whether they were helpful.

Results:
The pre-intervention survey found that nearly half of the student clinicians assigned to pediatric patients had no experience treating children. When asked about their patient encounters, students left comments like, "I feel useless in the peds room." 88% of students felt they would benefit from additional guidance on how to conduct pediatric encounters. At first, the resource binder was placed in a central location in the clinic, and students were asked to obtain the handouts they needed for their encounters themselves. Under this system, only 30% of students made use of the resources. Once the resources were included with the patient chart, 75% of students used them. Out of the students who utilized the new resources, 97% rated them "very useful." After the introduction of these resources, student's self-reported competence with pediatric encounters averaged 85/100, nearly 20 points higher than before the intervention. The overall quality of the pediatric encounters, as reported by the student clinicians, improved from 76/100 to 85/100.

Conclusion:
Our results show that, while many student clinicians are inexperienced in treating children, they report feeling significantly more capable of conducting high-quality pediatric encounters when given appropriate resources. In addition, the quality of pediatric encounters improves when students utilize these resources. The percentage of students who utilize available resources is significantly increased when physical copies are included in patient charts, making them more easily accessible. Equipping student clinicians with the resources they need to provide high-quality care at free clinics is one simple step we can take towards decreasing the health disparities that exist for local immigrant populations.

Abstract Title: Availability of Medical Language and Interpretation Services in Hampton Roads, VA

Investigator: Anna Baroody
Co-Investigator(s): Katherine Johnson, EVMS MD2025
Department(s): Global Health

Abstract

Background:
Limited English Proficiency (LEP) families of the Hampton Roads community have expressed the need for resources regarding linguistically competent medical care available to them. Despite the legal precedents guaranteeing language accessibility in medical care, the use of ad hoc or other, non-professional forms of interpretation, which can result in communication errors and have a negative effect on the health of LEP patients, are still prevalent. Studies have shown that LEP patients have poorer health outcomes such as lower quality of life related to chronic care management and an increased rate of pediatric emergency department revisits. Implementation of professional interpretation services are associated with improved follow-up rates, improved care management, and improved satisfaction among LEP patients.

Approach:
A literature review assessed the barriers and needs of LEP patients. Local LEP families reported specific issues such as the lack of transparency regarding the availability of language services. This needs assessment led to the creation of two medical language survey projects, which are currently underway. The purpose of the surveys is to collect information about the language services offered in the Hampton Roads medical community to provide LEP patients with the tools necessary to find linguistically competent care. The surveys were constructed to evaluate the regional availability of language services in pediatric medical practices, such as bilingual clinicians, in-person professional interpretation services, and video or telephone interpretation services. Survey results will provide LEP families with the information necessary to make an informed decision in choosing the healthcare providers best suited to their medical and language needs.

Outcomes/Future Directions:
This information will be compiled into an accessible resource to provide LEP families with the information necessary to identify clinical care best suited to their medical and language needs.

Abstract Title: Mapping the process and quality of discharge education in a children's hospital

Investigator: Heather Beatty
Co-Investigator(s): Benjamin Chilampath, EVMS\MD 2025; Kyrie Shomaker, MD Hospitalist\CHKD; Reyna Nikolaus, FNP Hospitalist\CHKD; Turaj Vazifedan, DHSc Pediatrics\CHKD
Department(s): CHKD Hospitalist Department

Abstract

Introduction:
Variation in the discharge process introduces potential for unsafe transitions home. In this hospital, the discharge process has not been standardized nor have responsibilities been assigned to the appropriate parties. The quality of discharge education is also an important factor in a safe discharge, and communication among all parties is imperative to reduce readmission and increase patient satisfaction. The primary aim of this study is to increase value added time by evaluating and documenting the discharge process.

Methods:
After attending rounds with physicians and meeting with the various stakeholders, we began constructing a process map of the different aspects of discharge. Through observation and discussion, we iteratively determined the existing process for the hospitalist team and potential areas of improvement. To evaluate the quality of the discharge education, we surveyed caregivers at the time of discharge then asked the nurse's perception of caregiver comprehension. A 20% discrepancy in actual versus perceived comprehension was deemed significant. Readmission data was collected if the patient returned to the ER or hospital within 7 days.

Results:
The final process map consisted of 75 steps, completed by 6 different healthcare provider roles. Summer scholars identified over 20 discrete opportunities for improvement. Of the 93 patients whose education was reviewed, only 46% identified as non-white, but these accounted for 73% of the 15 cases in which a discrepancy in comprehension was identified. The return visit rate was 6.6%, with only 1 of these 5 having a greater than 20% discrepancy in comprehension scores.

Conclusion:
Based on our observations, several potential areas for improvement were identified to increase efficiency and reduce potential for errors, for instance, establishing processes for prior authorizations and drafting discharge medication reconciliation for more senior review. While a significant correlation was not shown between discharge education quality and readmission rates, many questions raised throughout this project focused on assigning responsibility for certain tasks in the discharge process. Assigning tasks and outlining the process helps ensure every discharge home is safe and will hopefully reduce readmission rates.

Abstract Title: Risk stratifying patients, quantifying therapy efficacy, and detecting treatment/racial disparity in pancreatic cancer at Sentara-EVMS-VOA

Investigator: Abigail Bent
Co-Investigator(s): Zakary L. Kolkey, B.S. Leroy T. Canoles Jr. Cancer Research Center, Department of Microbiology and Molecular Cell Biology, EVMS 2. Rick J. Jansen, Ph.D. Department of Public Health, North Dakota State University; Janet S. Winston, M.D. Pathology Sciences Medical Group, Department of Pathology, Sentara Norfolk General Hospital; Dennis A. Rowley M.D. Pathology Sciences Medical Group, Department of Pathology, Sentara Norfolk General Hospital; Richard A. Hoefer D.O. FACS Sentara Cancer Network, Sentara Hospital Systems, Sentara Healthcare; Amy H. Tang, Ph.D. Leroy T. Canoles Jr. Cancer Research Center, Department of Microbiology and Molecular Cell Biology
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Pancreatic cancer (PDAC) remains one of the deadliest cancers in the world, ranking 10th in overall incidence (with an estimated 62,210 new cases) but 3rd in overall mortality (with an estimated 49,830) in the United States in 2022. Current treatment regimens rely on chemotherapy, radiation therapy, and surgery; however, even with state-of-the-art combinational therapeutics, the 5-year survival rate is only 11.5%. The dismal survival rate is associated with late diagnosis, metastatic presentation, ineffective treatment options, and high rate of inoperable tumors. Surgery represents the only "curative" measure for 20% of PDAC patients with clinically localized tumors, whereas the remaining 80% of PDAC patients with locally advanced and metastatic tumors are inoperable. Black/African American (AA) PDAC patients suffer a higher mortality rate locally and nationally.

Methods:
This retrospective study used a large cohort of 581 PDAC patients treated at Sentara Cancer Network between 2008 and 2016 in Hampton Roads Virginia. The cohort was stratified into two groups: 191 patients diagnosed with operable disease who underwent surgical resection, and 449 patients diagnosed with inoperable disease without surgical viability. Survival was calculated from date of initial diagnosis to date of last follow-up or death from all-cause mortality. Clinicopathological parameters (TNM classification) and Standard of Care (SOC) treatment modalities were reviewed, validated, and compared using electronic medical records from Sentara EPIC and VOA iKnow Medicine.

Results:
Both Black/AA and White PDAC patients in this Sentara cohort had a worse overall survival compared to the national average and SEER database, with less than 6% survival rates for both racial groups at 5 years compared to 11.5% nationally. Black/AA PDAC patients diagnosed at stage II were significantly less likely than White PDAC patients to receive surgery. Black/AA PDAC patients were diagnosed at younger ages in both the overall cohort (66.3 vs 68.4) and the inoperable cohort (66.4 vs 69.5). A younger age at diagnosis correlated with both a higher number of chemotherapy agents received and a longer survival. While this may potentially explain relatively similar survival rates in the Sentara cohort, this trend was not seen in the national SEER database, with Black/AA PDAC patients suffering higher mortality rates than their white counterparts both in the broader Hampton Roads area and nationally.

Conclusion:
While our local PDAC cohort suffers poorer outcomes compared to the national SEER database, there was no significant difference in length of survival between Black/AA and Whites in the Sentara catchment areas. This is remarkable given a lower rate of curative surgery received by Black/AA patients. The comparable survival of these younger Black/AA PDAC patients as compared to the older white PDAC patients may be due to their younger age of diagnosis, which was correlated with an increased number of chemotherapy agents prescribed and received, allowing for a more aggressive approach to manage their diseases and delay metastatic progression in the clinic. We aim to develop and validate better therapy-responsive prognostic biomarker(s) to risk stratify PDAC patients, quantify therapy efficacy, tailor treatment sequences and options, forecast tumor relapse, and predict patient survival in the clinic in the future.

Abstract Title: Vibrio vulnificus necrotizing fasciitis arising from crab inflicted wound

Investigator: Isabelle Brown
Co-Investigator(s): Uma Markan, MD2025; Mahmoud Khreis, Fellow, Internal Medicine, Infectious Disease; Catherine Derber, Associate Professor, Internal Medicine, Infectious Disease
Department(s): Infectious Disease, Internal Medicine

Abstract

Introduction:
Vibrio vulnificus is a Gram negative, siderophilic rod found in warm, brackish waters world-wide. *V. vulnificus* wound contamination can cause rapidly progressing necrotizing fasciitis and sepsis. Persons with liver disease are more susceptible to *V. vulnificus* infection due to elevated serum iron levels. The Chesapeake Bay is known to harbor *V. vulnificus,* and with the incidence of *Vibrio* cases increasing and concern for bay pollution leading to bacterial antibiotic resistance, greater awareness of the risks of *Vibrio vulnificus* infection and how to effectively treat it are needed. In this report, we describe the case of a 66-year-old male with a history of liver disease who presented with necrotizing fasciitis of the left upper extremity one day after sustaining a pinch wound from a blue crab in North Carolina.

Case Information:
The patient is a 66-year-old White male with a history of essential hypertension, hyperlipidemia, smoking, alcoholic hepatitis and alcohol dependence who initially presented with puncture wounds on his hands after handling live crabs.

He developed hemorrhagic bullae associated with pain radiating up his left arm. Within one hour of presentation, the patient became hypotensive with lactic acidosis and leukocytosis. Blood cultures were taken, and the patient received surgical wound debridement. Cultures grew Gram negative rods, and due to freshwater exposure, he was given cefepime and doxycycline for suspicion of *Pseudomonas aeruginosa* and *Vibrio vulnificus*. When the blood cultures speciated to pan-sensitive *V. vulnificus*, the patient was switched from cefepime to ceftriaxone with continuation of doxycycline. The patient's leukocyte count continued to rise following multiple debridement operations, and antibiotic coverage was broadened to cefepime and ciprofloxacin.
After a two week course of antibiotics and five debridement operations, the patient showed significant improvement and was discharged without significant loss of tissue and retained functioning of the left upper extremity.

Discussion:
This patient had multiple risk factors that predisposed him to severe infection with *Vibrio vulnificus,* including male sex, age over 50, and underlying liver disease.

The current Infectious Disease Society of America (IDSA) guidelines recommend treatment of necrotizing fasciitis secondary to *V. vulnificus* with doxycycline plus ceftriaxone or cefotaxime. The patient's clinical condition continued to deteriorate on ceftriaxone and doxycycline, however. With re-escalation of antibiotics to cefepime and ciprofloxacin, in addition to further debridement operations, the patient's condition improved. Of note, ceftriaxone was not specifically included in the susceptibility testing of the microbiology lab. Recent research on *V. vulnificus* and *V. parahaemolyticus* strains collected from crabs in Maryland Coastal Bays raised concerns for emerging resistance, with 35% of V. vulnificus strains demonstrating resistance to ceftriaxone and 21% demonstrating resistance to cefepime.

Conclusion:
This patient's treatment course was unique due to his clinical deterioration despite being on IDSA guideline antibiotic therapy, which may represent a clinical example of emerging antibiotic resistance in the *Vibrio* species of the eastern US. This case also highlights the importance of balancing the use of national guidelines with individual case presentations, and the importance of timely clinical decision-making in adapting to critical cases.

Abstract Title: Polymeric Nanoparticles in Brain Cancer Therapy: A Review of Current Approaches

Investigator: Chad Caraway
Co-Investigator(s): Hallie Gaitsch - Hunterian Neurosurgical Research Laboratory, Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD - NIH-Oxford-Cambridge Scholars Program, Wellcome-MRC Cambridge Stem Cell Institute and Department of Clinical Neurosciences, University of Cambridge, Cambridge CB2 1TN, UK; Elizabeth E. Wicks - Hunterian Neurosurgical Research Laboratory, Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD - University of Mississippi School of Medicine, University of Mississippi Medical Center, Jackson, MS; Anita Kalluri - Hunterian Neurosurgical Research Laboratory, Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD; Navya Kunadi - Hunterian Neurosurgical Research Laboratory, Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD; Betty M. Tyler - Hunterian Neurosurgical Research Laboratory, Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD
Department(s): Department of Neurosurgery, Johns Hopkins School of Medicine

Abstract

Introduction:
Translation of novel therapies for brain cancer into clinical practice is of the utmost importance as primary brain tumors are responsible for more than 200,000 deaths worldwide each year. While many research efforts have been aimed at improving survival rates over the years, the prognosis for patients with glioblastoma and other primary brain tumors remains poor. Safely delivering chemotherapeutic drugs and other anti-cancer compounds across the blood-brain barrier and directly to tumor cells is perhaps the greatest challenge in treating brain cancer. Numerous approaches aimed at overcoming these limitations have been developed over the years, with variable success. Some of the most promising techniques in development involve the use of nanocarrier systems to bypass the blood-brain barrier and blood-brain tumor barrier, selectively target brain cancer cells, and release anti-cancer compounds into diseased tissue while limiting toxicity to systemic and healthy brain tissue.

Main Body:
Nanoparticles-carriers ranging from 10-1000 nm in diameter-can be loaded with chemotherapeutic drugs, nucleic acids, antibodies, and other proteins and peptides. These carriers can be engineered from a variety of materials, with metal, lipid, and polymer-based nanoparticles being the most tested in neurological disease research. Polymeric nanoparticles are powerful, highly tunable carrier systems that may be able to improve brain tumor therapy. The general structure of polymeric nanoparticles consists of a core polymer with therapeutic agents either surface-bound or encapsulated and coated with targeting and/or hydrophilic molecules to increase circulation half-life and specific delivery.

In recent years, polymeric nanoparticles developed for central nervous system (CNS) tumor treatment have been modified with various moieties capable of interacting with the blood-brain barrier and tumor cells. Appropriate subtypes can be selected by assessing the polymer pharmacokinetics, modifiability, and payload delivery best suited for any given study. Additionally, polymers can be engineered to form other nanomaterials that may be useful for therapeutic development. For example, a recent study detailed the ability to produce optical nanofibers from polymers that can aid in phototherapy, drug delivery, sensing, and more. Others have explored the potential of novel noninvasive delivery methods, like loading polymeric nanoparticles into neutrophils or monocytes, to enhance their transport to brain tumors. Though many challenges remain, mounting evidence from promising preclinical studies utilizing a variety of approaches suggests polymeric nanoparticles may prove effective in the treatment of CNS malignancies.

Conclusion:
Appropriately constructed polymeric nanoparticles cross the blood-brain barrier, increase drug bioavailability, reduce systemic toxicity, and selectively target CNS cancer cells. This review includes a variety of polymeric nanoparticles and how their associated composition, surface modifications, and method of delivery impact their capacity to improve brain tumor therapy.

Abstract Title: Effect of Medicaid Expansion on 30-day Hospital Readmissions for Pneumonia, Heart Failure, and Acute Myocardial Infarction; A Nationwide Study

Investigator: Chloe Carr
Co-Investigator(s): Sami Tahhan, MD, Internal Medicine; Cynthia Avila, Internal Medicine; Rehan Qayyum, MD, Internal Medicine
Department(s): Internal Medicine

Abstract

Introduction:
In 2010, the US Congress passed the Patient Protection and Affordable Care Act (ACA) with the primary objective of increasing access to affordable health insurance through healthcare subsidies and Medicaid expansion. However, not all States allowed Medicaid expansion resulting in variable insurance coverage across the US. Hospital readmissions within 30 days after discharge are associated with poor health outcomes and are very costly, accounting for more than $17 billion in avoidable Medicare expenditures. The Centers for Medicare & Medicaid Services (CMS) created the Hospital Readmissions Reduction Program (HRRP) and hospitals with higher-than-expected 30-day readmission rates for selected clinical conditions have been penalized by up to 3%. Overall, the HRRP has resulted in a decrease in hospital readmissions. Hospital readmissions are a reflection of the discharge planning and the access to care after discharge. Because uninsured or underinsured patients are likely to have poor access to care after discharge, they may have high readmission rates. Thus, the US States that expanded Medicaid expansion may have larger readmission reductions than States that did not. To examine this hypothesis, we examined the national hospital readmissions since 2005 to determine if the readmission reduction trends of hospitals differ by the Medicaid expansion status of the States in which these hospitals were located.

Methods:
We obtained data from four sources: 1) hospital characteristics and severity of illness-adjusted readmissions data were obtained from CMS, 2) regional demographic and economic data were obtained from the US Census Bureau, and 3) hospital catchment area data from the Dartmouth Atlas of Healthcare, 4) States that allowed Medicaid expansion in 2014 from the Kaiser Family Foundation. We divided States into those that expanded Medicaid in 2014 and those that did not expand Medicaid until 2020; five States that expanded Medicaid between 2014 and 2020 were excluded from the analysis. Data were summarized using mean (SD) or percentages and differences between variables were examined using the Chi-square test or Wilcoxon rank-sum test as appropriate. We examined the relationship between Medicaid expansion and 30-day readmissions after hospitalizations for pneumonia, heart failure (HF), and acute myocardial infarction (AMI) in a difference-in-difference framework using multilevel levels models; such models allow for examination of changes in time-trends while accounting for correlation between repeated observations from the same hospitals. Adjusted models included the following potential confounding variables: hospital ownership, teaching status of the hospital, number of hospital beds, number of nurses, rural vs. urban location of the hospital, and hospital catchment area population characteristics (total population, median income, poverty percentage, African American percentage, and percentage with insurance).

Results:
Of the 3,015 hospitals, 52%(1,451) were located in States with Medicaid expansion. States without Medicaid expansion (N=19) had more for-profit hospitals (26% vs. 12%; P<0.001), hospitals in rural areas (38% vs. 21%; P<0.001), and non-teaching hospitals (79% vs. 61%; P<0.001). Before 2014, 30-day readmission rates were higher in hospitals located in the Medicaid-expansion States than in hospitals located in non-Medicaid-expansion States (pneumonia = 18.2% vs 17.9%; HF = 24% vs. 23.7%; AMI = 19.1% vs. 18.8%; all P<0.001). Across all hospital in the US, readmissions were significantly lower after 2014 than before 2014 for pneumonia (-1.2%, 95%CI = -1.2%, -1.1%; P<0.001), HF (-2.0%, 95%CI = -2.1%, -1.9%; P<0.001), and AMI (-3.0%, 95%CI = -3.1%, -2.9%; P<0.001). While absolute readmission rate remained higher for hospitals in the Medicaid-expansion States, the drop in readmission reductions before and after 2014 was larger for hospitals in the Medicaid-expansion States than for hospitals in the non-Medicaid-expansion States; difference-in-difference for pneumonia (-0.13%; 95%CI = -0.23%, -0.04%; P=0.006), HF (-0.23; 95%CI = -0.35%, -0.11%; P<0.001), AMI (-0.19%; 95%CI = -0.28, -0.10; P<0.001). These results remained significant after adjusting for hospital and regional population characteristics.

Conclusions:
Hospitals located in states that expanded Medicaid had larger reductions in 30-day hospital readmission for pneumonia, HF, and AMI than hospitals that were located in states that did not expand Medicaid. Better access to healthcare due to Medicaid expansion may be responsible for the observed difference.

Abstract Title: The COVID-19 Pandemic and Its Effect on Bystander CPR

Investigator: Chloe Carr
Co-Investigator(s): Kevin Guy, MD 2023; Aaron Lopacinski, MD 2023; Cameron Palmer, MD 2023
Department(s): Emergency Medicine

Abstract

Introduction:
Bystander cardiopulmonary resuscitation (B-CPR) and early use of automated external defibrillation (AED) are effective early interventions in the treatment of out-of-hospital cardiac arrests (OHCA) and have been demonstrated to improve survival. In Norfolk, Virginia, a city with a diverse population and a high percentage of African Americans who live below the poverty line, the B-CPR rate falls short (12% in 2013) compared to national norms (approximately 40%). However, with the revitalization of B-CPR in 2014, now focusing on early chest compressions without the use of mouth-to-mouth, the B-CPR rates in Norfolk have increased to 26% in 2019. The B-CPR community-engaged learning (CEL) initiative at Eastern Virginia Medical School (EVMS) in Norfolk provides educational sessions for the local community, focusing on understanding the importance of early intervention in OHCA and practicing compression-only CPR and using an AED. Due to the COVID-19 pandemic, the B-CPR CEL initiative has been limited in its ability to educate the community. This study aims to understand the effect that the COVID-19 pandemic has had on OHCA and B-CPR rates in Norfolk, Virginia, and identify areas for further improvement in B-CPR rates.

Methods:
This retrospective study analyzed non-traumatic cardiac arrests to which the Norfolk Fire and Rescue (NFR) responded in 2019, 2020, and 2021. Traumatic cardiac arrests were excluded from the analysis. Demographic data, including age and gender, were collected. Endpoints chosen were the return of spontaneous circulation (ROSC) upon arrival at the emergency department (ED) and whether CPR was started before emergency medical services (EMS) arrival and by whom (Bystander (non-related community member and not a healthcare worker), Family Member, or Healthcare professional/non-EMS) determined by NFR personnel while obtaining information about the incident.

Results:
Between 2019 and 2021, there were a total of 773 non-traumatic cardiac arrests in Norfolk, Virginia, as reported by NFR. There were 435 males (56.2%) and 338 females (43.8%). The mean age was 58.9 (range 1-98 years). Of the 773 patients with non-traumatic cardiac arrest, 249 (32%) received early CPR. This included CPR performed by bystanders (n=51, 6.6%), family members (n=79, 10.2%), non-EMS healthcare providers (n=112, 14.9%), and law enforcement officers (n=7, 0.9%). Comparing 2019 to 2021, the total number of cardiac arrests increased (n=221 to n=280), while the percentage of bystander-initiated CPR stayed relatively flat at 6.3% in 2019, 6.25% in 2020, and 7.14% in 2021, respectively. Interestingly, family member-initiated CPR decreased in 2020, down to 6.25% from 12.2% in 2019 and 12.5% in 2021.

Conclusion:
This study found that the total number of cardiac arrests NFR responded to increased stepwise from 2019-2021. One hypothesis is that patients may have elected to forego seeing a medical provider during the pandemic due to fear of contracting the virus and thus missing necessary preventative screening. This study also found a decrease in the percentage of family members providing CPR in 2020 compared to 2019 and 2021. This may be due to a reduction of in-home family members caused by lockdown regulations during the pandemic. This may have decreased the likelihood that someone else would be present during a cardiac arrest that could initiate B-CPR; however, further research is required. Overall, the percentage of B-CPR rates stayed relatively the same in Norfolk throughout the three years studied, possibly indicating that the pandemic did not prevent the initiation of B-CPR. It is also possible that rates of B-CPR did not increase during the pandemic due to the disruption of B-CPR CEL group training sessions; however, further studies are needed.

Abstract Title: BCR Signalling in Atherosclerosis

Investigator: Samuel Chan
Co-Investigator(s): Shelby Ma, MS; Elena Galkina, PhD
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Atherosclerosis is a multifactorial chronic inflammatory disease characterized by the accumulation of modified lipoproteins and leukocytes in the aorta, vascular dysfunction, low-grade chronic inflammation, and formation of dangerous atherosclerotic plaques within the medium and large size vessels. The response of immune cells in atherosclerosis has been shown to play a large role in the course of disease. B cells are an active player in atherogenesis and serve a subset-specific role. Regulatory and marginal zone B cells as well as B1 cells are protective via Tfh cell suppression and secretion of natural antibodies. Conversely, follicular (FO) and innate response activator (IRA) B cells are pro-atherogenic, supporting the Th1 response, production of inflammatory cytokines and immunoglobulins. IRA B cells is a recently discovered subset of B cells that differentiate from B1a cells in the response to a TLR engagement and have a protective effect in sepsis via GM-CSF production and neutrophil activation. While evidence suggests that TLRs induce a pathological IRA cell differentiation in atherosclerosis, it is not known whether B-cell receptor signaling is also involved in IRA cell differentiation.

Methods:
To test how BCR signaling is involved in IRA B cell generation, we used transgenic mice that express 15% of normal levels of CD45, s protein tyrosine phosphatase that is involved in BCR signaling. These CD45L/L mice demonstrate reduced BCR signaling. For this study, C57BL/6 mice served as the control group. CD45L/L and WT mice were injected intraperitoneally with either LPS or LPS for 4 days. After the treatment, a peritoneal lavage and spleens were harvested, cell suspensions were made, cells were counted and stained with FACS Abs for B1 cells (CD23- CD43+ CD5+ IgMhi IgDlo) and IRA B cells (GM-CSF+ CD19+). The content of B1a and IRA B cells were calculated using percentage of cells and cell numbers. A t-test was then used to calculate statistical significance.

Results:
Recently, it has been established that IRA B cells differentiate from B1a in the peritoneum upon TLR-induced inflammation and migrate to the site of the spleen for their complete differentiation and pro-inflammatory activities. Therefore, we first established staining for a rare population of IRA B cells in the spleen after LPS i.p. injection into C57BL/6 mice. We found only a few numbers of IRA+ B cells within the peritoneal cavity of the C57BL/6 recipients at homeostatic conditions. After 4 days of induction of LPS-induced inflammation, we identified an increase in GM-CSF+ IRA B cells in the spleens of C57BL/6 mice. The generation of IRA+ B cells was also orchestrated by the reduction of B1a cells in the peritoneum of the LPS-injected recipients in comparison with PBS-injected C57BL/6 mice. Next, we tested how CD45 signaling and therefore BCR-associated signaling affects the generation of IRA+ B cells. In contrast to C57BL/6 B1a cells, CD45L/L B1a cells did not differentiate to GM-CSF+ IRA B cells and remained mainly within the peritoneum of CD45L/L mice.

Conclusion:
Overall, our data demonstrate an implication of CD45 and therefore BCR signaling in the generation of GM-CSF+ IRA B cells. Further experiments will be focused on the dissection of mechanisms that might be involved in CD45-dependent generation of pathological IRA B cells in atherosclerosis.

Abstract Title: Resolution of food protein-induced enterocolitis syndrome: an 8-year review at a pediatric referral center

Investigator: Spencer Chee
Co-Investigator(s): Victoria Shum, MD, EVMS Pediatrics\ Pediatric Residency; Kristina Roth, MD, CHKD Pediatrics; Kelly Maples, MD, CHKD Pediatrics\Divison of Allergy and Immunology
Department(s):

Abstract

Introduction:
Food Protein-Induced Enterocolitis Syndrome (FPIES) is a non-IgE mediated allergic food disorder that commonly presents with delayed, repetitive emesis 1 to 4 hours after ingestion. Further symptoms may develop such as lethargy, diarrhea, and hypotension which in severe cases can progress to hypovolemic shock that requires hospitalization.[1] Any food can trigger FPIES, but the most common triggers include cow's milk, soy, and grains. Current understanding of FPIES pathophysiology, long-term treatment, and natural history is limited. Unlike IgE-mediated food allergies, there are no biomarkers to predict the resolution of FPIES. Oral food challenges (OFC) are the current gold standard for assessing tolerance development, however, they are resource-intensive with unpredictable outcomes. Current literature suggests attempting an OFC within 12 to 18 months after the most recent reaction to assess resolution, but this guideline is broad and does not consider the food type involved or other patient-specific characteristics. The purpose of this retrospective study is to assess characteristics and time to resolution for FPIES patients. We hypothesize that the ideal timing of food reintroduction is > 18 months after the most recent reaction and varies based on the food type and patient age.

Methods:
322 charts of patients diagnosed with FPIES at CHKD's Allergy and Immunology clinic between 1/1/2010 - 12/31/2018 were reviewed. Characteristics of initial FPIES reactions and outcomes related to food re-introduction (if applicable) were recorded by two independent reviewers. Each reaction was categorized as acute or chronic and graded for severity based on the International Consensus guidelines for the diagnosis and management of FPIES. We defined clinical resolution as the completion of an OFC without symptoms. Patients with concomitant IgE-mediated symptoms to the FPIES food trigger, biopsy-confirmed diagnosis of eosinophilic gastrointestinal disease, and patients with both allergic proctocolitis and FPIES to cow's milk or soy were excluded.

Expected Outcomes:
We expect the proportion of failed OFCs to be greater than the proportion of successful OFCs within the 12-18-month window of the patient's last reaction. We also expect the development of tolerance for the offending food to vary by food trigger class (cow's milk, soy, grains, fruits, etc.) and age of the child.

[1] NOWAK-WEGRZYN ET AL

Abstract Title: Case Report: Orofacial Granulomatosis as an Indicator for Crohn's Disease

Investigator: Cinyu Chi
Department(s): Otolaryngology

Abstract

Introduction:

Oral manifestations of inflammatory bowel disease (IBD) vary widely. The prevalence of oral lesions in IBD ranges from 0.7-37% in adults and 7-23% in children. Recent studies have shown an association between Crohn's Disease (CD) and Orofacial Granulomatosis (OFG), a term that has been used to describe isolated oral lesions without associated intestinal disease, even in the absence of gastrointestinal symptoms. The overall prevalence of OFG in CD is unknown but has been increasingly related to pediatric patients with CD. A systematic review conducted in 2014 found that 40.4% of children with OFG were concomitantly diagnosed with Crohn's disease and 51.4% anticipated the diagnosis of Crohn's disease. A consistent delay in reaching the final diagnosis was reported with a mean time to diagnosis of 13.1 months. Stomatologists, dentists, and oral-maxillofacial surgeons were most frequently involved in diagnosis (64.7% of cases) followed by gastroenterologists (49.7%). In contrast, otolaryngologists were only involved in 7.5% of cases. The purpose of this case report is to emphasize the association between intestinal disease and macrocheilia, the most common manifestation of OFG, and increase awareness among otolaryngologists. We present a case of macrocheilia associated with CD.

Case Information:

A 13 year-old male with a past medical history of obesity, asthma, and sleep apnea presented to our ENT clinic with a four month history of intermittent non-pruritic lower lip swelling. He was previously evaluated by Allergy/Immunology and started on a trial of Zyrtec with minimal improvement. His C1 esterase inhibitor was normal. He was then referred to our pediatric ENT clinic 9 months after his initial evaluation. The left cheek was biopsied, and pathology showed hyperplastic mucosal epithelium with spongiosis and patchy submucosal mixed lymphohistiocytic inflammation consistent with granulomatous cheilitis.

Given the association of granulomatous cheilitis with Crohn's disease, the patient underwent a chest x-ray to rule out sarcoidosis and evaluation by gastroenterology 3 months later who performed an upper endoscopy and colonoscopy. Chest X-ray was within normal limits. Biopsies of the intestinal mucosa showed mild active ileitis with a rare granuloma consistent with Crohn's ileitis. Gastroenterology recommended starting the patient on Humira. Unfortunately, the patient did not experience significant improvement in his oral symptoms when assessed at his four-month follow up though he did report temporary improvement in the macrocheilia while on a trial of Prednisone.

Discussion:

Previous studies have suggested that OFG remains a largely unknown clinical entity among physicians. This case report emphasizes the importance of bringing awareness to different specialties to avoid a delay in diagnosis. In this case, the patient was not evaluated by gastroenterology until approximately one year after his initial evaluation, which is consistent with the mean time to diagnosis in the literature. This highlights the importance of educating providers on characteristic oral lesions that are concerning for CD.

Oral lesions in CD can be specific or non-specific. Specific lesions are less common, characterized by non-caseating granulomas on histology, and are commonly associated with CD. Oral lesions that should raise suspicion for an underlying intestinal source include indurated tag-like lesions, cobblestoning, muco-gingivitis, lip swelling with vertical fissures, and granulomatous cheilitis. Nonspecific lesions that are commonly seen in IBD include aphthous stomatitis, pyostomatitis vegetans, and angular cheilitis, but these are not specific. Previous studies have shown that approximately half of patients with oral granulomas showed involvement of the intestinal mucosa in the absence of gastrointestinal symptoms. Thus, oral lesions that are suspicious for CD should be an indication for gastrointestinal evaluation.

As otolaryngologists become more involved in the diagnosis of OFG, prompt recognition of lesions that are suspicious for CD could mitigate delays in diagnosis and provide an opportunity for early intervention. Although the impact of long-term disease outcomes in the setting of CD with no intestinal symptoms is unclear, recent studies regarding the treatment of CD have suggested that early intervention with use of biologics improves clinical outcomes and increases rates of remission in patients with shorter disease duration. Given that OFG is more commonly seen in the pediatric population, further research into the role of early biologic use in asymptomatic CD is needed.

Conclusion

In this case, we have highlighted the relationship between OFG and CD and emphasized the need for broader education on this topic. According to the literature, otolaryngologists are rarely involved in the diagnosis of OFG, however, greater awareness of this topic is needed to mitigate delays in diagnosis which may improve long-term clinical outcomes for patients with CD.

Abstract Title: Complex Intercoastal Embolization Following Stabbing

Investigator: Vaisali Chilamkurthy
Co-Investigator(s): Laura Columbus, Radiology\Residency
Department(s): Interventional Radiology

Abstract

Introduction:
Historically, tube thoracostomy has been regarded as the gold standard for treating traumatic hemothorax with refractory cases usually undergoing exploratory thoracotomy or video-assisted thoracoscopic surgery (Mowery et al 2011, Lohan et al 2011). Transcatheter arterial embolization (TAE) of intercostal artery (ICA) injuries is a minimally invasive strategy that has been shown to be an effective alternative to controlling traumatic hemothorax. Our case is a patient that suffered hemothorax following a penetrating chest wound. This patient possessed a unique arterial anatomy that presented as a challenge requiring repeat TAE and surgery.

Case:
20-year-old M presented as a bravo trauma after a penetrating wound to the left 6th rib space. Upon arrival, he was mildly tachypneic with BP of 118/74, heart rate of 80 beats/min, and oxygen saturation of 98% on room air. Physical exam revealed a young male in mild distress with a 3 cm laceration. CT chest/abdomen on admission showed left moderate-sized hematoma in the thorax as well as a rim of hyperdense blood seen at the periphery of the lateral left diaphragm. There was a small focus of free air in the stab wound path at the left anterior upper abdomen/lower chest raising suspicion for injury to hollow vicus organ. The patient was taken to the OR for diagnostic laparoscopy of possible diaphragmatic and gastric injury. In the OR, left-sided diaphragmatic injury was repaired and a thoracostomy tube was placed. Following the procedure, the patient had a significant output of 2.3 L of blood from the thoracostomy tube although his condition remained stable. CTA showed left-sided hemothorax with extravasation from a diaphragmatic artery. Interventional radiology performed angiogram with successful embolization to an anterior intercostal branch off the internal mammary artery. Following embolization, the patient continued to have significant chest tube output prompting repeat exploratory angiogram with coil embolization of a small pericardial branch off the left internal mammary artery (IMA). Despite embolization, there continued to be prominent chest tube output prompting exploratory thoracotomy where persistent bleeding was identified from a pericardial branch on the inferior aspect of the heart. The vessel was identified and clipped which stopped the bleeding. The patient made a successful recovery and was discharged.

Discussion:
Evidence from retrospective studies shows that the primary technical success (PTS) of embolization of ICA's in the setting of hemothorax is around 87% (Chemelli et al 2009). PTS in these studies was defined on an intent-to-treat basis and as successful embolization on the first attempt. Existing literature points to a multivariate approach when assessing determining the outcome of proceeding with TAE, particularly considering factors such as age, hemoglobin on presentation and presence of comorbidities including diabetes and hypertension. Notably, failure of embolization of ICA is also seen more often with cases where there is presence of collateralization of blood supply to the bleed source from the internal mammary artery. For example, one such case of persistent bleeding following embolization was found to have a rich collateral supply from the musculophrenic artery off the IMA (Tamburini et al 2019).

Conclusion:
Our case is a patient with unique arterial anatomy that required tube thoracostomy, repeat TAE, and exploratory thoracotomy finally resulting in the discovery of a bleeding vessel on the inferior surface of the heart. This case serves to educate clinicians on a unique case of traumatic hemothorax and emphasize that there is often a rich collateral supply that exists in the thoracic cavity. It is necessary for surgeons and interventionalists to have this understanding to be able to assess when to proceed with a minimally invasive strategy or a thoracotomy.

Abstract Title: Investigating the Effects of the Test-Enhanced Learning Strategy on Student MCAT Self-Efficacy Within the Dr. L.D. Britt Premedical Scholars Program

Investigator: Benjamin Chilampath
Co-Investigator(s): Jessica Bergden, PhD \ EVMS Department of Anatomy and Pathology; Natascha Heise, PhD \ EVMS Department of Anatomy and Pathology; Mekbib Gemeda, EdD \ EVMS Department of Diversity and Inclusion
Department(s): Department of Pathology and Anatomy

Abstract

Introduction:
Self-efficacy is regarded as an individual's belief in their capacity to execute or perform to a specific standard. Students with higher self-efficacy are more likely to take on academic challenges and persevere during difficult academic situations. These lead to a higher chance of a student achieving academically. There is currently a gap in research regarding the role of self-efficacy on standardized examination performance for underrepresented pre-medical students. This project aims to investigate team-based learning and testing-enhanced learning to conduct a Medical College Admissions Test (MCAT) preparatory course for underrepresented premedical undergraduate students. The purpose is to assess the effectiveness of this premedical MCAT program designed to improve the self-efficacy of underrepresented students enrolled in the Dr. L.D. Britt Premedical Scholars Program at EVMS.

Methods:
This program included four, two-hour sessions with each session dedicated to one of the four subject areas tested on the MCAT. The scholars were delivered lectures by medical student volunteers followed by passage quizzes, passage reviews, and group work. Self-efficacy and program effectiveness were measured via various means. Pre-session and post-session MCAT self-efficacy survey questions assessed the change in student MCAT self-efficacy from participation in the session. Supplementary survey items were included to measure the change in scholar motivation to study for the MCAT before and after completion of the program. Additionally, a post-course focus group evaluation obtained student perceptions about the program after its completion.

Results:
Scholar MCAT self-efficacy improved (from M=33.75, SD= 0.85 to M=40.33, SD= 0.65) after the completion of the program, $t(12) = 15.69$, $p < 0.0001$. These results suggest a meaningful increase in self-efficacy scores of the scholars participating in the program indicated by a large effect size (Cohen's d= 0.86). When looking at scholar MCAT self-efficacy scores of the individual subjects, the data is trending towards participants improving in their self-efficacy for all MCAT subjects; however, the differences in the means are not significant. Survey results also showed the scholars were more motivated to study for the MCAT after participating in the preparatory course (from M=10.37, SD= 0.84 to M=11.33, SD= 0.68). Qualitative feedback after the course demonstrated that scholars found the sessions helpful and engaging.

Conclusion:
The Dr. L.D. Britt Premedical Scholars participated in an MCAT preparatory course with test-enhanced learning and team-based learning. Results showed a meaningful increase in overall MCAT self-efficacy and scholar motivation levels. Future scholar participation in this longitudinal program, and a larger sample size, may further elucidate the benefits of the MCAT preparatory program on the self-efficacy of underrepresented premedical students.

Abstract Title: Evaluating the Process and Quality of Discharge Education in a Children's Hospital

Investigator: Benjamin Chilampath
Co-Investigator(s): Heather Beatty, BS / EVMS MD Student; Kyrie Shomaker, MD / CHKD Department of Hospital Medicine; Reyna Nikolaus, FNP / CHKD Department of Hospital Medicine; Turaj Vazifedan, DHSc / CHKD Department of Biostatistics
Department(s): Department of Hospital Medicine

Abstract

Introduction:
The pediatric discharge education process currently struggles with a lack of standardization, miscommunication between care team members, and non-patient-centered discharge communication. These issues contribute to medical errors, increased readmissions, patient dissatisfaction, and unnecessary healthcare costs. The purpose of this study is to understand the current level of caregiver comprehension in our hospital, streamline the discharge process via process mapping, and thereby identify opportunities for improvement that have the potential to reduce miscommunication, errors, and preventable readmissions.

Methods:
Summer scholars attended interdisciplinary huddles and daily rounds with the healthcare team, observed discharge education provided by team members to families, and met with team members to formulate an understanding of the discharge process. The created process map was analyzed to identify any gaps with potential for improvement. Additionally, questionnaires were created to assess the caregiver's comprehension of the discharge education, nurse prediction of the caregiver's understanding, patient demographics, and revisit rates to the hospital or ER within seven days of discharge. Questionnaires were administered after education was completed. Caregiver responses were scored for accuracy, by comparison, to discharge education as documented in the patient's chart. A 20% discrepancy between nurse prediction and the caregiver comprehension score was deemed a priori to be significant.

Results:
The final process map consisted of over 75 steps, completed by six different healthcare provider roles. Summer scholars identified over 20 discrete opportunities for improvement. Of the 93 patients whose education was reviewed, only 46% identified as non-white, but these accounted for 73% of the 15 cases in which a discrepancy in comprehension was identified. The return visit rate was 6.6%, with only 1 of these 6 having a greater than 20% discrepancy in comprehension scores.

Conclusion:
Despite the relatively weak correlation between nurse prediction of caregiver understanding and patient readmission, several aspects of the discharge process were identified that could improve patient understanding and reduce the likelihood of error, which could further ensure safe patient discharge and reduce readmissions. These include a need for functional improvements in the electronic medical record, better communication between members of the healthcare team, and increased team member role clarity.

Abstract Title: Patterns and disparities in Health Issues and Services Utilization Among Chinese Americans in Eastern Virginia - Findings from a Mixed-Method Study Conducted in 2022

Investigator: James Chung
Co-Investigator(s): Elizabeth Li, Eastern Virginia Medical School Of Medicine; Tram H. Phung, Eastern Virginia Medical School Of Medicine; Timothy W. Liu, Eastern Virginia Medical School Of Medicine; Catilyn F. Ling, Eastern Virginia Medical School Of Medicine; Spencer G. Chee, Eastern Virginia Medical School Of Medicine; Tracy Dien, Eastern Virginia Medical School Of Medicine; Jamie Luis D. Almirante, Eastern Virginia Medical School Of Medicine; Marc Franco T. Nepomuceno, Eastern Virginia Medical School Of Medicine; Cynthia C. Romero, Eastern Virginia Medical School Of Medicine; Hongyun "Tracy" Fu, EVMS Department of Pediatrics
Department(s): Department of Pediatrics

Abstract

Background:
Chinese Americans have been stereotyped as "a model minority group" in many studies, although they comprise diverse subgroups of people with different social, economic, and health profiles. We explored the perceived health status, concerns, and service utilization as well as the disparities across subgroups, using data from a mixed-methods community health resource and needs assessment (CHRNA) conducted in 2022 among Asian and Pacific Islanders (APIs) in Eastern Virginia.

Methods:
The CHRNA quantitative survey was implemented online via REDCap in April/July 2022. Respondents were recruited from a range of social media channels and in-person events via the existing API networks in Eastern Virginia, following three criteria: 1) decedents of Asian and Pacific Islanders, 2) ages 18-85 years, and 3) residents of Hampton Roads and the Eastern Shore. Data from a subsample of respondents who self-reported as Chinese decedents (N=509) were analyzed, using descriptive statistics and multivariable logistic regression. Furthermore, key informants (N=23) were recruited through snowball sampling and referrals from Chinese community stakeholders. Semi-structured interviews (30-60 minutes) were conducted virtually via Zoom in English and Chinese by trained bilingual researchers. Semantic analysis was conducted to identify the key theme, guided by the grounded theory.

Results:
The most commonly raised health concerns included cardiovascular diseases (28.7%), cancer (23.2%), and diabetes (22.6%). About one-third (35.6%) of respondents had a flu vaccine, and less than half (49.7%) had a routine check-up during the past 12 months. Concern over COVID-19 infection (42.0%), language barriers (21.6%), and appointment cancelation (14%) were major barriers to healthcare utilization in the past year. While 7.1% received a diagnosis of mental health problems, 12.8% frequently experienced symptoms of depression. Significant disparities existed, with the odds of having physical and mental health problems being higher among individuals who were older, had lower education, worked in blue-collar professions, and had no insurance coverage.

Conclusions:
Findings revealed significant prevalence in health problems with few acute symptoms that take years to manifest and those involving regular screening such as cancer, diabetes, cardiovascular disease. This is suggestive of how Chinese place lower emphasis on conditions that can be asymptomatic and only on immediate detectable disease. This trend is also shown by how most mental health conditions in Chinese Americans in our study tend to go untreated or undiagnosed according to our results, further depicting the lack of attention and support to these health conditions. Findings also revealed significant disparities in health problems and access to healthcare services across subgroups of Chinese Americans, highlighting the heterogeneity of the Chinese community and the need for further studies and targeted intervention to support disadvantaged people to reduce health disparities.

Abstract Title: A Case Report of Thoracic Mycotic Aortic Aneurysm and Adjacent Osteomyelitis

Investigator: Mark Clark
Co-Investigator(s): Dylan Steffey MD, Radiology Resident; Christopher O'Neil MD, Radiologist
Department(s): Radiology

Abstract

Introduction:
Mycotic Aortic Aneurysm is an uncommon diagnosis, describing an infected dilatation of the aorta, which may be the primary result of infectious degeneration of the vessel wall, or may describe pre-existing aneurysms that become secondarily infected. Characteristic radiological findings include a lobulated, saccular appearance of the aneurysm, soft tissue inflammation surrounding the vessel, intramural air, or a perivascular fluid collection. This case is that of a 73-year-old gentleman with an unusual presentation of mycotic aneurysm and adjacent osteomyelitis/discitis.

Case Information:
MM is a 73 year old man with hypertension and 1 ppd cigarette usage, presenting to the Emergency Department for worsening abdominal pain which he has had, on and off, for the last 6 months. He denies any chest pain, shortness of breath, or numbness/tingling in his feet. Physical exam revealed an afebrile, nonseptic, well appearing man. Exam was only positive for mild tenderness to palpation in the epigastric region.

Laboratory results at time of presentation were grossly benign. CT Abdomen/Pelvis with contrast noted concern for a penetrating aortic ulcer at the level of the diaphragm with slow leak but no active contrast extravasation and an adjacent fluid collection concerning for an abscess. Subsequently, a CTA Chest/Abdomen/Pelvis characterized a focal 2.9 x 1.6 cm, saccular aneurysm of the distal descending thoracic aorta with surrounding soft tissue inflammation suggesting a mycotic aneurysm. Exam also revealed a subtle erosion of the anterior, inferior endplate of T10 concerning osteomyelitis/discitis.

Discussion/Clinical Findings:
A multidisciplinary approach was required for the treatment of this patient given the added concern for osteomyelitis/discitis, which was later biopsy confirmed. Medical management with long term antibiotics was sufficient for treatment of the osteomyelitis/discitis. For the mycotic aneurysm, the decision was made to proceed with open thoracoabdominal surgical repair with graft placement using cryopreserved aorta. Findings during surgery included a large posterior aneurysm cavity, but no gross pus. This patient had a complex postoperative course, including septic shock and acute hypoxic respiratory failure necessitating prolonged antibiotic and resuscitation as well as tracheostomy. He was eventually able to be discharged to a long-term care facility with suppressive antibiotics and close follow up.

Conclusion:
Thoracic mycotic aortic aneurysm with concomitant, adjacent thoracic vertebral osteomyelitis and discitis is a rare pathology with a highly morbid prognosis but may present with a subtle finding, often relying on radiological evidence. It is unknown whether the aorta or the vertebra were the source of infection in our patient, though he had no prior history of aneurysm. Nonetheless, in the reported instances of this pathology, aneurysm rupture is the most common cause of mortality. Classically, the literature describes an open repair procedure, followed by long term antibiotics, similar to the above patient. However, there are examples of endoscopic stenting being performed with successful outcomes.

Abstract Title: The Needle That Broke the Camel's Back: A Case of Spinal Gout

Investigator: Mark Clark
Co-Investigator(s): Mruna Patel MD, Internal Medicine Resident; Jody King MD, Internal Medicine
Department(s): Internal Medicine

Abstract

Introduction:
Gout is a common cause of inflammatory arthritis affecting approximately 8 million Americans. It is caused by deposition of monosodium urate (MSU) crystals in the synovial joints that commonly manifests as a monoarticular arthritis however spinal manifestations are rare. This case report highlights the importance of keeping our differentials broad and also sheds light on the right imaging modality needed to assess crystal arthropathy. Traditionally, the gold standard for gout diagnosis has been microscopic confirmation of needle-shaped MSU crystals. However, this is not always feasible because of difficulty accessing small joints that may be affected by disease. Dual-energy computed tomography (DECT) is a recently developed advanced imaging method which is a non-invasive method to assess urate deposition.

Case Information:
A 25 year-old man with a past medical history of Bartter Syndrome, Chronic Kidney Disease IV, and Gout presented to the emergency department for evaluation of 6 days of progressively worsening back pain located in the lower mid back. Pain was not prompted by any movement or recent injury. He denied any fever, chills, nausea, vomiting, weakness, numbness, tingling, bowel or bladder changes. He did report frequent Emergency Department (ED) visits due to gout pains, primarily in the lower extremities and is managed with allopurinol 200mg daily.

In the ED, vital signs were normal and stable. Physical exam revealed no bony vertebral tenderness, normal muscle tone, 5/5 strength and sensation intact to light touch to bilateral upper and lower extremities. Labs revealed a worsening creatinine in the setting of CKD4, hypokalemia, hypomagnesemia, and mild leukocytosis of 11.6. He received supplemental magnesium, IV fluids, and morphine for pain.

Initial CT scan showed a soft tissue lesion centered at the left T10/T11 neural foramina possibly arising from the left T10/T11 facet joint. Lumbar and thoracic MRIs was obtained without contrast due to renal disease and revealed characteristic findings of chronic inflammatory arthropathy with resultant minor cord contact but no cord edema or atrophy.

Discussion/Clinical Findings:
There was concern for spinal epidural abscess. Patient became intermittently febrile to 102.9F on day 3 of hospitalization and developed a worsening leukocytosis to 16.4. Infectious etiology could be explained by a distant history of dental infections although there had been no recent infections and physical exam did not show any current abscess or obvious infection. Patient was started on Vancomycin and Ceftriaxone.

CT-guided aspiration of the left paraspinal fluid collection revealed 5-6cc of cloudy/turbulent non-purulent appearing fluid. Pathology revealed sterile fluid with negative cultures. Since culture negative spinal epidural abscess could not be ruled out, the plan was to complete 6 weeks of Vancomycin and Ceftriaxone with weekly lab monitoring.

Further infectious imaging workup included TTE, MRI C-spine, and Panorex dental imaging which were all negative. Given the unclear etiology of patient's persistent back pain, a dual energy CT was obtained and fortunately revealed a 4.9cm lesion urate crystal at the left T10/T11 neuroforamen with additional associated erosive changes at the left T8/T9 level measuring 9mm confirming a spinal gout flare. The patient was treated with IV solumedrol inpatient with plan for a 2 week oral prednisone taper upon discharge.

Conclusion:
Dual energy computed tomography (DECT) is a recently developed imaging modality which aids in visualization of mono-sodium crystal depositions and has previously shown excellent accuracy in detecting uric acid kidney stones. It uses two x-ray sources to run simultaneously with two corresponding detectors which provides two spiral data sets that are acquired in a single scan. Imaging modalities like DECT, which has shown excellent accuracy, should be more utilized as a non-invasive diagnostic option for detecting and monitoring gout.

Abstract Title: Implementation of Standardized Radiology Education in Pediatric Residency Curriculum

Investigator: Laura Columbus
Co-Investigator(s): Daniel O'Neal, Interventional Radiology\University of Pittsburgh Medical Center
Department(s): Radiology\Florida Atlantic University

Abstract

Introduction:
An integral part of residency is didactic education. Imaging is vital to the diagnosis and treatment of patients. It is important for physicians to learn how to comfortably order and, at times, preliminarily interpret imaging within a narrow scope. At our institution, pediatric residents periodically selected cases to review with a pediatric radiologist. It was felt that increased structure, while maintaining a heavy emphasis on cases, would be beneficial.

Methods:
The curriculum involved five parts; a pre-curriculum survey, a pretest, a standardized lecture series, a posttest, and a post-curriculum survey. The pre-curriculum survey gauged interest in reformatting a radiology curriculum, confidence in interpreting and ordering studies, and which topics they wanted to cover. This data was used to create 8 standardized lectures, which were given during the 2021-2022 academic year. The lectures consisted of appropriately 10-15 minutes of didactic material, presented to optimize adult learning. The topics were basic and tailored to the need of the over-night trainee. Each lecture gave images and education of the topic. Most of the session was spent working through basic radiographic cases with the use of the audience response software Poll Everywhere (Poll Everywhere TM). Following the completion of the lecture series, a posttest and survey were administered. The types of questions asked included multiple choice, free response, word cloud, true/false, and clickable images. Following the completion of the lecture series, a posttest and survey were administered. Both the pre and post-test questions were identical with 10 multiple choice questions, followed by 14 free choice questions based on images presented, totaling a maximum score of 24 points. Half credit was given if part of a free choice question was correct.

Results:
A total of 28 residents completed the pretest, and 15 completed the posttest. There was a statistically significant increase in the mean test score of the posttest compared to the pretest (p value of 0.03).

The survey questions were structured as a 5-point Likert scale ranging from negative (1) to positive (5). The answers were analyzed using a Wilcoxon Signed Ranks Test ($p<0.05$ considered statistically significant). A total of 21 residents completed the pre-survey, and 16 completed the post survey. The questions analyzed were "How important are imaging studies to your ability to practice medicine?", How comfortable are you in interpreting radiographs?", "How comfortable do you feel ordering imaging studies?", and "Do you feel that you receive adequate training to order the optimal studies for your patients?". No statistical difference was found between the pre and post curriculum survey answers with p values of 0.18, 0.56, 1.00, and 0.66 respectively.

Conclusion:
There was a statistically significant increase in mean posttest scores compared with pretest scores, suggesting that pediatric residents acquired and retained radiological knowledge over the course of the academic year.
There was, however, no statistical difference in residents' perceptions of their radiology education. Many factors likely influenced these findings, including lower response on the post survey compared to the pre-survey (16 vs 21). Statistical analysis was also limited due to the anonymous nature of the surveys.

Abstract Title: Geographic Adjustments in Medicare Compensation for Trigger Finger Release at Ambulatory Surgery Centers Compared to Cost of Living

Investigator: Parth Contractor
Co-Investigator(s): Thomas B Marhsall, EVMS MD 2024; Carlo DelDonno, EVMS MD 2025
Department(s): Pathology and Anatomy

Abstract

Introduction:
Medicare reimbursement is currently adjusted to accommodate for regional differences in healthcare delivery input costs such as wages paid to employees. These input costs vary based on a variety of factors including geographic location and adjustment is made by the Center for Medicare and Medicaid Services using the Hospital Wage Index and Geographic Practice Cost Indexes. However, it is unclear whether the current adjustment model adequately corrects for geographic input cost differences leading to potential increased healthcare costs. Prior studies have shown that Medicare reimbursements have decreased over time compared to consumer price index and that geographic adjustments have decreased. No study to date has examined the relationship between compensation adjustment for a single procedure and regional cost of living. Trigger Finger release is a common orthopedic procedure performed for flexor tenosynovitis of A1 pulley. We evaluated the relationship between Medicare allowed payments and regional cost of living for trigger finger releases performed at ambulatory surgery centers in the state of Virginia.

Methods:
Medicare reimbursement data for trigger finger release performed at ambulatory surgery centers in Virginia in 2020 was retrieved from the Medicare Physician & Other Practitioners database on CMS.gov. Livingcost.org, a crowdsourced database that calculates living cost as a consumer basket for a modern lifestyle, provided the cost of living data for one person in the location of each ambulatory surgery center. Surgery centers in locations without cost-of-living data were excluded. A regression analysis of the data was conducted in Microsoft Excel.

Results:
Fourteen surgery centers met inclusion criteria providing 1193 services in total. Average allowed reimbursement ranged from $393.30 to $636.11 (Mean = $528.98, SD = $62.99). Cost of living ranged from $1562 to $2704 (Mean = $2065.57, SD = $372.63). Unstandardized analysis showed an intercept of 310.19 and coefficient of 0.106 ($r^2 = 0.393$, $p = 0.00215$). This indicates an increase in compensation of $0.106 for each $1.00 increase in regional cost of living. Standardized regression analysis showed an intercept of 4.3E-05 and coefficient of 0.627 ($r^2 = 0.393$, $p = 0.0165$). This indicates a 0.83 standard deviation increase in compensation for each 1 standard deviation increase in cost of living.

Conclusion:
Our findings indicate a significant positive linear relationship between Medicare allowed reimbursement and regional cost of living. For every $1.00 increase in cost of living there is a $0.106 increase in allowed compensation to the ambulatory surgery center in Virginia. Our data strengthens the idea that the CMS database can be used as a valid tool for examination of reimbursement rates. Further investigation is required to determine whether adjustments in reimbursement adequately compensate for regional differences in input costs. Further research should examine reimbursement for multiple procedures to determine generalizability of these findings.

Abstract Title: Therapeutic Alliance in Telemental Health

Investigator: Julia Cornelius
Co-Investigator(s): Nicole Wells, PhD, CHKD Children's Specialty Group
Department(s): CHKD Children's Specialty Group

Abstract

Introduction:
Mental health concerns in youths are increasing, especially since 2020 (Racine et al, 2021). Telemental health (TMH) increases access to mental health care (Myers et al, 2008) and was quickly adopted during the pandemic, but its future availability may be threatened by third-party payer regulations and limited empirical support. While TMH offers logistical advantages to in-person care, the therapeutic patient-clinician alliance, a strong predictor of clinical outcomes (Shirk et al, 2008; Hawley and Weisz, 2005), has not been studied extensively in TMH settings. This study examined family satisfaction and quality of therapeutic alliance in TMH early in the COVID-19 pandemic.

Methods:
Between April and October 2020, the CHKD mental health program invited caregivers of all 2,045 scheduled patients to complete a survey about caregiver perception of alliance (Munder et al, 2010) and caregiver satisfaction (Myers et al, 2008). Descriptive and correlational statistics were performed using nonparametric tests in SPSS.

Results:
Caregivers of 306 children responded to the survey; of those responses, 297 had completed their first TMH appointment and were analyzed for this study. Patient age ranged from 2 to 26 years old, with a mean of 12.15 years old. There were 137 females (46%) and 161 males (54%). Most caregivers reported that their child would not have received mental health care without TMH. On all caregiver satisfaction items, the mean score was above 4.0 on a 5-point Likert scale. On all alliance items, the mean score was above 6.0 on a 7-point scale. Neither satisfaction nor alliance differed between patients new to the mental health program or established with the program prior to telehealth ($p>0.05$). No differences across child gender, across age, among reported race, or among insurance types were identified for either satisfaction or alliance ($p>0.05$). Notably, satisfaction was similar for families seeing therapists compared to prescribing clinicians ($p>0.05$), but alliance was higher for therapists than prescribing clinicians ($U=8122$, $p<0.023$). Unsurprisingly, caregivers reporting interest in telehealth prior to the pandemic reported higher satisfaction ($H(4)=78.8$, $p<0.001$) and alliance ($H(4)=17.3$, $p<0.01$).

Conclusion:
Our findings demonstrate high caregiver satisfaction and positive caregiver perceptions of alliance in a TMH setting. Notably, even caregivers who were not previously interested in TMH were highly satisfied and reported strong alliance. This study is the first to demonstrate that therapeutic alliance, a key predictor of mental health outcomes, can be achieved in TMH settings, supporting continued use beyond the pandemic. TMH offers a platform to address child mental health in a way that is satisfying to families and supports a strong therapeutic alliance. TMH can play an important role in delivery of child mental health services.

Abstract Title: Pathologic Examination of a Neonate with Probable Larsen Syndrome: Unique physical findings

Investigator: Emery Cuellar
Co-Investigator(s): Makailla Kastner, Pathology Assistant Program
Department(s): Pathology

Abstract

Introduction:
Larsen syndrome is a rare genetic disorder caused by mutations in the FLNB gene affecting an integral protein in cytoskeleton development, filamin B. This disorder affects 1 in 100,000 newborns with common findings being characteristic facial features including frontal bossing and ocular hypertelorism as well as significant skeletal and joint deformities. With medical management primarily focused on orthopedic interventions these patients often have a normal life expectancy with normal intellectual development although the syndrome is associated with so many orthopedic deformities its management has been described as a "herculean task" (1).

Case information:
The patient is a 24 day old female neonate presented for autopsy. Her medical history is significant for multiple congenital anomalies and respiratory distress requiring transfer to the NICU and a genetics consult. She also had significant neonatal maternal substance exposure and was small for gestational age with congenital hypothyroidism. Upon initial genetics consultation, the patient was noted to have several features seen in Larsen syndrome, including dislocations of the knees and hips, frontal bossing, flat nasal bridge, cleft palate, and abnormal metacarpal bones. A full DNA testing panel was sent for further evaluation. She was discharged in the care of a foster family with her medical course further complicated by failure to thrive requiring supplemental nasogastric tube feeds with her normal oral feeds. She was found in bed without signs of life with no return of cardiac activity despite prolonged medical intervention. Upon postmortem examination, several findings were documented consistent with Larsen syndrome including hypertelorism, spatulate fingers, rhizomelia, bilateral clubfeet and cleft palate. She also had findings previously undocumented in association with Larsens including a widely open anterior and posterior fontanelle, a large heart relative to patient's size and melanotic finger/toe tips. Pertinent negatives upon pathologic examination include no signs of trauma externally or internally and this patient appeared well cared for. Genetic testing revealed 8 unique variants of uncertain significance including an abnormal variant at FLNB, the gene associated with Larsen syndrome. The final diagnosis is probable Larsen syndrome based on the genetic testing and characteristic features found in the patient. The final pathological diagnosis for this patient is sudden unexplained infant death associated with Larsen syndrome with additional diagnoses of patent foramen ovale, ovarian cysts, and inability to rule out fetal alcohol effect.

Discussion:
This case is noteworthy as few postmortem exams exist in the literature regarding a patient with Larsen syndrome. This patient also died unexpectedly without a clear cause and while most patients with Larsen syndrome reportedly have a normal life expectancy, respiratory failure and early respiratory death have been reported as part of the syndrome (1). Upon literature review, there is a reported association between Larsen syndrome and tracheomalacia and laryngomalacia with one patient presenting with respiratory difficulty secondary to tracheal stenosis (2). In another case, a 9 month old female with Larsen's suffered attacks of respiratory failure thought to be caused by softening of the larynx and trachea with microscopy revealing a reduced number of elastic fibers in the larynx, trachea and bronchi (3). Apart from tracheo/larynogomalacia causing pulmonary compromise or death in these infants, the etiology could involve cord compression or flaccid paresis leading to respiratory weakness and failure making a throughout neurological evaluation very important in these patients to identify cervical kyphosis (1). This patient did have cervical kyphosis identified on bone survey with no noted interventions.

Conclusion:
This is a rare case as it is estimated only 5,000 individuals in the United States have Larsen Syndrome with unique physical exam findings previously unreported as characteristics of this disorder. This patient was at risk for sudden unexplained infant death due to the increased risk of respiratory failure from both her upper airway as well as centrally from cervical kyphosis both features of Larsen syndrome.

Abstract Title: ADHD Prescription Patterns and Medication Adherence in the COVID-19 pandemic

Investigator: Peter Cunniff
Co-Investigator(s): Amil Ahsan, EVMS MS2; Catherine MCrary, EVMS; Tracy Dien, EVMS MS2; Tristan Kuhn, EVMS MS2; Turaj Vazifedan MS, CHKD; John Harrington MD, CHKD GAP
Department(s): CHKD GAP

Abstract

Introduction:
COVID-19 has altered the traditional classroom model of education from an in-person to virtual and hybrid platforms, which has put students with attention deficit hyperactivity disorder (ADHD) at risk of disruptions in their medication regimen and school performance. In addition, telehealth appointments have become increasingly more common during the pandemic. One way to analyze ADHD management is through medication adherence, which can be measured through the prescription refill schedule of patients. Our study aims to identify if ADHD medication regimens were disrupted during the pandemic and if telehealth management demonstrates a higher rate of adherence.

Methods:
A total of 396 General Academic Pediatric (GAP) patients between the ages of 8-18 with a history of ADHD for three or more years managed with medications were recruited. A retrospective chart review collected age, sex, race, refill schedule, and appointment schedule.

Results:
The total percentage of patients who had their ADHD medications refilled pre-pandemic between January 2019 and March 2020 ranged from 40-66%, as opposed to 31-44% between April 2020 and May 2022, $p<.001$. Additionally, the total percentage of patients who had quarterly ADHD management appointments between January 2019 and March 2020 ranged between 61-70% as opposed to 33-50% between April 2020 and June 2022, $p<.001$. The number of months that an ADHD prescription was refilled was significantly correlated with total number of ADHD appointments ($r=0.40$, $p<0.001$), virtual appointments ($r=0.27$, $p<0.001$), and in-person ($r=0.35$, $p<0.001$) ADHD appointments. There was a negative correlation between increasing age and number of months that ADHD prescription was refilled ($r=-0.12$, $p=0.012$). Also, increasing age was negatively correlated with total number of ADHD appointments ($r=-0.30$, $p<0.001$) and number of in-person appointments ($r=-0.31$, $p<0.001$).

Conclusion:
Since the start of the pandemic in the US in March 2020, ADHD patients have neither refilled their medications nor been seen as frequently by a physician. Even before the pandemic started, many ADHD patients were not on a consistent management regimen. This data suggests a need to re-evaluate the ADHD symptoms of GAP patients periodically and return them to a more consistent medication regimen as well as implement methods to increase adherence to greater than pre-pandemic levels. Telehealth appointments are a potential solution to increase adherence among ADHD patients.

Abstract Title: Investigating the Diagnostic Utility of Structural and Functional Measures of Nerve Function for the Identification of Peripheral Neuropathy in Subjects with Type 2 Diabetes

Investigator: Courtny Cushman
Co-Investigator(s): Carolina M. Casellini M.D, Strelitz Diabetes Center; Henri K. Parson, PhD, Strelitz Diabetes Center; Elias S. Siraj M.D., Strelitz Diabetes Center
Department(s): Strelitz Diabetes Center at EVMS

Abstract

Introduction:
Diabetic peripheral neuropathy (DPN) is the most common long-term complication of diabetes, yet it has no cure. However, identifying DPN in the clinic can be challenging. The purpose of this study is to identify reliable diagnostic tools for the detection of DPN in subjects with Type 2 Diabetes Mellitus (T2DM).

Methods:
Two hundred and thirty-two healthy controls (HC) and subjects with T2DM, with (DM-DPN) and without DPN (DM-no DPN) were recruited. DPN was defined according to the 2010 Toronto Consensus Guidelines. All patients were evaluated with the following measures: neuropathy deficit scores, nerve conduction studies, quantitative sensory testing for thermal (WST & CSD) and vibration perception thresholds (VDT), in vivo corneal confocal microscopy for the quantification of corneal nerve fiber density and length, sudomotor function testing (feet and hands electrochemical skin conductance (ESC)), and cardiac autonomic reflex testing (CART). Receiver operating characteristic (ROC) areas under the curve (AUC) with respective sensitivity and specificity values were calculated for each measure analyzed

Results:
All groups were well balanced for gender and race (59% females and 48% African Americans). DM-DPN subjects were older and had longer duration of DM. As expected, T2DM subjects were more overweight and had worse metabolic profiles. Both structural and functional measures of DPN were significantly worse in DM-DPN subjects. Of all the measures evaluated, neuropathy scores, WST, VDT, and feet ESC showed the best accuracy for detecting DPN (AUC of 0.838, 0.820, 0.755, and 0.710 respectively and sensitivity/specificity of 82/44, 80/52, 78/57, and 71/62 % respectively).

Conclusions:
This study shows that different functional measures evaluating somatic and autonomic nerve fiber function have better accuracy than structural measures for the detection of DPN. Future studies need to investigate the best combination of methods to detect DPN and monitor progression of disease.

Abstract Title: An Unexpected Case of Meningococcal Pericarditis

Investigator: Kaivalya Dandamudi
Department(s): Internal Medicine/Infectious Disease

Abstract

Introduction:
Neisseria meningitidis is most commonly known to cause bacterial meningitis. Meningococcal pericarditis is a rare manifestation and current literature classifies the disease into three categories: pericarditis with disseminated meningococcal disease, isolated meningococcal pericarditis, and immunologic meningococcal pericarditis. We present a case within the first category, meningococcal pericarditis with bacteremia in a patient with human immunodeficiency virus (HIV).

Case Information:
A 31-year-old male presented to the ED for chest pain, shortness of breath, and intermittent nausea and vomiting for 3 days. The patient went to the ED 2 days prior for similar symptoms, had a negative workup, and was discharged home on Acetaminophen and Ibuprofen for a presumed viral infection. The patient returned due to persistent symptoms. Medical history was significant for HIV with intermittent antiretroviral therapy (ART) use and a sick contact 5 days ago. He noted the sick contact to be his partner who awoke in the middle of the night with fevers, chills, diarrhea, and vomiting. Upon arrival, his EKG showed diffuse ST segment elevation and his Troponin was 30 ng/L. Cardiology was consulted and a transthoracic echocardiogram (TTE) demonstrated a large pericardial effusion measuring 2.32cm, mildly reduced left ventricular systolic function, and an ejection fraction of 45%. The patient was diagnosed with acute pericarditis and admitted to the hospital.

Infectious disease was consulted for the management of the patient's HIV ART in the setting of acute pericarditis. His vitals during physical exam were as follows: blood pressure 128/110, heart rate 117, and temperature 97.2ºF. A pericardial friction rub was auscultated and the patient was actively vomiting clear emesis. The remainder of the exam was unremarkable. Labs were significant for a leukocyte count of 18.5 K/uL with 76% segmented neutrophils, 14% bands, 4% lymphocytes, absolute CD4 77 (CD4 % 11.1), and HIV viral load 77 copies.

On day 2, diagnostic testing revealed blood cultures positive for gram-positive cocci (GPC) and the patient was started on empiric Vancomycin for GPC bacteremia. On day 3, the original blood cultures re-speciated to gram-negative cocci (GNC) and all subsequent blood cultures also grew GNC, eventually speciating *N. meningitidis*. The patient was immediately started on Ceftriaxone (2g q 12hrs). On day 4, a pericardiocentesis was completed and 335cc of purulent pericardial fluid was removed. A lumbar puncture was also performed which was not consistent with meningitis. Gram stain of the pericardial fluid was positive for gram-negative diplococci and the patient was ultimately diagnosed with meningococcemia with meningococcal pericarditis.

He reported significant improvement in symptoms following the pericardiocentesis. Ceftriaxone was continued for the remainder of the hospital stay, ART was restarted, and Vancomycin was discontinued. Blood cultures from day 4 showed no growth at 5 days, his leukocyte count dropped to 10.6 K/uL and repeat TTE showed a reduced pericardial effusion (1.46cm). The patient was discharged on hospital day 9 with a PICC line to receive Ceftriaxone outpatient for a total duration of 4 weeks.

Discussion / Clinical Findings:
Although *N. Meningitidis* is an uncommon cause of purulent pericarditis, it can lead to a severe form of the disease. While our patient was promptly diagnosed with acute pericarditis, there was initially minimal evidence to suggest a bacterial etiology or systemic meningococcal disease except for the leukocytosis with left shift. Our case demonstrates the importance of having a high clinical suspicion for meningococcal pericarditis despite the absence of classic features of meningococcal disease, severe symptoms, and when pericarditis symptoms present in conjunction with acute meningococcemia. This is especially important in patients who are immunocompromised and may not have the ability to mount an appropriate immune response as evidenced by our patient.

Conclusion
Meningococcal pericarditis is a rare form of *N. meningitidis* infection and can have any atypical presentation inconsistent with systemic meningococcal disease. This case demonstrates the importance of prompt recognition and management in order to prevent progression to cardiac tamponade and shock.

Abstract Title: A Proposed Case of Branchio-oto-renal (BOR) Syndrome First Diagnosed on the Psychiatric Ward

Investigator: Riccardo De Cataldo
Co-Investigator(s): Steven Forte, EVMS M4; Chelsey Rountree, MD, EVMS Psychiatry; Dylan Golomb, MD, EVMS Psychiatry; James Rapley, MD, EVMS Psychiatry
Department(s): Psychiatry

Abstract

Introduction:
Branchio-oto-renal (BOR) syndrome, also known as Melnick-Fraser Syndrome, is an inherited, autosomal dominant mutation in several genes, primarily Eyes Absent Homolog 1, EYA1. Mutation of this gene results in embryonic malformation of the neck, ears, and kidneys. Specifically, one may find cystic structures derived from the brachial clefts along the lateral aspects of the neck; low-set and malformed external ears; hearing impairment or loss due to middle-ear malformations; and lastly absent or hypoplastic kidneys that commonly present with bladder malformations. 1,2 BOR syndrome has a prevalence of 1/40,000. Treatment focuses primarily on symptomatic management, emphasizing the preservation of renal function to delay transplant or dialysis as long as possible.3 Other treatments may include ear and bladder reconstructive operations and cochlear implants with education for hearing loss. Typically this constellation of symptoms is diagnosed in childhood, however, we present a case of a 30-year-old man without a formal diagnosis who was hospitalized for psychiatric concerns resulting from the symptoms of this syndrome. Interestingly, no apparent family history of this disease possibly suggests the development of BOR from a spontaneous mutation or unrecognized disease in family members.

Case Information:
LS is a 30-year-old, African American male with a past medical history of posterior urethral valves, single kidney, and obstructive uropathy. He has had many surgeries to correct his congenital obstructive uropathy with a single hypoplastic kidney, which have included: gastrocystoplasty (bladder augmentation with a segment of the stomach) and an appendicovesicostomy (the appendix is used as a conduit for urine from the bladder to abdomen/navel). This patient has also had a failed renal transplant at age 13, in part to patient nonadherence to medications, and numerous AV fistula operations with revisions for his dialysis ports since then. The patient presented to the ED with suicidal ideations with plan as well as reporting poor sleep, depressed mood, and chronic fatigue resulting from these conditions and chronic anemia (Hgb baseline ~6.5) secondary to chronic hematuria from his gastrocystoplasty, which is due for a revision.

Discussion:
His extensive medical history has required significant interventions with frequent hospital/doctor visits, which has resulted in a multifactorial medical and psychiatric cause for his chronic fatigue. This constellation of significant symptoms without a formal diagnosis in three decades of medical care potentially suggests a case where multiple healthcare providers focused on treatment of symptoms and disease states without considering the patient as a whole. This syndrome is commonly diagnosed in childhood, but family and the patient were never informed of any syndromic diagnosis. The addition of residents and medical students allowed the care team to spend time investigating this possible diagnosis for a patient who had been suffering for 30 years with no explanation for his failing health. Offering a potential diagnosis of this patient's syndromic condition enabled the psychiatric team to more fully address the psychosocial factors impacting his depressed mood, which led to an improved clinical response versus just treating his mood biologically. Furthermore, given the genetic inheritance component of BOR would suggest family members should undergo genetic testing if they desire.

Conclusion:
Rare and debilitating diseases contribute to psychosocial stressors and impact the psychiatric health of patients. Adequate diagnosis of rare conditions, such as branchio-oto-renal syndrome, should not be overlooked on the psychiatry wards as diagnosis and education can improve the psychiatric care of patients by providing closure and allowing better-informed discussions regarding goals of care.

Abstract Title: Investigating Urine Biomarkers to Determine Progression of Bladder Cancer

Investigator: Rose Dever
Co-Investigator(s): Caleb Smack, MD 2025
Department(s): Leroy T. Canoles Jr. Cancer Research Center and Deptartment of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Bladder Cancer is the 6th most common cancer in the United States, representing nearly 5% of all cancer diagnoses. It is four times more common in men than women, and is the eighth most deadly cancer in the U.S.1 Bladder cancer is pathologically staged as pTa (non-invasive), pT1 (invasion of lamina propria), or pT2 (muscle invasive disease). Patients with T1 disease can undergo transurethral resection of the bladder tumor (TURBT), while the treatment for those with T2 disease is a radical cystectomy, with or without an adjunctive chemotherapy treatment2. Given the distinct treatments and the implications on quality of life, differentiating between the two disease states is highly advantageous to both patient and physician. It is difficult to distinguish between the two conditions, however, and even more challenging to determine whether a T1 bladder cancer will progress to a T2 disease. As such, a prognostic test in the high-risk urothelial patient would be welcome and could affect clinical decision-making.

Methods:
Analyzing urine samples is a favorable method for studying bladder cancer, as urine is in close contact with the diseased cells. Since 2013, a urology clinic specializing in high-risk cases of bladder cancer has been collecting and storing urine samples from its patients for future study. Patients were selected to participate if they had bladder cancer. Informed consent was obtained prior to the collection. As of September 2022, over 800 urine samples have been collected. The specimens include newly diagnosed samples as well as follow-up urine samples on the same patients throughout their disease and treatment.

To begin analyzing the samples, the patients were organized into five cohorts based on the number of urine samples obtained, with Cohort 1 having the most samples and Cohort 5 having the least samples. Cohort 1 contains 67 patients, Cohort 2 contains 28 patients, Cohort 3 contains 66 patients, Cohort 4 contains 70 patients, and Cohort 5 contains 84 patients, for a total of 315 participants with urine samples. Each patient must have their relevant demographic data collected from the urology clinic's EMR and input into the research database, Redcap. Relevant data collected includes patient age, sex, race, TNM staging, median follow up (months), and whether the patient underwent a TURBT or cystectomy. As of the writing of this abstract, this has been accomplished for Cohort 1 and Cohort 2. We have analyzed the demographics collected from the patients in these two cohorts (Table 1). Further analysis will be performed as more patients are added to the research database from the EMR. As the pool of patients increases, we expect some of these metrics may change. However, these preliminary demographics give a sense of the participant pool being studied.

Results:
There are 95 total patients in Cohort 1 and 2. The median age at diagnosis was 67, ranging from 35 to 90. There are 63 males and 32 females. The predominant race in the two cohorts is white, with 65 Caucasians, followed by 17 Black, 2 Latino, 3 Asian, and 9 patients with an unknown race. Staging data was obtained from 89 patients, and most of these patients (69.7%) had T2 disease. The second most represented group was patients with T3 disease (20.2%), and the remaining patients had T0, T1, and T4 disease. The predominant group of patients had no nodal involvement upon initial diagnosis (N0: 87.6%) and no metastases (M0: 97.8%). (Table 1)

Conclusion:
Bladder cancer is common in the U.S, yet there is a gap in knowledge on how to distinguish between T1 and T2 disease and how to predict when T1 will progress to T2. Although preliminary, the demographic data from Cohort 1 and 2 demonstrate trends we expect to continue. We will analyze the corresponding urine samples with the goal of discovering biomarkers predictive of T2 disease.

N=95					
Median Age at Diagnosis, Years (Range)	67 (35-90)	Sex (Male/Female)		63/32	
Race		Median Follow Up, Years (Range)		3.9 (28.7-0.9)	
White	65	Over 5 Years		35	
Black	17	Over 10 Years		22	
Latino	2	Over 15 Years		9	
Asian	3				
Unknown	9				
Clinical T Stage		Clinical N Stage		Clinical M Stage	
T0	2	N0	78	M0	87
T1	4	N+	11	M+	2
T2	62				
T3	18				
T4	3				
TURBT (Yes/No)	87/8	Cystectomy (Yes/No)		19/76	

Table 1: The demographic data of Cohort 1 and Cohort 2 (N=95). Staging data was only obtained for 89 patients

Abstract Title: Satisfaction and Efficacy of Pediatric Obesity Prevention Program, Healthy You for Life, Through Telehealth versus In-Person Visits

Investigator: Tracy Dien
Co-Investigator(s): Tristan Kuhn, EVMS; John W. Harrington, CHKD
Department(s):

Abstract

Introduction:
Childhood obesity has been a long-standing public health concern in the United States. Unfortunately, this issue has only been exacerbated by the COVID-19 pandemic, with a meta-analysis in 2021 demonstrating an increase in body weight (MD 2.67 kg) and BMI (MD 0.77 kg/m2) amongst school-age children during this time. Obesity prevention programs have also had to adapt and move online during this time. However, while patient satisfaction is high through these online programs, there has not been significant data to demonstrate the efficacy of these virtual platforms.

Methods:
A retrospective chart review was conducted to compare the BMI values of Healthy You for Life patients at the start of the program to their BMI's 6-12 months afterward to evaluate the efficacy of the telehealth versus in-person modalities. In addition, a satisfaction/compliance survey of parents of the program was conducted over the phone. The three cohorts that were compared for the study were (1) patients who had only in-person visits, (2) patients who had only telehealth visits, and (3) patients who had a combination of telehealth and in-person visits.

Results:
Based on preliminary data from 88 patients, the difference in BMI changes among the three cohorts appears not significant. However, further statistical analysis is still ongoing. Regarding the survey conducted amongst 107 patients total, although those who had both in-person and telehealth visits reported better overall experiences during their in-person visit, there was not any significant difference in following provided recommendations after the visit ($p=0.29$). Moreover, they agreed that the level of care provided during the telehealth visit was equal to the quality that was provided in person ($M= 0.98$, 95% CI [0.75, 1.22), $p<0.001$). There was no significant difference in the survey outcomes amongst those who had only in-person versus only telehealth visits.

Conclusion:
Results at this point indicate similar efficacy between in-person versus online visits. Therefore, obesity prevention programs could consider promoting telehealth visits to help combat their primary obstacle of high drop-out rates due to transportation and timing conflicts. Future studies that further analyze reasons for non-compliance with the program's guidance will also help strengthen the current results.

Abstract Title: Stratifying high-risk patients, quantifying therapy efficacy, and detecting treatment/racial disparity in triple-negative breast cancer (TNBC) at Sentara-EVMS-VOA

Investigator: Taylor Drake
Co-Investigator(s): Caroline Dasom Lee, M.D., Leroy T. Canoles Jr. Cancer Research Center, Department of Microbiology and Molecular Cell Biology, EVMS; Emily L. Breeding, M.D., Leroy T. Canoles Jr. Cancer Research Center, Department of Microbiology and Molecular Cell Biology, EVMS; Brandon Euker, B.S., Leroy T. Canoles Jr. Cancer Research Center, Department of Microbiology and Molecular Cell Biology, EVMS; Janet S. Winston, M.D., Pathology Sciences Medical Group, Department of Pathology, SNGH; Billur Samli, M.D., Pathology Sciences Medical Group, Department of Pathology, SNGH; Rick J. Jansen, Ph.D., Department of Public Health, North Dakota State University; Michael A. Danso, M.D., Virginia Oncology Associates; Richard A. Hoefer, D.O., Sentara Cancer Network, Sentara Hospital Systems, Sentara Healthcare; Amy H. Tang, Ph.D., Leroy T. Canoles Jr. Cancer Research Center, Department of Microbiology and Molecular Cell Biology, EVMS
Department(s):

Abstract

INTRODUCTION:
Metastatic breast cancer (MBC) is the 2nd leading cause of cancer-related deaths in American women. While improvements in local and systemic therapies have significantly improved survival, 43,250 MBC patients are expected to succumb to their disease in the United States in 2022 alone. Incidence of breast cancer in Norfolk is 8% higher than the national average (136 vs. 126 per 100,000 females, respectively). Triple-negative breast cancer (TNBC) represents 15% of all breast cancer and is defined by the lack of expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). TNBC is the most aggressive subtype of breast cancer, known for its early relapse rate, chemo-resistance, and reduced survival. TNBC is also nearly twice as common in African American (AA) than in White women. In this study, we aim to ascertain if there is cancer disparity in a large cohort of Black/AA TNBC patients compared to their White counterparts in Hampton Roads, as well as to the national Surveillance, Epidemiology, and End Results (SEER) database.

METHODS:
A retrospective chart review and survival study of 554 TNBC patients who received standard of care (SOC) treatment at Sentara-EVMS-VOA was performed. Kaplan-Meier survival curves were generated. Statistical analyses were conducted to determine if any clinicopathologic parameters, chemotherapy regimens, insurance, or socioeconomic status could be used to predict patient survival and risk stratify Black/AA and White TNBC patients in this Sentara cohort.

RESULTS:
According to the national SEER TNBC database, 5-year survival rates for Black/AA and Whites are reported as 71.65% and 78.98%, respectively, compared to 70.33% and 75.53% within our local TNBC cohort. The Kaplan-Meier curve, which stratified our TNBC patients by race, predicted significant reduction in breast cancer-specific survival among Black/AA patients as compared to their White counterparts at all TNBC stages, especially in advanced and metastatic settings. This disparity is notably pronounced at stages II and III, as the Black/AA survival curves trend below that of the White TNBC patients for years following surgical intervention. A higher percentage of Black/AA patients were uninsured or under Medicaid coverage and did not receive standard AC-T regimens (Doxorubicin [Adriamycin] and Cyclophosphamide, followed by Paclitaxel), particularly for TNBC patients with stage II disease, likely contributing to a reduced 5-year survival in the Black/AA TNBC cohort. We detected a racial disparity in prescription of monotherapy or combination chemotherapy that might have also linked to reduced survival in the Black/AA patients from the Sentara catchment areas.

CONCLUSION:
Low socioeconomic status is a major impediment for access to health care. Multipronged combination chemotherapy regimens are critical in treating high-risk and high-grade TNBC patients. Therefore, it is imperative that Medicaid coverage includes AC-T regimens to improve TNBC survival, especially in our Black/AA patients in Hampton Roads, Virginia.

Abstract Title: Biofilms in Necrobiotic Granulomas

Investigator: Iain Noel Encarnacion
Co-Investigator(s): Alice A. Roberts, MD, PhD, Department of Dermatology, EVMS; Herbert B. Allen, MD, Department of Dermatology, Drexel University College of Medicine, Philadelphia, PA
Department(s): Dermatology

Abstract

Introduction:
Biofilms in dermatopathology have been previously demonstrated in multiple dermatologic conditions, including atopic dermatitis (AD), psoriasis (PSO), and leprosy. More recently, biofilms have been identified in two of the benign necrobiotic granulomas, namely Granuloma annulare (GA) and Rheumatoid arthritis nodules (RA). Here we include the finding of biofilms in dermatopathology specimens of Necrobiosis lipoidica (NL), completing the triad of benign necrobiotic granulomas.

Methods:
Specimens representing GA, RA, and NL were collected for pathological processing. Routine hematoxylin and eosin revealed the diagnosis of necrobiotic granulomas. Periodic acid Schiff (PAS), colloidal iron (CFe), and Congo red stains were utilized to identify potential biofilms.

Results:
All specimens were positive for necrobiotic granulomas. The presence of biofilms for each specimen was confirmed by positive staining for CFe and Congo red. Congo red stains the amyloid that makes the infrastructure of the biofilm. In GA, RA nodules, and NL, PAS was much more muted (or absent) while the Congo red was positive. The PAS stain highlights the extracellular (outside the microbe) mucopolysaccharides that form the bulk of the biofilm. The PAS positivity was replaced by staining with colloidal iron that stains for acid mucopolysaccharides, particularly hyaluronic acid. These findings demonstrate that biofilms were identified in each of the triad of benign necrobiotic granulomas, namely GA, RA, and NL.

Conclusion:
In contrast to the biofilms in other skin diseases (i.e. AD, PSO, leprosy, and others) which stained with PAS and Congo red, the necrobiotic granulomas stained positive for CFe and Congo red. Where AD and PSO have been associated with gram positive organisms, evidenced by positive PAS staining, necrobiotic granulomas may be associated with different organisms. In RA nodules, we previously showed a possible link to gram negative organisms. The demonstration of biofilms is a novel feature in these diseases and, inasmuch as biofilms are made by microbes, points to the likelihood of these diseases being infectious in origin. This contrasts with the prevailing theory that these diseases are "reactive".

Abstract Title: Monkeypox: An Early Snapshot in a Novel Global Outbreak

Investigator: Iain Noel Encarnacion
Co-Investigator(s): J. Klint Peebles, MD, Department of Dermatology, Kaiser-Permanente Mid-Atlantic Permanente Medical Group, Rockville, Maryland
Department(s): Department of Dermatology, Kaiser-Permanente Mid-Atlantic Permanente Medical Group, Rockville, Maryland

Abstract

Introduction:
As of July 23, 2022, the World Health Organization declared monkeypox (MPX) a global health emergency. With the current outbreak rapidly spreading, particularly among groups currently felt to be at higher risk including men who have sex with men (MSM), it is imperative that dermatologists be equipped with information and tools to discern the disease from other entities that may present similarly. This study sought to describe patient demographics as well as morphology and disease course of reported monkeypox cases.

Methods:
The search term, "monkeypox," was used in the internal PubMed search engine, which yielded 224 results. Data collection began 7/8/22 and ended 7/27/22. Each article was individually screened and was included for analysis if it was a case report or case series. Morphology of lesions, demographics, and photographs were collected from each article.

Results:
Sixteen articles were included in the final analysis, with 23 patients total. All patients identified as male. The anogenital region (83%) was the predominant location of lesions at the initial encounter. A wide array of morphologies was observed at initial encounter: papules being the main primary lesion (38%), followed by pustules (22%), ulcers (9%), then vesicles (7%). Lesions tended to be clustered together and umbilicated. Thirteen patients were re-examined at later dates, with pustules (35%) being the predominant primary morphology for new lesions followed by papules (25%), then vesiculopapular (12%). New lesions at follow-up encounters were more commonly noted on the extremities (41%) and trunk (31%), with a tendency to be discrete/scattered with overlying crust.

Conclusions:
Prior to 2022, knowledge of MPX has been largely limited to prior outbreaks and experience with the disease in endemic regions around the world. However, the current outbreak has shown marked differences in both patient predilection as well as disease course. The current outbreak has shown a disproportionate impact on sexual minority individuals for reasons that remain to be fully elucidated, particularly MSM, as well as atypical anogenital lesion distribution. Given the rising number of current cases globally, there is an opportunity to better understand the full spectrum of morphologies and clinical presentations of the MPX virus, which may have been lacking in studies of previous smaller outbreaks.

Abstract Title: A Case of Treatment-Refractory Nausea and Vomiting in a Patient with PTSD Treated with Mirtazapine.

Investigator: Gabriel Enciso
Co-Investigator(s): Manasa Vallabhaneni, MD2023
Department(s): Psychiatry

Abstract

Introduction:
Mirtazapine is an atypical antidepressant commonly used for its side effects of sedation and appetite stimulation, particularly in patients with major depressive disorder who experience sleep and appetite disturbances. However, mirtazapine uses are expanding to other conditions, including post-traumatic stress disorder, somatization, nausea, and vomiting. This is likely due to its various mechanisms of action. In this article, we discuss a case of treatment refractory nausea and vomiting secondary to post-traumatic stress disorder somatization that was resolved with use of mirtazapine.

Case Information:
Patient description: The patient is a 23-year-old transgender male with a past medical history of emergency hernia repair with celiac plexus ablation and chronic gastroparesis who presented to the hospital with altered mental status, hematemesis, nausea, abdominal pain, and severe malnutrition.

History and physical examination results: He was admitted to another hospital one day prior for nausea and hematemesis but left against medical advice due to symptom resolution. The following day, the patient became altered with drooling and decreased responsiveness. During psychiatric evaluation, the patient reported childhood trauma with chronic negative emotions and restricted range of affect. He also stated that during a recent vacation, he experienced sexual assault from a stranger.
On physical exam, he was vitally stable, was slow to respond, showed dysmetria, large and sluggish pupils, and intermittent tremulousness of the bilateral upper extremities and had diffuse abdominal pain on palpation.

Diagnostic procedures: Urine Drug Screen showing cannabis; Abdominal X-RAY and CT Abdomen and Pelvis showing no acute process.

Treatment plan: The patient's nausea, vomiting, and abdominal pain were unresponsive to pantoprazole, zofran, hydromorphone, and IV ketorolac. Given the patient's presentation of nausea, vomiting, and decreased appetite with history of trauma, the top differentials included PTSD, somatic symptom disorder, THC use disorder, or major depressive disorder. Based on these differentials, the patient was started on mirtazapine 7.5 mg with meals.

Outcome: One day after starting mirtazapine, the patient's affect improved significantly with less dysarthria. His abdominal pain and nausea also improved and he tolerated increased food intake. Given this improvement, the patient's mirtazapine was increased to 15 mg three times daily with continued avoidance of opioids. The next day, the patient had complete resolution of nausea and vomiting, minimal pain and significantly improved mentation. Due to relief of the patient's symptoms, the patient was discharged on duloxetine 30 mg once daily and mirtazapine 15 mg three times daily; with instructions to follow-up with an outpatient psychiatrist and psychologist for continued support for his PTSD.

Discussion:
This case report provides an example of significant improvement in a patient with PTSD, likely experiencing somatizations manifesting as nausea, vomiting, and gastroparesis, who was treated with mirtazapine. Given Mirtazapine's 5HT-3 antagonist properties, this medication can be used to treat nausea and vomiting, which is similar to ondansetron's mechanism of action. In addition, mirtazapine also demonstrates appetite stimulating and anxiolytic effects due to 5HT2-receptor blockade. Similarly, mirtazapine also has H1-receptor antagonistic properties which also help to increase appetite. In early studies of mirtazapine's antidepressant effects, the drug also demonstrated significant anti-anxiety effects in patients with major depression and comorbid anxiety symptoms with improvement of both depression and anxiety scoring measures.

Conclusion:
Interestingly, this case report provides an example of a rapid response rate, within hours to days, after initiation of mirtazapine. It also demonstrates a significant improvement of likely somatic symptoms of PTSD, including nausea, vomiting, and gastroparesis that were previously refractory to standard medical treatment.
Further research is needed to fully expand on the FDA approved indications for mirtazapine use. Given this example, mirtazapine can be utilized as an appropriate treatment option and should be considered in patients who experience somatic symptoms related to PTSD.

Abstract Title: Duration of Antibiotic Prophylaxis For Ballistic Fractures To The Extremities

Investigator: Nathaniel Faber
Co-Investigator(s): Noah Kathe, Medical Student, 2024; Jay Collins, M.D., EVMS Department of Surgery
Department(s): Surgery

Abstract

Introduction:
In the U.S. there are thousands of ballistic firearm injuries to the extremities and subsequent infections, yearly. There is a lack of consensus regarding the ideal duration of antibiotic treatment to prevent infection of these wounds. Our study investigated infection rate among ballistic extremity fracture patients based on antibiotic prophylaxis duration, wound severity, and fracture location.

Methods:
Retrospective chart review of ballistic extremity fracture patients from a single trauma center from 01/01/2010-12/31/2020.

Results:
231 of 1,611 fracture cases screened met our inclusion criteria. Infection rate was significantly higher among patients who received antibiotics for ≥48 hours (16.6%), compared to those who received antibiotics for <48 hours (3.6%) (Chi2 = 10.57, p = 0.001). Infection rate was significantly higher among patients with Gustilo grade III wounds (18.5%), compared to Gustilo I & II wounds (5.15%) (Chi2 = 5.09, p = 0.024). When stratified by Gustilo grade, there was no difference in the rate of infection between patients who received antibiotics for ≥48 hours and those who received antibiotics for <48 hours (Gustilo I & II Chi2 = 0.53, p = 0.82; Gustilo III Chi2 = 2.15, p = 0.14). Infection rate was not correlated with joint involvement or fractured extremity location.

Conclusion:
Our results indicate that infection likelihood for extremity ballistic fractures is correlated with wound severity and not antibiotic prophylaxis duration, joint involvement, or fracture location. Prophylactic antibiotic administration greater than 48 hours for most ballistic fractures is unwarranted.

Abstract Title: Role of the microRNA miR-888 cluster in prostate cancer cell plasticity and castration resistant disease

Investigator: Trevor Fachko
Co-Investigator(s): Katherine Routon, MS, Department of Microbiology and Molecular Cell Biology; Aurora Esquela Kerscher, PhD, Department of Microbiology and Molecular Cell Biology
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Prostate cancer (PCa) is the second leading cause of male cancer-related deaths. Androgen deprivation therapy (ADT) is a first-line therapy for advanced disease. Prolonged ADT treatment results in castration-resistant prostate cancer (CRPC), an aggressive form of PCa. A clinical association exists between ADT and treatment-emergent neuroendocrine PCa (T-NEPC), a subset of CRPC characterized by tumor acquisition of neuroendocrine (NE) characteristics and down-regulation of androgen receptor (AR). As CRPC is a lethal disease with mean survival of 2-3 years, new therapeutic targets are needed. We hypothesize that the noncoding RNA miR-888 cluster promotes PCa progression and NE transdifferentiation. Our lab identified the miR-888 cluster as preferentially elevated in prostatic fluids from high-grade PCa patients. Members of this cluster, notably miR-888 and miR-891a, promote prostate cell growth and invasion *in vitro,* and accelerate prostate tumor load in mice. Cluster members are predicted to suppress AR. Using a human prostate LNCaP cell culture assay for NE, we aimed to test if the miR-888 cluster influences PCa plasticity by quantifying neurite outgrowth and stemness marker expression.

Methods:
miR-888 and miR-891a expression was modulated in LNCaP cells using lentiviral miRNA mimic overexpression (OX) vectors or generating CRISPR-specific miRNA knockout (KO) cell lines. Cells were deprived of hormones by culturing in phenol-free RPMI media with 10% charcoal-stripped fetal bovine serum. KO cells were harvested at day 0 and weekly for 8 weeks; and OX cells were harvested at day 0 and every 48 hours for 3 weeks. Cells were fixed with 4% paraformaldehyde, stained with an antibody against neurite marker beta-3-tubulin and neurite length was measured using immunofluorescence and NeuronJ. Total RNA and protein lysate from these timepoints were analyzed for stem cell markers (H19, SOX-2, NANOG, BRN2) and NE markers (SCGN) by qRT-PCR and western blot.

Results:
LNCaP cells overexpressing miR-888 and miR-891a displayed significantly accelerated neurite outgrowth after 9 days compared to controls. miR-888 and miR-891a deleted cells showed neurite outgrowth delay of 5 weeks compared to controls. Stem cell marker studies are in progress.

Conclusion:
Our results indicate that the miR-888 cluster accelerates NE transdifferentiation. These findings could lead to novel anti-miRNA therapies for CRPC.

Abstract Title: Genetics, its role in preventing the pandemic of coronary artery disease

Investigator: Jacques Fair
Co-Investigator(s): Dr. Robert Roberts, Dignity Health Heart and Vascular Institute
Department(s): Dignity Health Heart and Vascular Institute

Abstract
Epidemiologists have claimed for decades that about 50% of predisposition for coronary artery disease (CAD) is genetic. Advances in technology made possible the discovery of hundreds of genetic risk variants predisposing to CAD. Multiple clinical trials have shown that cardiac events can be prevented by drugs to lower plasma low-density lipoprotein cholesterol (LDL-C). A major barrier to primary prevention is the lack of markers to identify those individuals at risk prior to the development of symptoms of the disease. Conventional risk factors are age-dependent, occurring mostly in the sixth or seventh decade, which is less than desirable for early primary prevention. A polygenic risk score, derived from the number of genetic risk variants predisposing to CAD inherited by an individual, has been evaluated in over 1 million individuals. The risk for CAD is stratified into high, intermediate, and low. Polygenic risk scores derived from retrospective genotyping of several clinical trials evaluating the effect of statin therapy or PCSK9 inhibitors show the genetic risk is reduced 40%-50% by decreasing plasma LDL-C. Prospective randomized placebo-controlled clinical trials document a 40%-50% reduction in cardiac events in individuals at high genetic risk associated with favorable lifestyle changes and increased physical activity. The polygenic risk score is not age-dependent and remains the same throughout life. Thus, the GRS is superior to conventional risk factors in identifying asymptomatic individuals at risk for CAD early in life for primary prevention. These results indicate clinical embracement of the GRS in primary prevention would be a paradigm shift in the treatment of the number one killer, CAD.

Abstract Title: Determining your risk for carpal tunnel syndrome

Investigator: Jacques Fair
Co-Investigator(s): Harshit Amin; Caitlin Shi; Thomas Amabile; Sarah Abernathy - EVMS MD Student Curtis Caughey - EVMS MD Student Kush Shah - EVMS MD Student Grace Yi - EVMS MD Student James Bennett - EVMS Pediatric Orthopedic Surgeon
Department(s): Pediatric Orthopedic Surgery

Abstract
Carpal tunnel syndrome (CTS) involves the entrapment of the median nerve between the transverse carpal ligament and carpal bones. Nerve compression leads to numbness in the distribution of the median nerve, paresthesia, and pain. It is known to be associated with rheumatoid arthritis, hypothyroidism, diabetes, and amyloidosis, however, is largely idiopathic.

Analysis of the human Genome via the HapMap project has provided the ability to utilize unbiased genome-wide association studies leading to the discovery of genetic risk variants that predispose to CTS. The genetic risk for CTS can be expressed in a single number based on the number of risk variants one has, combined with their associated risk. Genome-wide association studies of CTS have been conducted in 48,843 cases and 53 sequence variants were located at 50 loci associated with the syndrome. At least 22 genes have been associated with an increased risk for CTS.

Further analysis of these genes has provided the suggestion that they are associated with growth and extracellular matrix architecture. Utilizing the risk for CTS based on conventional risk factors such as diabetes and rheumatoid arthritis are age dependent, occurring primarily later in one's lifetime which is too late for primary prevention. The genetic risk score would allow for the determination of one's risk independent of age. Incorporation of the genetic risk score into clinical practice could transform the primary prevention for CTS, the world's most common entrapment neuropathy.

Abstract Title: The Role of Computerized Tomography in Early Diagnosis and Treatment of Acute Hemorrhagic Pancreatitis

Investigator: Aidan Findley
Co-Investigator(s): Laura Columbus, MD, Radiology\ Eastern Virginia Medical School
Department(s): Radiology

Abstract

Introduction:
Hemorrhagic pancreatitis can arise as a late sequela of acute pancreatitis or as a complication of a ruptured pancreatic pseudoaneurysm. It is characterized by the rupture of pancreatic vessels and successive hemorrhage in or around the pancreas. The goal is to report a case of hemorrhagic pancreatitis and stress the significance of the associated radiographic findings on computerized tomography scan in early diagnosis and treatment.

Case:
A 52-year-old male with a past medical history significant for alcohol use disorder presented with constant epigastric pain with radiation to the back with onset two hours prior. Additionally, the pain was associated with nausea and vomiting. Upon admission, labs were significant for hemoglobin and hematocrit values of 12.9/38.8 and lipase value of 4202. CT abdomen/pelvis was ordered, which revealed a moderate amount of peripancreatic interstitial edema with a 7.9 x 5.1 cm hyperdense bilobed hematoma involving the pancreatic head and uncinate process, and the second portion of the duodenum. There was a small focus of enhancement posteriorly along the hematoma, possibly due to a distal pseudoaneurysm. Additionally, the ventral wall of the duodenum was non-enhancing and not well seen with an additional hematoma measuring 3.9 cm located more caudally at the medial uncinate process, possibly intraluminal of the second and third portion of the duodenum. There was no evidence of active extravasation. The patient was admitted to the medicine, with the general surgery and GI services consulted. The patient was treated conservatively with intravenous fluids, bowel rest, pain management, serial labs, and empiric antibiotics. His lipase continued to downtrend and normalized while his diet was slowly advanced without increased abdominal pain. He was appropriate for discharge on hospital day four.

Discussion:
Hemorrhagic pancreatitis is a rare condition resulting from necrotizing acute pancreatitis or pancreatic pseudoaneurysm with a range of clinical outcomes from mild and self-limiting to life threatening. Etiologies include biliary tract disease, more commonly in women, and chronic alcoholism, more commonly in men. A retrospective autopsy study found that patients with acute pancreatitis died significantly earlier than a control autopsy population and major etiologic factors included alcoholism, bile duct stones and prior abdominal surgeries. A retrospective study assessing pathophysiology, radiographic diagnosis, and treatment of hemorrhagic pancreatitis found that while hemorrhagic complications of acute pancreatitis are rare and the severity and amount of hemorrhage varies, early radiographic diagnosis and intervention improve mortality.

Conclusion:
Hemorrhagic pancreatitis is a rare condition that results from late-stage acute pancreatitis and ruptured pancreatic pseudoaneurysms. Alcoholism is a key etiologic factor in the development of hemorrhagic pancreatitis. The use of computerized tomography scans in diagnosis is essential for early diagnosis and intervention of this potentially lethal condition.

Abstract Title: Venous bullet embolism following thoracic gunshot wound

Investigator: Kari Flicker
Co-Investigator(s): Lauren Jutras, Radiology; Hampton Andrews, Radiology
Department(s): Radiology

Abstract

Introduction:
Bullet embolism is a rare complication of gunshot wounds in which a small-caliber, low-velocity bullet penetrates the vasculature and enters the bloodstream.

Case Information:
A 25 year old patient sustained a thoracic gunshot wound with ballistic course, resulting in injury to the anterior right hemidiaphragm and Grade 5 liver laceration with extension into the intrahepatic inferior vena cava (IVC). The patient arrived with shortness of breath and physical examination was remarkable for mild chest wall emphysema and small right hemopneumothorax with pleural effusion, prompting chest tube placement. Initial contrast-enhanced tomography revealed a bullet fragment in the pelvis in the location of the left external iliac vein whereas follow up scan revealed a clear pelvis with new bullet placement in the right upper quadrant, suggesting intravascular location. After failed extraction of the bullet from both the IVC and the right renal vein as well as continued bullet migration, the bullet was removed from the common femoral vein using catheterization and fluoroscopy. Following the procedure, the patient remained stable and was discharged after four days.

Discussion:
While arterial bullet emboli often present with early signs of ischemia, venous bullet emboli can be asymptomatic. Venous bullet emboli can pose a risk for pulmonary embolism, cardiac valvular incompetence, sepsis, endocarditis, or stroke. It is recommended that symptomatic bullet emboli always be treated, but there is no current consensus on whether asymptomatic venous bullet emboli must be removed and these cases are often treated on a case-by-case basis with possible treatments including conservative monitoring, surgery, or endovascular retrieval. The rarity of bullet emboli contributes to the controversies surrounding treatment, often delayed diagnoses, and the current lack of standardized clinical approach. This report details the successful removal of an asymptomatic bullet emboli through endovascular approach with the hope of shedding further light into whether these cases should be treated versus carefully monitored.

Conclusion:
Physicians who manage gunshot wounds must be acutely aware of the possibility of a bullet embolism as this diagnosis is dependent on a high degree of suspicion. Management varies case-by-case but primarily consists of conservative treatment, endovascular, or surgical options.

Abstract Title: Investigation of Gap Junction Factor Connexin 43 on Exosomal Characteristics and Function

Investigator: Ariel Flotte
Co-Investigator(s): Alexandra Fleck, Leroy T. Canoles Jr. Cancer Research Center\EVMS; David Mu, PhD, Leroy T. Canoles Jr. Cancer Research Center\Department of Microbiology and Molecular Cell Biology\EVMS
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Gap junctions are a form of intercellular communication structures which mediate the exchange of small molecules between cells in close proximity. They are composed of connexin (Cx) proteins which form hexameric channels that connect adjacent cells. In humans, there are 21 Cx isoforms and Cx43 is the most ubiquitously expressed. Another form of intercellular communication is through exosomes that are secreted by donor cells and carry cargo to target cells. The hypothesis of the project was that these two forms of intercellular communication were connected. In the project, Cx43 was mutated to examine the effect on exosomal characteristics and exosomal uptake by target cells.

Methods:
Human lung cancer A549 cells with endogenous wild-type Cx43 expression were mutated at the Y17 position of the Cx43 allele using lentiviral CRISPR-Cas9 vectors. For exosome preparation, cells were cultured in exosome-depleted media consisting of Opti-MEM with 1% exosome-depleted fetal bovine serum and 1% penicillin/streptomycin for 48 hours. Exosomes were collected by differential ultracentrifugation from the conditioned media of A549 clonal control and Cx43-mutant cell clones. The size and concentration of exosome particles were examined with nanoparticle tracking analysis. The protein concentrations of exosome preparations were measured via micro BCA assay. Exosomal marker proteins were characterized using Western Blot with SDS PAGE. For the uptake assays, lipophilic fluorescent dyes (PKH26 and DiD) were used to label exosomes and recipient cells, respectively. Cellular uptake and internalization were quantified using imaging flow cytometry to examine the overall PKH26 fluorescence intensity within recipient cells.

Results:
Exosomes from Cx43-mutant cell clones showed an increase in the exosomal marker protein CD63 as compared to exosomes from A549 clonal control cells. Since CD63 is thought to be involved in the cellular internalization of exosomes, uptake studies were started to examine whether this increase in CD63 had functional implications regarding the uptake of exosomes by target cells.

Conclusion:
Since Cx43 mutants lead to altered exosomal CD63 abundance, the results indicate that Cx43 may be involved in regulating the adhesion characteristics of exosomes to target cells. In the future, further studies will elucidate the impact of increased CD63 abundance on exosomal function.

Abstract Title: Bipolar Beyond the DSM-V-TR: A Proposed Case of Other Bipolar and Related Disorder with Hyperthymic Temperament

Investigator: Steven Forte
Co-Investigator(s): Riccardo De Cataldo, EVMS; Dylan Golomb, EVMS Department of Psychiatry and Behavioral Sciences; James Rapley, EVMS Department of Psychiatry and Behavioral Sciences
Department(s):

Abstract

Introduction:
Bipolar and related disorders affect 4.4 percent of the population with the majority of these patients not reaching the threshold of either Bipolar I (BPI) or Bipolar II (BPII). In clinical practice, when a patient presents in a major depressive episode (MDE), and does not meet criteria for BPI or BPII, they are often diagnosed with MDD when Other Bipolar and Related Disorders (OBRD) may more accurately reflect their symptom constellation. In fact, it is estimated that 40% of patients with MDD have a missed bipolar diagnosis. OBRD with hyperthymic temperament is characterized by major depression that occurs later in life and superimposed on a baseline mood below that of hypomania and above that of euthymia. Although not recognized in DSM-5-TR, it is starting to gain support in the literature,. We present a case of OBRD with hyperthymic temperament to support recognition of this condition.

Case Information:
A 58 year old Caucasian male with a medical history of hypertension, diabetes mellitus type II, well-controlled HIV, obstructive sleep apnea, and psychiatric history of persistent depressive disorder, major depressive disorder, and attention deficit hyperactivity disorder (ADHD) inattentive subtype presents for evaluation and management of firm suicidal intent.

Collateral information was obtained from the patient's sister and was consistent with the history provided by the patient. The patient struggled in high school despite being highly intelligent. He attended one semester of university before dropping out. After this, he embarked on a highly successful career in the nuclear industry.

Throughout his adult life, the patient has had stable and significant dysfunction in self and interpersonal functioning. Collateral described the patient as being preoccupied with being "the most interesting person in the room." Collateral says he has "never been okay holding a normal job," only considering prestigious careers. He has spent much of his life traveling throughout the world and collecting items of objective value.

Over the past three years, sad feelings have become pervasive. He embarked on a several-month "farewell voyage" around the world. Shortly after returning, he lost his job as a nuclear consultant and has since been unemployed. Over the past six depressive symptoms have become more severe. He reported trouble falling asleep, lost interest in pleasurable activities, feelings of guilt, decreased energy, decreased concentration, and suicidal ideation. On the day of admission, he was evicted from his friend's house.

Notable on mental status exam was a superficial affect. He interacted socially in the milieu, making jokes, thanking staff, organizing rooms, and "helping others" while endorsing severe depression.

The patient was concerned about his inability to complete tasks. Neuropsychiatric tests were never performed. His primary care physician diagnosed him with ADHD and prescribed stimulants.

Psychiatrically, the patient continued his home regimen of amphetamine/dextroamphetamine 30mg daily. Home duloxetine was tapered to discontinuation on hospital day 5. Patient was placed on sertraline at admission and titrated to 100mg daily by hospital day 5. Lithium 300mg twice a day (BID) was added on hospital day 5 for antisuicidality and therapeutic level was reached by hospital day 10. Aripiprazole 5mg nightly was added on hospital day 11 to augment sertraline. Mirtazapine 15mg nightly was added on hospital day 12 for augmentation and persisting insomnia.

By discharge, the patient's firm suicidal intent had diminished. On day 13 follow-up, patient sustained clinical improvement.

Discussion:
The DSM-V-TR has made significant improvements in identifying subthreshold bipolar patients. Currently, the DSM-IV-TR does not account for OBRD with hyperthymic temperament although this pathology seems to be related to BPI and BPII. Early diagnosis ADHD, MDD and persistent depressive disorder may have led to suboptimal treatment in this patient as literature suggests that mood stabilizers are most effective in OBRD with hyperthymic temperament. In fact, literature supports that a large proportion of patients currently diagnosed with treatment-resistant depression actually have an undiagnosed bipolar spectrum disorder.

Conclusion:
Further recognition of OBRD with hyperthymic temperament and treatment with mood stabilizers may result in better diagnostic clarity, treatment decisions, and clinical outcomes.

Abstract Title: Disparities in Gestational Diabetes in Virginia Mothers and the effect of COVID-19 Pandemic: Results from 2009-2020 Pregnancy Risk Assessment Monitoring System Data

Investigator: Lauren Gilgannon
Co-Investigator(s): Dr. Hongyun Fu, EVMS Department of Pediatrics: Community Health and Research Dr. Katharine Hawkes, Isabella Health Foundation, Inc.
Department(s): Department of Pediatrics: Community Health and Research

Abstract

Introduction
The United States has the worst maternal and child health (MCH) indicators among industrialized countries, with African American women carrying a disproprotionate burden of negative outcomes. It is widely acknowledged that intrauterine exposure to maternal obesity is associated with adverse MCH outcomes. This study examines factors associated with pre-pregnancy obesity and gestational diabetes in Virginia mothers using the Virginia Pregnancy Risk Assessment Monitoring System Data.

Methods
This study included a sample of 6,453 mothers who participated in the 2009-2022 VA-PRAMS - a probable based sample survey that covered a wide range of information from new mothers about their socioeconomic background; experiences before, during, and after their recent pregnancies; and health outcomes. Multivariate logistic regression was used to identify factors associated with gestational diabetes, adjusting for confounding factors and sampling weights.

Results
Overall, 20.8% of mothers were obese before pregnancy, 8.6% had hypertension, and 5% had gestational diabetes during pregnancy, with rates of gestational diabetes being significantly higher in African Americans (6.4%), Hispanics (6.2%), and women of other races/ethnicities (9.1%). An elevated risk for gestational diabetes was revealed after the COVID-19 lockdown in March 2020, with the odds of having gestational diabetes (OR: 2.32, 95% CI: 1.37-3.97) doubled in women who had birth after the COVID-19 outbreak.

Conclusion
Findings demonstrate racial disparities in gestational diabetes in Virginia mothers and elevated risks for gestational diabetes after the outbreak of the COVID-19 pandemic, which highlighted the need for targeted intervention to improve MCH outcomes.

Abstract Title: Maternal Outcomes in Pregnancies with Preeclampsia Complicated by Fetal Growth Restriction

Investigator: Lauren Gilgannon
Co-Investigator(s):
Department(s): Department of Obstetrics and Gynecology

Abstract

Introduction:
It has been suggested that fetal growth restriction (FGR) is associated with a more severe preeclampsia phenotype. We sought to determine whether the presence of FGR among women with preeclampsia was associated with increased odds of adverse maternal outcomes compared to those without FGR.

Methods:
This was a retrospective study of patients with preeclampsia and singleton pregnancy who were delivered at 23 weeks' gestation or greater from January 1, 2010, to December 31, 2020. The primary outcome was a composite of maternal mortality and severe preeclampsia-associated complications. We stratified analyses based on the onset of preeclampsia (early-onset vs. late-onset). Early-onset preeclampsia was defined as the development of preeclampsia before 34 weeks' gestation. Outcomes were compared between patients with FGR and those without FGR. Adjusted odds ratios (aORs) and 95% confidence intervals (95% CI) were calculated using multivariable logistic regression, controlling for confounders.

Results:
Of 559 patients, 235 (42%) had early-onset preeclampsia and 324 (58%) had late-onset preeclampsia. Rates of FGR were 40% (94/235) and 10% (32/324) in patients with early-onset and late-onset preeclampsia, respectively. In patients with early-onset preeclampsia, patients with FGR compared to those without were more likely to be delivered at earlier gestational age and were less likely to have pregestational diabetes. In this group, patients with FGR compared to those without had similar odds of the primary outcome (12.8% vs. 14.2%; aOR 0.58; 95%CI 0.25-1.35). In patients with late-onset preeclampsia, patients with FGR compared to those without were more likely to be younger and delivered at earlier gestational age. In this group, patients with FGR compared to those without had increased odds of the primary outcome (15.6% vs. 4.1%; aOR 5.80; 95%CI 1.75-19.23).

Conclusion:
In patients with late-onset preeclampsia, the presence of FGR compared increased the odds of severe maternal morbidity.

Abstract Title: Eccentric vs. Concentric Contraction in Pectoralis Major Ruptures While Weightlifting: An Online Video Analysis

Investigator: Eric Gullborg
Co-Investigator(s): Dr. Robert Ablove, Jacobs School of Medicine
Department(s): Jacobs School of Medicine

Abstract

Introduction:
Bench press is the most common cause of pectoralis major rupture. It is thought to occur during the eccentric phase of this exercise [1]. The purpose of this study is to analyze online video evidence of pectoralis major ruptures and determine if they occurred during the eccentric or concentric phase of contraction.

Methods:
We queried YouTube.com for videographic evidence using the search terms: "pectoralis major ruptures", "pec tear", "pec rupture", "bench press pec tear", "bench press pec rupture", and "weightlifting pec injury". We looked for videos that clearly showed when the ruptured occurred, and what phase of contraction the muscle was in while performing a chest press exercise. These videos were then watched in slow motion and evaluated. We also measured number of repetitions at injury and weight used (if visible).

Results:
26 videos were identified. Of these 26, 12 videos (46.2%) demonstrated the rupture occurring during the eccentric phase, and 14 videos (53.8%) demonstrated the rupture occurring in the concentric phase.

Conclusions:
Pectoralis major ruptures caused by a bench press exercise can occur during both the eccentric and concentric phase of muscle contraction. This is distinct from previous studies.[1, 2] This information should lead to a better understanding of how and when a pectoralis major rupture occurs during weightlifting.

[1] Ordas Bayon A, Sandoval E, Valencia Mora M. Acute pectoralis major rupture captured on video. *Case Rep Orthop* 2016;2016:1-4. 10.1155/2016/2482189

[2] Wolfe SW, Wickiewicz TL, Cavanaugh JT. Ruptures of the pectoralis major muscle. An anatomic and clinical analysis. Am J Sports Med. 1992 Sep-Oct;20(5):587-93. doi: 10.1177/036354659202000517. PMID: 1443329.

Abstract Title: Validation of the HOSPITAL Score to Predict 30-day Readmissions in a Health System Across Virginia and North Carolina

Investigator: Gagan Gupta
Co-Investigator(s): Sami G. Tahhan, Internal Medicine; Benjamin M. Goodman, Internal Medicine; Caroline Benz, MS4; Nina Tserediani, MS3; Shaheer A. Hasan, MS4; Michael Bittner, HADSI; Rehan Qayyum, Internal Medicine
Department(s):

Abstract

Introduction:
Hospital readmissions are incredibly expensive with an estimated cost between 15-20 billion dollars annually. Previous studies of general medicine patients have found that 26.9% of 30-day readmissions were potentially preventable. Identification of patients at a high risk of potentially avoidable readmissions allows hospitals to efficiently direct additional care transition services to the patients most likely to benefit. Prediction models may provide a more efficient and accurate means to identify those patients at highest risk. The HOSPITAL score consisting of 7 readily available clinical predictors is one such predictive model that may accurately identify patients at high risk of avoidable readmissions. To assess its applicability to our patient population, we aimed to validate the HOSPITAL score in patients discharged from the Sentara Health System across Virginia and North Carolina.

Methods:
A randomly selected sample of patients from regional hospitals was used for this analysis. Data on patient demographics, HOSPITAL score, and 30-day readmission status was collected from electronic health records. The study design was approved by the EVMS IRB. Patients' baseline characteristics are presented as proportions, means with standard deviation (SD), and as medians with interquartile ranges (IQR) as appropriate. The risk for 30-day readmission was categorized into 3 groups according to the total number of HOSPITAL score points: low risk (0 to 4 points), intermediate risk (5 to 6 points), and high risk (≥7 points). These categories have an associated 5%, 10%, and 20% risk of readmission, respectively. The score was evaluated according to its overall performance, its discriminatory power, and calibration. We used the Brier score to quantify how close predictions are to the actual outcome (overall performance); a useful prediction model has a Brier score <0.25 (the lower the better). For the discriminatory power, i.e., the ability to discriminate the readmissions from the non-readmissions based on both sensitivity and specificity, we used area under the curve (AUC). For calibration, we used the logistic regression model and compared predicted readmission probabilities with observed readmission rates. All tests were conducted as 2-sided at a 0.05 level of significance using Stata 16.1.

Results:
The 379 patients in our sample were randomly selected from 8 Sentara hospitals. Within 30 days after discharge, 61(16.1%) patients were readmitted. Patients had a mean (SD) age of 60.6 (17.4) years and had a median (IQR) length of stay of 82 (75) hours. The HOSPITAL score ranged from 0 to 13, with a mean (SD) HOSPITAL score of 3.6 (2.0). Using the score, 269 patients (71.0%) were categorized as low risk for a potentially avoidable readmission; 74 (19.5%), intermediate risk; and 36 (9.5%), high risk. The Brier score was 0.14, suggesting that HOSPITAL score was a good predictive model. The AUC was 0.69 (95%CI = 0.60 to 0.78) showing good discrimination. For calibration, the predicted risk of readmission calculated with HOSPITAL score was similar to observed risk; the estimated Hosmer-Lemeshow goodness-of-fit statistic was 8.53 (P=0.13) suggesting a good fit of data to the model.

Conclusion:
In this multi-hospital study, we found that the HOSPITAL score had good discriminative ability and calibration for predicting the risk of 30-day hospital readmission. The HOSPITAL score is easy to use and can be calculated before discharge, which makes it a practical tool for identification of patients within our community at high risk for readmission. This may allow timely administration of high-intensity interventions designed to improve transitions of care.

Abstract Title: May-Thurner Syndrome Diagnosed in a Young Male: Case Report

Investigator: Neha Gupta
Co-Investigator(s):
Department(s): EVMS Department of Radiology

Abstract

Introduction:
May-Thurner Syndrome (MTS) is a vascular condition in which the left common iliac vein crosses under and is compressed by the right common iliac artery. This relatively common anatomic variation may be an underdiagnosed contributor to the development of left-sided deep vein thrombosis.

Case Information:
We report on a 27-year-old male with no past medical history, who presented with left lower extremity swelling that began two days prior. CT revealed a significant clot in the left common iliac, external iliac, and common femoral veins, in addition to significant stenosis at the common iliac vein, suggestive of MTS.

Discussion:
Distinguishing MTS cases can be imperative as long-term anticoagulation alone is generally inadequate to prevent future complications in these patients. Our patient also underwent endovascular stenting, which has become a mainstay of therapy as it addresses the underlying anatomical problem. The underdiagnosis of MTS may be attributable to lack of knowledge regarding the condition, a satisfaction of search when there are other explanations for a hypercoagulable state, or a combination of the two.

Conclusion:
Possible complications from MTS can be serious, therefore, it should be considered in the differential during diagnostic workup of patients who present with lower extremity swelling and pain, regardless of whether there is an obvious cause as it can influence treatment planning.

Abstract Title: Racial Disparity in Treatment of Acute-Onset Severe Hypertension in Pregnant and Postpartum Women

Investigator: Neha Gupta
Co-Investigator(s): Fatima Arif, MD2023; Saritha Attanagoda, MD2023; Madison Cauble, MD2024; Kari Flicker, MD2024; Matilda Francis, MD2024; Lauren Gilgannon, MD2023; Kenyibe King, MD2025; Danielle Long, MD2025; Aref Rastegar, MD2025; Rohini Siva Srinivas, MD2023; Maya Vishnia, MD2024; Madeleine Wright, MD2025
Department(s): EVMS Department of Obstetrics and Gynecology, Maternal-Fetal Medicine

Abstract

Introduction:
Hypertensive disorders of pregnancy are a leading cause of maternal morbidity and adverse pregnancy outcomes. There are disturbing racial disparities in pregnancy outcomes as non-Hispanic black women are more likely to experience hypertension-related morbidities compared to non-Hispanic white women. Using new quality metric guidelines, we sought to examine factors associated with delayed treatment of acute-onset severe hypertension (HTN) with a focus on race and ethnicity. Delayed treatment was defined as occurring greater than 60 minutes after the onset of the first severe HTN.

Methods:
This was a retrospective study of patients with preeclampsia who were delivered from January 1, 2010, to December 31, 2020. Analyses were limited to patients who developed severe HTN during the hospital stay. Outcomes were compared between patients who had appropriate treatment (anti-hypertensive medication within 60 minutes) and those who had delayed treatment. Variables with P-values of less than 0.1 by bi-variable analysis were considered in a multivariable logistic regression analysis to calculate adjusted odds ratios (aORs) and 95% confidence intervals (95%CI). Race and ethnicity were included in this logistic regression analysis regardless of P-value.

Results:
Of 409 patients with preeclampsia, 129 (31.5%) had delayed treatment and 280 (68.5%) had appropriate treatment. Variables with P-values less than 0.1 including multiple gestation and body mass index (BMI) 40 kg/m2 or greater as well as race were included in the multivariable logistic regression. BMI 40 kg/m2 or greater compared to BMI <40 kg/m2 was associated with increased odds of delayed treatment (aOR 1.58; 95%CI 1.03-2.42). Multiple gestation compared to singleton pregnancy was associated with decreased odds of delayed treatment (aOR 0.32; 95%CI 0.12-0.85). Race was not associated with increased odds of delayed treatment.

Conclusion:
We found that there was no racial disparity in delayed treatment. Given that approximately 30% of women had delayed treatment, an innovative approach such as autonomous hypertensive treatment should be considered to facilitate a timely treatment.

Abstract Title: The Provider Awareness and Cultural Dexterity Toolkit for Surgeons Trial (PACTS): Can We Improve Cultural Competency In Surgery?

Investigator: Abby Hankins
Co-Investigator(s): Molly Brittain, Department of General Surgery; L.D. Britt, Department of General Surgery
Department(s): General Surgery

Abstract

Introduction:
Racial and cultural disparities in health care are a widely documented phenomena that exist even in circumstances in which socioeconomic status, insurer status, age and comorbid conditions are controlled for. These differences in health care are thought to be related to a combination of underrepresented racial and ethnic minorities in healthcare, bias and overall poor communication between patient and provider. Some studies suggest that improved cultural competency of providers can bridge a gap that leads to improved patient satisfaction and improved health outcomes on the basis of augmented communication quality, shared decision-making, understanding of information and partnership building. The Provider Awareness and Cultural Dexterity Toolkit for Surgeons Trial (PACTS) is a curriculum established for general surgery residents to take aim at mitigating healthcare disparities and improving communication with patients of all cultures and ethnicities. The PACTS study aimed to assess resident cross-cultural knowledge, attitudes and skills when interacting with patients from a variety of different backgrounds.

Methods:
A randomized clinical trial supported by the National Institute on Minority Health and Health Disparities (NIMHD) and American College of Surgeons (ACS) included 2800 participants ranging over the course of July 2019 to June 2022. Participants included general surgery residents and patients on a variety of surgical services at eight different institutions across the United States, including Eastern Virginia Medical School. During the first year, curriculum was enacted to develop cognitive skills in residents, targeted to ensure patient-centered care. The primary outcome of the study was to evaluate resident questionnaire scores prior to curriculum versus afterwards. Secondary outcomes addressed patient satisfaction and clinical outcomes. Clinical outcomes included length of stay, surgical complications and 30-day mortality, morbidity and complications. Patients' self-satisfaction with residents was evaluated via surveys, dispersed by non-surgical team members on the project, at baseline, as well as twice annually in the following two years.

Results:
Preliminary studies reveal that approximately 50% of surveyed patients report receiving culturally dexterous care at baseline and 30% of patients reported not receiving culturally dexterous care. White patients were more likely to reports dexterous care, while black patients were less likely. This aligned with 50% of residents reporting that they viewed themselves providing dexterous care, with non-white residents reporting greater adeptness. Limitations to this study include that patient perception of residents is likely multifactorial and biased by the care they receive from all providers and staff aside from residents. Additionally, the service patients were evaluated on may impact time spent interacting with residents, as busier services, such as trauma, may not allow the same depth of conversation and patient decision-making due to emergent nature of disease process. This study was performed during the covid-19 pandemic and studies have shown hinderance of communication with patients due to hospital protocol, personal protective equipment and restriction of physical presence of providers in some circumstances.

Conclusion:
It is crucial to ensure that surgical residents obtain the skills to adequately communicate with patients of all cultural and ethnic backgrounds. Early reports of this study show nearly a third of the patient population was dissatisfied with the interactions they had with surgical residents. The PACTS curriculum presents a potential solution to addressing a key healthcare disparity. The support from intuitions and residents, as well as adequate application of these concepts is crucial in ensuring an impactful curriculum that brings about change. Finalized results of this study will bring greater insight into the potential success of the PACTS curriculum thus far.

Abstract Title: A rare case of Loeys-Dietz: A radiologist's perspective

Investigator: Esai Hernandez
Co-Investigator(s): Esai Hernandez, EVMS MD student; Garrett Hamblin MD, EVMS Radiology
Department(s): EVMS Radiology

Abstract

Introduction:
Loeys-Dietz syndrome is a rare connective tissue disorder that can present with craniofacial, musculoskeletal, and vascular abnormalities. This disease is often confused with Marfan's syndrome as it can result in early-onset aortic root aneurysm, extensive aortic dissection, and thoracic abdominal aortic aneurysm. However, non-aortic aneurysmal dilatation most commonly of the iliac, splenic, and popliteal arteries are a characteristic feature of Loeys-Dietz syndrome that helps distinguish it from Marfan's syndrome. Making this distinction is crucial, as there are important differences in management. Here we describe a rare case of Loeys-Dietz syndrome, provide an overview of the disease and its radiographic features, and discuss a unique method of treatment known as a debranching procedure which was utilized in this case.

Case information
A 45-year-old Caucasian male presented to the emergency department after developing left sided pain while working as a plumber. The pain began suddenly and progressed to radiate to his chest and back. He complained of nausea but denied any other associated symptoms. CT angiography of the chest, abdomen, and pelvis was performed and demonstrated acute type B aortic dissection with extension into the left kidney causing poor renal perfusion. Shortly after this diagnosis, the patient underwent a thoracic endoscopic aortic repair (TEVAR) with in-situ laser fenestration. Due to extensive dilation throughout the aorta, branched stents were placed in the left subclavian and left renal arteries. 3 months after TEVAR, he was found to have persistent abdominal aortic aneurysmal dilatation up to 4 centimeters in diameter, and left iliac artery aneurysm. These findings necessitated an aortic graft and total visceral debranching.

Discussion:
Loeys-Dietz syndrome is an autosomal dominant connective tissue disorder which has many features similar to Marfan syndrome. The disorder is caused by mutations in the genes encoding transforming growth factor-beta receptor 1 (TGFBR1) or 2 (TGFBR2). Although inheritable, De novo mutations account for approximately 75% of cases. Loeys-Dietz can present with musculoskeletal abnormalities such as craniosynostosis, scoliosis, and pectus carinatum. Additionally, blood vessels are greatly affected by the connective tissue mutation, resulting in tortuous vessels, aortic and non-aortic dilation, and aortic dissection. Patients who do not have any musculoskeletal findings may only exhibit vascular findings, which are known to be difficult to diagnose clinically and often require imaging. The best imaging modality for diagnosis is CT angiography. This allows for the detection of any structural abnormalities in the aorta or its branches. Treatment for patients with Loey-Dietz can be complex due to the sheer number of vascular abnormalities that can be present throughout the aorta and its branching vasculature. Patients commonly require vascular stents and valve replacements. Due to the extensive nature of the aneurysms in Loeys-Dietz, the more intensive debranching procedure may be necessary in addition to aortic stenting. This is done when a graft needs to be applied to a large region of the aorta and includes surgically removing and transposing superior branches of the aorta to originate from the more inferior common iliac arteries. Our patient underwent this debranching procedure, which was demonstrated on subsequent imaging. After his procedure, he was found to have post-operative changes of the superior mesenteric, right renal ,and celiac arteries, which all ascended from the left common iliac artery. Additionally, a graft was placed to support the thoracic and abdominal regions of the aorta.

Conclusion
This case provides the reader with an introduction to the rare condition of Loeys-Dietz syndrome. Diagnostic imaging of our patient provides an excellent overview of the distinguishing vascular features of the disease and its unique treatment.

Abstract Title: Diabetic Ketoacidosis and Acute Mesenteric Ischemia in Adults: An Underreported Association

Investigator: Kelly Hogan
Co-Investigator(s): Lydia Sa MPH, Global Health; Kenyone King, MD 2025; Chukwuka Ukekwe
Department(s): Global Health

Abstract

Background:
The HOPES (Health Outreach Partnership of EVMS Students) Clinic, established in 2011, was created to provide free primary care to the Norfolk area. In 2016, the clinic expanded to serve Spanish-speaking patients in the Clinica Comunitaria Esperanza (CCE). However, little research has been done to explore patient characteristics and clinical outcomes between these two uninsured populations. In the United States, there is a higher prevalence of type two diabetes in Hispanic populations and a higher frequency of undiagnosed diabetes. The aim of this study is to determine if there is a higher prevalence of type two diabetes among patients in the CCE clinic than in the HOPES clinic, and to determine if diabetes is managed differently in the HOPES and CCE clinics.

Methods:
A retrospective chart review will be done to determine the prevalence of diabetes in each clinic. Due to inconsistencies in charting, as well as a lack of full patient panel export function in the utilized electronic medical system, records must first be standardized and consolidated. A separate RedCap survey was created to manage manual export of the data, which will then be analyzed using chi square analyses.

Conclusions:
Building a survey to export the described data will allow for subsequent analysis and identification of differences in the burden and management of diabetes between English- and Spanish-speaking patients at a free clinic in Norfolk, as well as additional analyses comparing health characteristics of these two patient communities.

Abstract Title: Unintended Public Health Effects of Environmental Regulation: Inhalant Abuse Cases Reported to United States Poison Control Centers, 2001-2021

Investigator: Lee Hogge
Co-Investigator(s): Gary Smith, MD, DrPH, Center for Injury Research and Policy, The Abigail Wexner Research Institute of Nationwide Children's Hospital, Columbus, OH; The Ohio State University College of Medicine, Department of Pediatrics, Columbus, OH; Child Injury Prevention Alliance, Columbus, OH; Henry A. Spiller, MS, D.ABAT, The Ohio State University College of Medicine, Department of Pediatrics, Columbus, OH; Central Ohio Poison Center at Nationwide Children's Hospital, Columbus, OH; Sandhya Kistamgari, MPH, BDS, Center for Injury Research and Policy, The Abigail Wexner Research Institute of Nationwide Children's Hospital, Columbus, OH; Dr. Marcel Casavant, MD, Center for Injury Research and Policy, The Abigail Wexner Research Institute of Nationwide Children's Hospital, Columbus, OH; Dr. Natalie Rine, PharmD, BCPS, BCCCP, Central Ohio Poison Center at Nationwide Children's Hospital, Columbus, OH
Department(s): Center for Injury Research and Policy, The Abigail Wexner Research Institute of Nationwide Children's Hospital, Columbus, OH

Abstract

Introduction:
Inhalants describe a broad range of substances that produce chemical vapors to induce a psychoactive effect. Abuse of these substances is one of the most prevalent forms of drug abuse within American society and can have significantly damaging effects on multiple organ systems. Despite this, inhalant abuse remains one of the least researched forms of drug abuse and has been termed "the hidden epidemic". This study investigates the characteristics and trends of inhalant abuse cases reported to United States (US) poison control centers (PCCs) from 2001 through 2021.

Methods:
Data from the National Poison Data System, a database maintained by the American Association of Poison Control Centers and considered the data warehouse for US PCCs, were retrospectively analyzed.

Results:
US PCCs managed 26,446 first-ranked cases of inhalant abuse during the study period, which equaled an annual average of 1,259 cases. Most inhalant abuse cases involved abuse by teenagers, by males and of a single substance. The rate of total inhalant abuse mirrored that in which teenagers abused freon and other propellants, which increased from 7.02 per 1,000,000 US population in 2001 to 16.13 in 2010, before decreasing to 2.83 in 2021 ($p<0.0001$). This decline in rates of teenage abuse of freon coincides with the Environmental Protection Agency's (EPA) ban on freon production, import and use except continuing servicing needs of existing equipment. This regulation was installed as part of the US's commitment to reducing ozone depleting hydrochlorofluorocarbons as part of the Montreal Protocol. Abuse of freon and other propellants was more likely to result in a serious outcome (OR: 1.13; 95% CI: 1.07-1.19), and reductions in teenage abuse of freon and other propellants in 2010 corresponded with a decline in both serious outcome and health care facility admittance rates among teenagers. These findings suggest that the EPA's regulation of freon likely had the unintended consequence of decreasing access to an inhalant popularly abused by teenagers, thereby reducing teenage morbidity and mortality.

Conclusions:
The timing of the Environmental Protection Agency's 2010 regulation of freon with the decline in freon abuse among teenagers, which had previously been rising, exemplifies the potential impact that environmental conservation efforts can have on public health. With treatment of acute intoxication of inhalants primarily consisting of stabilization and supportive care, prevention of abuse serves as the most effective strategy currently available for reducing morbidity and mortality from inhalant abuse. Further research is needed to identify other areas where agencies within public health and environmental conservation can effectively collaborate for mutual benefit.

Abstract Title: Assessing Barriers to Prescription Medication Access at HOPES Clinic

Investigator: Rachel Holmes
Co-Investigator(s): Miranda Teixeira, Medical Student/MD 2024
Department(s): Community Engaged Learning, EVMS

Abstract

INTRODUCTION:
The first student-run clinic in Virginia and the only free clinic in Norfolk, the Health Outreach Partnership of Eastern Virginia Medical School Students (HOPES) Clinic was established in 2011 to meet the needs of the uninsured population of Hampton Roads, Virginia. Since the patients seen at HOPES are required to make less than twice the federal poverty level and be uninsured or underinsured, obtaining medications is often a barrier to proper treatment. To meet this need, in February 2022 we have begun dispensing over-the-counter (OTC) and prescription medications directly to patients in clinic. While this has been effective in meeting the immediate medication needs, we are now conducting research via in-clinic surveys to determine the underlying specific barriers that our patient population face in obtaining prescription medications. Specifically, our needs assessment seeks to answer the questions:

1. Do HOPES clinic patients who are uninsured fill the prescriptions they are being prescribed?
2. If the patients are not filling prescriptions what is preventing them?

METHODS:
A paper survey was developed, in both English and Spanish, to be provided to patients during HOPES clinic and the Spanish-speaking Esperanza clinic within HOPES. Demographic information about the patient including l language preference, medical conditions, and number of medications prescribed is obtained from the patient information already provided in the Practice Fusion electronic medical record (EMR). All patients that come in for appointments are asked if they are willing to answer a few questions for a project pertaining to their prescription access. If they agree, we give them the written survey. Once the survey is collected, the information is entered into Redcap and connected to the corresponding patient demographic information. Once the two data sets are connected, the information is deidentified.

RESULTS:
We expect to have at least 25 patients' data completed over the next month by the EVMS Research Day submission deadline of September 25, 2022, comprised of a mix of English and Spanish-speaking patients. We expect that most patients will cite medication cost and lack of pharmacy accessibility as the leading barriers to proper treatment.

CONCLUSION:
Research in progress.

Abstract Title: Where is the Cookie Theft? A Multifaceted Clinical Presentation and Unique Imaging Findings in a Case of Balint Syndrome

Investigator: Connor Jahelka
Co-Investigator(s): Dr. David Spiegel, Psychiatry and Behavioral Science.
Department(s): Psychiatry

Abstract

Balint Syndrome (BS) is a clinical syndrome associated with bilateral parieto-occipital lobe lesions that results in a triad of symptoms: simultanagnosia, optic ataxia, and ocular apraxia. In this presentation, we discuss the case of a 49 yo male with a PMHx of HIV, hypertension, type 2 diabetes and hyperlipidemia that presented to the ER with stroke like-symptoms, and was found to have a clinical presentation consistent with Balint syndrome. Imaging findings, however, were unique for this patient.

Over the course of a few weeks, the patient had complaints of worsening blurry vision, a non-radiating headache, and impaired depth perception that resulted in multiple admissions. CT imaging initially showed a left occipital lobe infarct with high grade atherosclerosis. The patient then developed dizziness, weakness, a severe posterior headache, and difficulty ambulating without colliding with items within a room. Follow-up MRI imaging revealed acute areas of infarction in the left posterior cerebral artery distribution. On clinical exam, the patient had notable supralateral quadrantanopia, ocular ataxia and oculomotor apraxia. The patient also showed difficulty with perceiving more than one object at a time when tested with parts of the Boston Diagnostic Aphasia exam. Notable difficulties were present with the clock-drawing test as well.

The patient was determined to have the triad present in Balint syndrome. The patient likely developed symptoms from damage to the PCA supply at the parietal-occipital junction, thus leading to an inability to integrate dorsal "where" steams of the visual pathways with the ventral "what" streams of the visual pathway. This patient is an example of the presentation of Ballint syndrome that resulted from lesions that were unilateral, as opposed to the more common bilateral parietal lobe lesions. It is a unique presentation of a rare condition, within a clinical setting.

Abstract Title: CD40L-CD40 mediate hippocampal network activation in experimental epilepsy

Investigator: Gary Jean
Co-Investigator(s): Madeline Sun, Department of Pathology and Anatomy / MD Student; Faith Reid, Department of Pathology and Anatomy / MD Student; Esther Pototskiy, Department of Pathology and Anatomy / RA; Katherine Vinokuroff, Department of Pathology and Anatomy / RA
Department(s): Pathology and Anatomy

Abstract

Introduction:
Temporal lobe epilepsy (TLE), the most common form of epilepsy in adults, has no cure or effective treatment in a subset of patients. TLE is a product of underlying progressive complex biological events denominated limbic epileptogenesis (LE) which is notable for up-regulation of pro-inflammatory mediators in the limbic system. CD40L, a small protein belonging to the TNF superfamily that interacts with the CD40 receptor protein, is upregulated in the brain in human epilepsy and after seizures. The goals of this research were to elucidate the role of CD40L-CD40 in ictogenesis and epileptogenesis.

Methods:
Adult male CD40 deficient mice (CD40KO) and its respective wild type were used in this study. Acute and recurrent seizures were induced using the pentylenetetrazole (PTZ) and pilocarpine model of epilepsy respectively. Anti-CD40L antibody or SiRNACD40 were administered intranasal or intraventricular respectively in wild type (WT) mice and then seizures were induced by PTZ. Seizures were characterized through spontaneous video-electrical recordings using Ethovision for automatic recognition of seizures and through a multimicroarray electrodes inserted in a silicon probe chronically implanted in hippocampal-cortex axis. Type and frequency of seizures, neuronal network activity including individual neuronal activity were analyzed using a signal analysis software. Concentration of neuroinflammatory molecules in the brain were evaluated using ELISA; neuronal tissue was evaluated using basic staining and immunohistology.

Results:
Preliminary observations demonstrated that CD40L increased progressively in the brain during the development of epilepsy. Anti-CD40L administration limit seizure severity. siRNA CD40 attenuated seizure susceptibility. CD40 deficiency limited the onset of recurrent seizures and is associated with reduced neuronal damage and gliosis. In addition, Netrin G2, part of the netrin family of proteins that mediate cell and axonal migration, is upregulated in neurons and fibers after seizures.

Conclusion:
These preliminary findings indicate that the up-regulation of CD40L-CD40 could mediate ictogenesis and epileptogenesis by influencing inflammatory mechanisms that involve neuronal damage and rearrangement of neural circuitry. Therefore, the CD40L-CD40 interaction could be an innovative target for an immuno-therapeutic approach for TLE that could be expanded to other neurological disorders with similar disruptive neuronal networks including Alzheimer's disease and post-traumatic stress disorder.

Abstract Title: Neurotensin Stimulates Ovarian Endothelial Cell Migration

Investigator: Hannah Jensen
Co-Investigator(s): Andrew Pearson, Department of Physiological Sciences
Department(s): Department of Physiological Sciences

Abstract

Introduction:
Ovulation is well-regulated process in which a follicle matures within an ovary to release an oocyte. Angiogenesis plays vital role in ovulation and is controlled by several growth factors. Neurotensin (NTS), a small peptide, acts on the follicle via paracrine signaling to regulate angiogenesis. NTS targets three different receptors: NTSR1, NTSR2 and SORT1. SORT1 has the highest expression in ovarian vascular endothelial cells, so this study investigates the role of SORT1 in NTS-stimulated migration of monkey ovarian microvascular endothelial cells (mOMECs) as a measure of angiogenesis.

Methods:
Ovarian microvascular endothelial cells (mOMECs) from cynomolgus monkeys were isolated from follicle aspirates. mOMEC migration was measured using a transwell migration assay. Wells beneath the inserts were treated with NTS, a general NTS-receptor antagonist (SR142948), a combination of NTS and SR142948, or left untreated. Migration was quantified as the number of cells that moved through the pores to the bottom of the insert. To investigate the role of SORT1, expression was knocked down using small-interfering RNA (siRNA) designed to cleave SORT1 mRNA. RNA from knockdown cells was reverse-transcribed for quantitative PCR to evaluate the SORT1 knockdown percentage in comparison to a non-specific siRNA control. Migration assays were then performed with the knockdown cells in untreated and NTS-treated groups.

Results:
NTS treatment showed a moderate increase in migration compared to untreated mOMECs or mOMECs treated with SR142948. Migration observed in the presence of SR142948 and NTS was intermediate between the control and NTS only. qPCR revealed a 90% knockdown of SORT1 in mOMECs after siRNA transfection. Migration assays with mOMECS after SORT1 knockdown resulted in no NTS-stimulated migration above basal levels.

Conclusion:
Increased migration in NTS-treated groups as compared to the untreated group demonstrates the pro-angiogenic function of NTS. Inhibition of NTS-stimulated migration by SR142948 would indicate the importance of receptor-binding for NTS action. SORT1 knockdown resulted in no change in migration above the control. These findings indicate that SORT1 may be a key target of NTS-stimulated endothelial cell migration. Future studies should examine the role of NTSR1, NTSR2 or interactions between multiple NTS receptors.

Abstract Title: Identification of Medical Language Services and Development of Community Resource Directory for Limited English Proficiency Families of Hampton Roads

Investigator: Katherine Johnson
Co-Investigator(s): Anna Baroody, MD Program, Class of 2025
Department(s): Department of Global Health

Abstract

Introduction:
Antidiscrimination provisions in federal law require healthcare institutions and practitioners that receive federal funding to provide individuals with limited English proficiency (LEP) access to language assistance services. Language services include bilingual medical providers and professional interpretation services, both of which are essential for favorable patient outcomes. Despite federal law, many LEP patients struggle to establish and receive care from healthcare practices with suitable language services, leading to negative health effects. There is currently no single resource for pediatric LEP patients and their families to direct them to medical practices that offer comprehensive language services and/or bilingual subspecialized providers in Hampton Roads.

Methods:
A thorough needs assessment was conducted to examine the relationship between the LEP community and medical language services. A literature review revealed a broad spectrum of known language-based disparities in medical care for this population. Additionally, local LEP families directly indicated concerns over a lack of transparency regarding the availability and accessibility of language services. Our needs assessment led to the creation of two implementation-ready surveys. The first survey will identify bilingual and subspecialized medical providers at pediatric medical practices in Hampton Roads. The second survey will investigate the use of professional interpretation services including in-person, video, and telephone at the same pediatric medical practices.

Results/Conclusion:
Survey information will be compiled into an accessible resource directory and made available to LEP families of Hampton Roads. We hope to equip LEP patients with the tools necessary to find linguistically competent medical care.

Abstract Title: Filling the Gaps in Comprehensive Sex Education for School-age Youth in Hampton Roads through Capacity Building Intervention - Findings from the Teen Health 360 Program

Investigator: Katherine Johnson
Co-Investigator(s): Rebecca J. Slimak, Department of Pediatrics; Brady Goggin, MPH Program; Danielle Long, MD Program; Tram Phung, MD Program; Amil Ahsan, MD Program; Janvi Agrawal, MD Program; Rose Dever, MD Program; Lauren T. Gilgannon, MD Program; Taylor Wallace, MD Program; Kelli J. England, Department of Pediatrics; Amy C. Paulson, Department of Pediatrics; Matthew C. Herman, Department of Pediatrics; Hongyun "Tracy" Fu, Department of Pediatrics
Department(s): Department of Pediatrics

Abstract

Introduction:
Access to comprehensive sex education (CSE) for school-age youth is limited in Virginia due to a range of socioeconomic, cultural, and structural barriers. The Pediatrics Department at Eastern Virginia Medial School launched the Teen Health 360 program in July 2020 to promote CSE for school-age youth in Hampton Roads, with a major focus on the capacity building of public-school teachers, program staff at local community organizations, and students in medicine and public health (SMPH) to implement the Get Real CSE curriculum in school and community-based settings.

Methods:
Four rounds of Get Real Training of Educator (TOE) trainings were conducted virtually via Zoom between August 2020 and March 2022. A total of 82 health educators were trained/certified, including 56 physical education/ family life education teachers, 18 MPH students, and 6 staff from community-based organizations. Around 70% of TOE participants (57/82) completed an online quantitative survey and 9 participated in in-depth interviews, which collected information about their experience of and attitudes towards CSE, TOE training, and future recommendations. Survey data were analyzed using SPSS software. The profile of participants including background characteristics, experiences with CSE, and differences across subgroups were explored using descriptive statistics. In-depth interview data were analyzed using content analysis and grounded theory.

Results:
Participants on average had 3 years of experience in teaching sex education; 39% received CSE training in the last five years. While 85% considered CSE necessary for high-school students, 34% considered it necessary for middle-school students. The most discussed CSE topic was puberty, development and abstinence (79%) and the least discussed was sexual orientation, gender role, identify and expression (10%). Key challenges related to teaching CSE included 1) the stigma associated with sex and sex education for youth; 2) current sex education curriculum is outdated; 3) restrictions about discussing sensitive topics, such as homosexuality, abortion, and masturbation; 4) concerns over potential rejection from parents/guardians; and 5) comfort/confidence level in teaching certain sex education topics. The vast majority of TOE participants (84%) rated the virtual TOE as "good"/"excellent", and considered the *Get Real* curriculum a good fit for school-age youth.

Conclusion:
Findings highlight the unmet needs for CSE capacity building in public schools and community organizations to fill the gaps in CSE for school-age youth in Virginia. The virtual TOE trainings provided through digital platforms are a feasible and effective approach to promote CSE for school-age youth under the context of the COVID-19 pandemic.

Abstract Title: Delineating the molecular mechanism(s) of a potent anti-EGFR/HER2/KRAS strategy against undruggable and incurable human cancer in preclinical settings

Investigator: Maurice Johnson
Co-Investigator(s): Andrew P. Howell, Department of Microbiology and Molecular Cell Biology; Jonathan M. Baker, Department of Microbiology and Molecular Cell Biology; Ashleigh Hannah, Department of Microbiology and Molecular Cell Biology; Amy H. Tang, Ph.D, Department of Microbiology and Molecular Cell Biology
Department(s):

Abstract

INTRODUCTION:
The oncogenic EGFR/HER2/K-RAS pathway activation is a pivotal driving force associated with treatment-resistant tumor relapse and progression, local invasion, and systemic metastasis. Multiple targeted therapies against several key signaling modules in the EGFR/HER2/K-RAS pathway have received the FDA approval for clinical applications; however, their antitumor effects were often transient and drug resistance emerges rapidly. Seven-in-Absentia Homolog (SIAH), an evolutionarily conserved RING-domain E3 ubiquitin ligase, is the most downstream signal gatekeeper and a druggable cancer target in the EGFR/HER2/K-Ras pathway. Inhibiting SIAH was found to be highly effective in eliminating tumor growth in the xenograft models of human cancers. Although complete tumor eradication was achieved following SIAH inhibition, the molecular mechanism remained unclear and warranted an investigation detailed in this study. By using Reverse Phase Protein Array (RPPA) and Principal Component Analysis (PCA) analyses, we found that phospho-Cofilin S3 & cleaved PARP were upregulated in response to SIAH inhibition. Cofilin is a cytoskeleton protein involved in actin depolymerization. PARP is a critical component in the DNA repair machinery. Dysregulation of the kinases/phosphatases that phosphorylate and cleave Cofilin/PARP will be used as a readout of anti-SIAH targeted therapy efficacy. To validate these novel findings and delineate the roles of Cofilin and PARP in ERBB-KRAS-driven human cancer cells, Western Blot (WB), Immunofluorescent (IF) microscopy, and flow cytometry [fluorescence activated cell sorting (FACS)] experiments were performed.

METHODS:
Five stage IV metastatic human cancer lines were used in this study, including MiaPaCa (pancreatic cancer) and MDA-MB-231 (triple-negative breast cancer), and A549 (non-small cell lung cancer). A potent SIAH inhibitor, SIAH2PD, is expressed under the control of doxycycline (DOX)-inducible Tet-ON system. No SIAH2PD inhibitor is expressed in the control cells without DOX induction. The relative ratio and cytoplastic partition of an inactive phosphorylated form (Cofilin S3)/cleaved PARP and total Cofilin/PARP were validated and quantified by WB, IF, and FACS analyses.

RESULTS:
Multiple DOX-inducible Tet-ON stage IV human cancer cell lines were successfully established. The DOX-induced expression of a potent SIAH inhibitor, SIAH2PD, impeded tumor growth and suppressed endogenous SIAH expression. We expect to detect a markedly increase in Cofilin S3 and/or cleaved PARP in both MDA-MB-231, MiaPaCa, and A549 cell lines upon SIAH inhibition.

DISCUSSION:
Cofilin and PARP phosphorylation and cleavage identified via RPPA analysis will be authenticated and quantified in here. The mechanistic insights of how SIAH inhibition is linked to actin remodeling, DNA repair defects, and tumor eradication phenotype will be further investigated in this study.

Abstract Title: Utility of Participant Commentary to Evaluate the Benefit of a Virtual Educational Technology Program for Older Adults

Investigator: George Jones
Co-Investigator(s): Joseph Carton, MD program; Joshua Edwards, CEL; Madeline Dunstan, Glennan Center
Department(s): Glennan Center for Geriatrics and Gerontology

Abstract

Introduction:
Social isolation is a common issue in the geriatric population and has been exacerbated during the COVID-19 pandemic. Meanwhile, technology has become an increasingly prevalent force in our society, yet many older adults lack the skills or resources to use technology effectively. This deficit hinders older adults from connecting with their family and friends, and in turn, promotes further social isolation. A formal program ("HealthWise") was initiated to teach technological skills to geriatric participants to help them better connect with those they hold dear. Previously, we reported a decrease in social isolation, as measured by the quantitative Lubben Social Network Scale (LSNS), among participants who completed this program. While this finding is encouraging, it may not reflect the full benefit that HealthWise provides. We investigated whether the use of qualitative participant commentary feedback on the program could further support the value of an educational technology intervention for older adults with respect to reducing social isolation.

Methods:
The HealthWise program involves two one-hour sessions between a coach and an older adult each week for approximately 12 weeks. Sessions are conducted via Zoom. Participants learn about Wifi, telehealth, email, Zoom, and the Birdsong entertainment platform, and can also tailor sessions to learn about other digital platforms or capabilities that may be of particular interest to them. Two authors contacted participants via phone call after they completed the program to administer a REDCap survey between December 2021 and July 2022. The survey included LSNS questions and allowed for participant narrative feedback as well. We focused on the responses to three questions: (1) "Would you recommend the HealthWise program to others?"; (2) please explain your answer to (1); and (3) "Is there anything else you would like to share about your experience in the HealthWise program?" Themes, characterized by certain words or phrases, were identified from the comments, and all comments were analyzed based on whether they included these themes.

Results:
Of the 38 respondents, 36 (94.7%) stated that they would recommend the HealthWise program to others. Thirty-four participants (89.5%) offered a positive piece of feedback, while 6 (15.8%) had a negative piece of feedback. The most frequently identified positive themes were that (1) the program was helpful, useful, beneficial, valuable, or worthwhile (16/38; 42.1%), and (2) the coach was good (13/38; 34.2%). Less common positive themes included a belief that the program was good or positive (11/38; 28.9%) and that the participant learned, improved their technological ability, became more comfortable with or less intimidated by technology, or grew as a person (10/38; 26.3%). Among respondents who offered negative feedback, some were unsatisfied with the program due to poor communication (2/38; 5.3%) or technical obstacles (2/38; 5.3%). Others were unsatisfied with the amount they learned or reported feeling uncomfortable with technology (2/38; 5.3%). One participant stated a general belief that it was a poor program (2.6%).

Conclusion:
Overall, the amount of positive commentary received regarding older adults' experience in a virtual educational technology program substantially outweighed the negative commentary. This finding suggests that the previously reported quantitative data illustrating a positive impact of the program on older adults' social well-being did not fully reflect the benefit of this educational intervention. We found that participants had positive views of the program and coaches, found the program to be valuable, and grew as human beings, such as in their aptitude or comfort with technology. Granular analysis of negative feedback revealed opportunities for improvement, ranging from enhancing communication with coaches to alleviating technical barriers. We advocate for the development of similar programs to promote older adults' ability to connect with others, as well as for the use of both narrative feedback and quantitative data to more thoroughly evaluate the efficacy of such interventions.

Abstract Title: Patient Perception of Provider Compassion in the HofHeimer Hall Primary Care Clinic

Investigator: Rajita Kanapareddy
Co-Investigator(s): Jennifer Ryal, MD, EVMS Department of Internal Medicine; Zooha Altaf, MBBS, EVMS Department of Internal Medicine; Kristin Olsen, EVMS/MD2025
Department(s): Internal Medicine

Abstract

Introduction:
Clinician compassion is an essential part in providing high quality of care. Improved patient perception of clinician compassion has been associated with better adherence to recommended therapy by patients and better patient outcomes [4]. Compassion is defined as "the emotional response to another's pain and suffering involving an authentic desire to help."[4] Examining patient perception of clinician compassion is particularly relevant, given that the COVID-19 pandemic has amplified the mass shortage of healthcare personnel across the country. As part of this research study, we surveyed patients in the Hofheimer Hall, Primary Care Clinic to better understand patients current perception of provider compassion as part of a larger patient satisfaction assessment.

Methods:
Patients interested in study participation were given a one-page (double-sided) questionnaire. This questionnaire contains demographic and clinical questions followed by five validated patient perception of provider compassion questions. [4] These questions come from a reliable tool designed to measure perception of compassion on a large scale. No patient identifiers were collected in the questionnaire. Hard copies of the questionnaire were distributed to subjects by IRB-approved research team personnel.

Results:
In response to "How often do you feel your provider cares about your emotional or psychologic being?", 19 (6.8%) selected "Never" or "Sometimes, and 263 (93.3%) selected "Usually" or "Always". To the question "How often do you feel your provider is interested in you as a whole person?" 9 (3.2%) selected "Never" or "Sometimes" while 275 (96.9%) responded "Usually" or "Always". In response to "How often do you feel your provider is considerate of your personal needs?", 5 (1.8%) selected "Never" or "Sometimes" while 279 (98.2%) selected "Usually" or "Always". In response to "How often do you feel your provider is able to gain your trust?", 13 (4.7%) responded "Never" or "Sometimes" while 269 (95.3%) responded "Usually" or "Always". In response to "How often do you feel your provider shows you care and compassion?" 7 (2.5%) responded "Never" or "Sometimes", while 274 (97.5%) responded "Usually" or "Always".

Of the 289 patients who consented, 102 (35.3%) were Male and 174 (60.2%) were Female. 13 (4.5%) selected "Other or prefer not to say". 139 (48.9%) were White, 131 (46.1%) were African American, and 14 (4.9%) selected "Other or prefer not to say". 14 (5.2%) identified as "Hispanic or Latino". 179 (63.0%) of patients completed "College", while 101 (25.6%) had only completed "High School or GED" and 4 (1.4%) had completed "middle school" as their highest level of education. 100 (34.7%) reported being "Single", 111 (38.5%) are married, and 24 (14.9%) are widowed. 88 (31.2%) have Medicare, 75 (26.6%) have Medicaid, 117 (41.5%) have private insurance, and 2 (0.7%) have no health insurance. 90 (32.4%) had an income of less than 25,000, 62 (22.3%) have an income between 25,000 and 50,000, 79 (28.4%) have an income between 50,000 and 100,000, and 27 (16.9%) had an income of greater than 100,000.

Conclusion:
These results are preliminary data points for a larger patient-satisfaction and compassion survey study on clinic staffing models. These early survey results suggest potential areas to increase patient perception of provider compassion. Early survey results may suggest a need for further provider education on how to address patient emotional and psychologic being. Further data is needed to achieve our primary study objective to understand how clinic staffing models impact patient satisfaction.

Abstract Title: Bronchoesophageal Fistula Diagnosed on Modified Barium Swallow, a Unique Presentation

Investigator: Mihir Karande
Co-Investigator(s): Matthew Kang MD, Radiology Frances Lazarow MD, Radiology
Department(s): Radiology

Abstract

Introduction:
Bronchoesophageal fistula (BEF) can form as a sequelae of esophageal malignancy, commonly presenting with recurrent episodes of aspiration pneumonia. Lack of serosa around the esophagus can facilitate invasion of esophageal malignancy to adjacent structures within the mediastinum. BEF also occurs due to bronchogenic carcinoma, prolonged endotracheal intubation, and certain infections. The barium esophagram is considered the most sensitive in detecting BEF, but it may also be detected by CT imaging. Prompt recognition of BEF is important, as the median survival after diagnosis of BEF is reported to be between 1-6 weeks.

Case Information:
A 79 year old female resident of an assisted-living facility with significant smoking history presented with shortness of breath associated with chest pain and mild hemoptysis for one week. Her only medication was Naproxen for pain. The patient denied fever, palpitations, or abdominal pain. On physical examination, the patient appeared ill and was in acute respiratory distress. She had decreased breath sounds, crackles, and wheezing on the left side along with tachycardia. A CTA of the chest showed no evidence of a pulmonary embolism, but revealed a large left lower lobe consolidation with parapneumonic effusion, significant endoluminal debris, and possible narrowing in the left mainstem bronchus, which raised concern for a mass. After ICU admission and antibiotic treatment her condition did not improve, raising concern for recurrent aspiration.

A modified barium swallow (MBS) study showed that the patient had a small amount of aspiration with thin consistency barium with coughing. Contrast material was seen moving retrograde through the trachea and into the pharynx, which led to concerns of fistulous communication between the enteric and pulmonary tracts. A subsequent esophagram demonstrated severe luminal narrowing of the esophagus and a large concentric filling defect at the T8-T10 level. After a coughing fit, a layer of contrast outlined the trachea and right mainstem bronchus. Based on these findings, a BEF and paraesophageal mass within the lower posterior mediastinum were diagnosed. Endoscopic evaluation with biopsy was suggested, but were not pursued due to her limited prognosis along with the patient's wishes not to pursue further aggressive therapies. The patient chose to seek hospice care.

Discussion:
BEF is a rare sequelae of esophageal cancer, seen in 5 to 15% of patients with esophageal cancer. It is seen less commonly in patients with bronchogenic carcinoma, prolonged endotracheal intubation, endoscopic interventions, and infections, from tuberculosis, HIV, and syphilis. Most commonly, BEF presents with dysphagia, recurrent pulmonary infections, chest pain, hemoptysis, malnutrition, coughing after oral fluid intake (Ono's sign), and sepsis. Increased mortality from BEF is the result of recurrent aspiration pneumonia. Recurrent aspiration and paroxysmal coughing can contribute to decreased oral intake as well, leading to malnutrition. In terms of imaging, the barium esophagram is considered the most sensitive exam for detection of BEF, providing a correct diagnosis 78% of the time. Definitive imaging findings of BEF can be subtle, as demonstrated by this case presentation. As the esophagus lacks a serosa, no anatomic barrier exists between mucosa and mediastinum, facilitating invasion as seen by abnormal soft tissue appearance along the trachea or bronchus.

Conclusion:
Signs of communication between the respiratory tract and esophagus can be subtle or suboptimally demonstrated by CT. This case follows an atypical presentation of BEF during a routine MBS initially performed for aspiration pneumonia. The finding of interest was outside the field of view initially and retrograde contrast within the trachea could have been dismissed as previously aspirated contrast. This case highlights the importance of the radiologist maintaining a high degree of awareness and critical thinking while performing a MBS, a relatively routine study with limited potential for identifying pathology originating from an intrathoracic source.

Abstract Title: Chylothorax and Thoracic Duct Embolization

Investigator: Mihir Karande
Co-Investigator(s): Matthew Kang MD, Radiology, Daniel O'Neal MD, Radiology, Hampton Andrews MD, Radiology
Department(s): Interventional Radiology

Abstract

Introduction:
Chylothorax is a result of thoracic duct damage with chyle leakage from the lymphatic system into the pleural space. It manifests as a pleural effusion on radiographs and computed tomography (CT). Causes of chylothorax can broadly be separated into non-iatrogenic or iatrogenic. Non-iatrogenic causes are most often related to malignancy, however traumatic injury can also cause chylothorax. Thoracic surgery or traumatic cannulation of thoracic vasculature can cause iatrogenic chylothorax.

Chylothorax can present as a clinically impactful entity with potential to increase mortality. This can occur through loss of plasma proteins, fat-soluble vitamins, triglycerides, electrolytes, and intravascular volume. It has also been associated with increased risk of complications and death following surgical procedures such as esophagectomy when compared to patients without chylothorax.

Utilizing fluorography and interventional radiology techniques, the thoracic duct and cysterna chyli can be opacified using carefully injected radiopaque materials and anatomic landmarks. Thoracic duct lymphangiography (TDL) and embolization (TDE) is a relatively unique procedure that requires patience and dexterity to cannulate small structures. The purpose of this educational exhibit is to familiarize current and future radiologists with this procedure, review relevant anatomy, and demonstrate challenging cannulation of non-vascular structures.

Methods:
We documented cases of TDE performed at Sentara Norfolk General Hospital and observed patterns with access and the procedure itself. A literature review was conducted to further observe the procedure and pathology of chylothorax. This educational exhibit was created to: (1) recognize pleural effusion on diagnostic imaging, (2) overview thoracic duct anatomy, (3) review necessary tools and commonly used materials used in the procedure, (4) outline and discuss TDL and TDE, (5) discuss risks and complications of the procedure.

Results:
From our search, we found that initial therapy for chylothorax is conservative, including drainage of the chylous effusion and dietary modifications. TDE can be a technically challenging procedure due to the small size of lymphatic structures and targets for cannulation. The benefits of TDE include high success rates, minimal invasiveness, and the ability to localize chyle leaks and variations in thoracic duct anatomy. Some pitfalls that were found include rupture of lymphatic structures during lymphangiography and TDE, Methylene blue necrosis, anaphylaxis to lipiodol, pulmonary emboli from lipiodol, and extravasatin of lipiodol into other tissues.

Conclusion:
Chylothorax is a clinically impactful entity that can increase morbidity and mortality. When compared to surgical ligation, TDE has improved clinical outcomes and decreased rates of morbidity and mortality. Additionally, TDL can identify variant anatomy, which is often a complicating factor in the case of necessary surgical ligation. Although TDE can be a technically difficult procedure, it has few complications, primarily related to injected medications or intravascular device deployment.

Abstract Title: Retrospective Review of Pediatric Pedestrian vs. Auto Incidents in Norfolk, Virginia

Investigator: Christine Kim
Co-Investigator(s): Karen Soohoo, EVMS MS4; David Marriott, MD, EVMS Department of Pediatrics; James Burhop, DO, CHKD Pediatric Emergency Medicine; Paul Mullan, MD, CHKD Pediatric Emergency Medicine; Brooke Davidson, PGY2, EVMS Department of Pediatrics
Department(s): Children's Hospital of the King's Daughter, Pediatric Emergency Medicine

Abstract

Introduction:
Pedestrian injury is a problem both worldwide and in the United States. According to the World Health Organization (WHO), road injuries are the leading cause of death for children and young adults between 5 and 29 years of age. In the United States, it is estimated that a pedestrian is killed every 2 hours and injured every 7 minutes. Children are especially vulnerable to pedestrian injuries. In the United States, 20% of pediatric pedestrian injuries are "serious-severe" and 10% are "critical-unsurvivable." Children who survive pedestrian accidents while sustaining injuries may suffer life-long consequences. Additionally, according to the American Academy of Pediatrics, even minor pediatric pedestrian injuries can lead to long-term damage such as post-traumatic stress disorder. Analyzing patient information from Children's Hospital of The King's Daughters (CHKD) retrospectively will elucidate the characteristics of those who were involved in a pediatric pedestrian injury as well as when and where these events tend to occur.

Methods:
All patients under 18 years of age, who were seen in the CHKD ED after a pedestrian versus auto incident and whose accident occurred in Norfolk from January 1st, 2016 to December 31st, 2020, were included in this study. The sex, race, age at time of accident, severity of accident, location of accident, and date and time of accident were extracted from the patient chart. Age ranges were divided into birth-27 days, 28 days-12 months, 13-23 months, 2-5 years, 6-11 years, and 12-18 years based on the age stages determined by the National Institute of Child Health and Human Development. The time of accident was divided into the following intervals: 6AM to 9:59AM, 10AM to 1:59PM, 2PM to 6PM, 6PM to 9:59PM, and 10PM to 5:59AM. Location of accident was confirmed through cross-reference of data in the patient chart with the DMV Crash Location Map by Jurisdiction feature.

Results:
38 pediatric patients were involved in a pedestrian versus auto accident. The average age was 8 years and 10 months. Children most commonly injured were between the ages of 6-11 years old. 61% of patients injured were male. 71% of patients injured were black. Of the 38 patients whose incidents occurred in Norfolk, the exact accident location (GPS coordinates) for 34 patients was identified. Pediatric pedestrian events on average occurred 1.72 miles from home; however the majority of accidents (21 out of 34) occurred less than 0.5 miles from home. Injuries most frequently happened between 2 PM and 6 PM. The most common season of injury was Spring (45%). Of the 38 patients seen at CHKD, 15 were sent home, 14 were admitted to the floor, 2 were admitted to the ICU, 6 went to the operating room, and 1 was declared dead on arrival.

Conclusion:
Pediatric pedestrian vs. auto accidents most frequently occurred less than 0.5 miles from home. Males and children between the ages of 6-11 were the most commonly affected. Although 40.1% of the population in Norfolk in 2020 was black, 71% of pediatric patients who were injured in a pedestrian vs. auto accident between 2016 and 2020 were black. Future directions include extracting and analyzing patient data from the years 2015, 2021, and 2022. Additionally, a heat map will be generated based on the locations of the accidents and census tract data. With this information, we hope to prompt safety measures, especially in neighborhood streets given that many pediatric vs auto accidents occur close to home. Furthermore, we plan to explore the relationship between socioeconomic and racial disparities based on census tract data and the locations at which these incidents take place.

Abstract Title: Prevalence of Hypertension in Clínica Comunitaria Esperanza and HOPES Clinic

Investigator: Kenyone King
Co-Investigator(s): Kelly Hogan, BS, MD Program; Chukwuka Ukekwe, MS, MD Program; Lydia Sa, MPH, Department of Pediatrics; Brynn Sheehan, PhD, Department of Psychiatry and Behavioral Sciences; Alexandra Leader, MD, MPH, Department of Pediatrics
Department(s): Department of Pediatrics

Abstract

Background:
The EVMS student-run free clinics, HOPES (Health Outreach Partnership of EVMS Students) and CCE (Clínica Comunitaria Esperanza), provide health care services at minimal to no cost. While the patients served in HOPES and CCE share similar geographical location, economic and insurance status, CCE's Spanish-speaking patients face additional barriers to healthcare including cultural and language barriers. To our knowledge, CCE and HOPES data have not been fully examined to compare patient characteristics and clinical outcomes between the two patient communities. The Hispanic/Latino American population is a major ethnic group in the United States and hypertension is prominent within this population. With potential health disparities and the increased risk of mortality, it is important to consider the socioeconomic, cultural, and language barriers that impact treatment and overall health outcomes within the population.

Objectives:
To investigate differences in the prevalence and distribution of hypertension between CCE's Spanish-speaking patients and HOPES' English-speaking patients and to identify clinical setting characteristics that may indicate barriers to care, including no-show rates, the rate and type of specialty referral, and referral attrition in patients with hypertension.

Methods:
Practice Fusion data was cleaned and consolidated by transferring text fields into discrete variable fields, recoding text diagnoses to reflect accurate ICD-9 and ICD-10 diagnosis codes, and categorizing medications prescribed. Due to a lack of crosswalk or report extraction from Practice Fusion, an implementation-ready REDCap survey was designed to extract data from all HOPES and CCE patient records. If there is significant population size variability in Spanish and English-speaking datasets, random samples of each will be used for analysis. Descriptive statistics and statistical analysis using Chi-Square will be used to compare prevalence and distribution of hypertension between the two patient groups.

Conclusion:
With this implementation-ready survey and the cleaned and consolidated electronic medical records, for the first time in HOPES/CCE history, a comprehensive report of all patients will be generated, allowing for analysis and greater understanding of the patient population served in these clinics. This analysis may facilitate future targeted efforts in disease screening and management and resource distribution based on health disparities identified within patient communities in HOPES/CCE.

Abstract Title: Acute Ischemic Stroke: Considering all the Factors

Investigator: Nicholas Kochakian
Co-Investigator(s): Kanishk Sharma, EVMS Internal Medicine; Shripadh Chitta, EVMS Internal Medicine
Department(s): Internal Medicine

Abstract

Introduction:
The association of Factor V Leiden (FVL) mutation with venous thromboembolic events (TE) is well recognized. Relationship between FVL and arterial thrombosis is less clear. Furthermore, thrombophilia testing in the US has translated to Medicare spending between $300-$672 million. With this in mind, it is imperative to carefully select patients with thromboembolic events (TE) for testing and in the appropriate setting. Here we present a case of a 46-year-old white male with a right MCA stroke found to have heterozygous FVL mutation.

Case Information:
A 46-year-old white male with a history of prior MI (at age 37) presented to ED with left-sided weakness, facial droop, and decreased left-arm sensation. He did not have a history of obesity, hypertension, smoking, excess alcohol consumption, or hyperlipidemia but had a family history of a sister who had a stroke in her 30s. With NIHSS score of 12 and last known normal time forty-five minutes before arrival, stroke alert was called. tPA was given after ruling out an acute intracerebral bleed on the CT head without contrast. CTA head showed a right M1 occlusion. Thus, TICI 3 revascularization was performed. Transthoracic echocardiogram showed a 48% ejection fraction without structural heart disease or septal defect. Patient received Atorvastatin 40 mg and aspirin 325 mg. Hypercoagulability panel included testing for Factor V Leiden (FVL), prothrombin gene mutation, and anti-cardiolipin and B2 glycoprotein antibodies were ordered. The patient's symptoms rapidly improved and upon discharge he had complete return of muscle strength and no neurologic deficits. He was later found to have heterozygous FVL mutation and was referred to a hematologist to discuss further management.

Discussion/Clinical Findings:
FVL is a mutation that blunts the coagulation cascade's ability to self-regulate thrombin activation, leading to a seven-fold and 20-80 fold greater risk for venous thrombosis in heterozygous and homozygous patients, respectively. Additionally, within the population with a TE, the mutation prevalence is 10-20%. The relationship between FVL and arterial thrombosis such as acute ischemic stroke remains controversial. Our patient had suffered two arterial thrombotic events at a relatively young age and lacked additional risk factors. Therefore, the decision to test for hypercoagulability was made. Anticoagulation therapy and recent TE disease affect results of thrombophilia testing. Heparin interacts with antithrombin, prevents protein C and S activation, and increases coagulation parameters. It causes inaccurate laboratory measurements of these proteins and distorting assays of lupus anticoagulant. During the acute phase of thrombosis, consumption of protein C, protein S, and antithrombin occurs, leading to unreliable measurements. Tests for Factor V Leiden, prothrombin gene mutation, anticardiolipin antibodies, and anti B2 glycoprotein antibodies are not affected by anticoagulants or the acute phase of thrombosis. Heterozygous FVL patients may have a higher risk of arterial thrombosis than homozygous mutations.6 Data regarding treatment is sparse, but published cases have been treated with antiplatelet therapy and high-intensity statins.

Conclusion:
For patients who experience unprovoked TE and TE events at a young age, conscientious inpatient thrombophilia testing reduces cost burden and increases the accuracy of diagnosis. Heterozygous FVL mutation may have more arterial thrombosis risk than homozygous mutation.

Abstract Title: The Risks of Retained Foreign Bodies

Investigator: Sai Kottapalli
Co-Investigator(s): Veer Gariwala MD, Radiology
Department(s): Radiology

Abstract

Retained foreign bodies following penetrating thoracic trauma are unfortunately common. Whether to remove these foreign bodies is often weighed against the risks of the surgery itself. When asymptomatic, these foreign bodies are often left alone.

Herein we describe a case of a 76 year old male with a 4.2 cm foreign body in the right costophrenic sulcus following impalation by a glass door who presented asymptomatically. Months later, the patient presented with a large volume pneumothorax attributed to this previously asymptomatic retained foreign body. While initially asymptomatic, we discuss the risks and general unpredictability of retained foreign bodies and subsequent management decisions.

Abstract Title: Satisfaction and Efficacy of Pediatric Obesity Prevention Program, Healthy You for Life, Through Telehealth versus In-Person Visits

Investigator: Tristan Kuhn
Co-Investigator(s): Tacy Dien, MD Class of 2025; Peter Cunniff, MD Class of 2025; Amil Ahsan, MD Class of 2025
Department(s): CHKD GAP Clinic

Abstract

Introduction:
Childhood obesity is a major public health concern in the U.S. which has only been exacerbated with the COVID-19 pandemic. A 2021 meta-analysis across multiple countries found an increase in BMI (MD 0.77 kg/m2) and body weight (MD 2.67 kg) in school-age children during the COVID-19 pandemic. To combat this, some obesity prevention programs such as Healthy You for Life (HYFL) have utilized a telehealth appointment option. This study aimed to evaluate the level of satisfaction and efficacy of HYFL during the COVID-19 pandemic for telehealth only, in-person only, and patients who did both types of appointments.

Methods:
To accomplish this, we surveyed parents/guardians of patients enrolled in Healthy You for Life for the COVID-19 pandemic via phone call and compared the satisfaction/compliance survey results across the different subject groups (telehealth-only, in person-only, both).

Results:
For 107 total surveys completed, we found that there was no significant difference between telehealth only and in-person only survey outcomes for both the telehealth only group vs the in person only group and for within the group that had both types of visits ($P>0.05$). Additionally, there was higher patient satisfaction for those who had both types of visits compared to those with only one type of visit but there were no significant differences in following recommendations provided after the visit ($p=0.29$). Further, for those who had both types of visits, patients agreed that the level of care provided during the telehealth visit was equal to the quality that was provided in person ($M= 0.98$, 95% CI [0.75, 1.22), $p<0.001$). Later, we will compare the BMI of HYFL patients from initiation at start of the program and 6-12 months afterwards. Currently, based on preliminary data review, it appears there is no significant difference in BMI between the groups, but further analysis is still being conducted to definitively verify this.

Conclusion:
Programs could incorporate more telehealth appointments to combat childhood obesity as compliance and satisfaction levels appear to be similar across groups. Future studies could examine what aspects of appointment type have made them more or less likely to attend/comply.

Abstract Title: Relationship Between Serum Klotho Protein Levels and Skin Cancer

Investigator: Nargiza Kurbanova
Co-Investigator(s):
Department(s): Department of Internal Medicine

Abstract

Introduction:
Studies have reported that Klotho protein is associated with an increased risk of several types of cancers. However, no large epidemiological studies investigated a relationship between Klotho protein levels and skin cancer risk. Klotho protein has anti-neoplastic effects through modulation of oncogenic signaling pathways, such as Wnt/β-catenin, fibroblast growth factor, and PIK3K/AKT. Therefore, we investigated the association between serum Klotho levels and skin cancer.

Methods:
We used National Health and Nutrition Examination Survey (NHANES) data from 2007 through 2016. Self-report of the diagnosis of skin cancer of any type was the main outcome measure. Soluble serum Klotho levels were measured in individuals who were between the ages of 40 and 79 years using the enzyme-linked immunosorbent assay (ELISA). Only those participants with information on the main outcome and serum Klotho levels were included. We conducted survey-weighted logistic regression analysis without and with adjustment for age, gender, race, smoking, and alcohol use.

Results:
Among 13,765 participants, the mean (standard deviation [SD]) age was 57.9 (10.9) years, 7,098 (51.6%) were female, 5,921(43%) were Non-Hispanic White, and 2,737 (19.8%) Non-Hispanic Black. Of the 523 (3.8%) subjects with a history of skin cancer, 110 had melanoma. Mean (SD) serum levels of Klotho were 0.85 (0.31) ng/mL. Subjects with a history of skin cancer had significantly lower serum Klotho levels than those with no history (0.80 vs. 0.86 ng/mL; P<0.001). In unadjusted models, each ng/mL increase in Klotho was associated with a significant 40% lower odds of skin cancer history (Odds ratio [OR]=0.60; 95%CI =0.40, 0.90; P = 0.01). However, 37% lower odds of melanoma history were not statistically significant (OR=0.63; 95%CI = 0.24, 1.62; P=0.33) likely due to few subjects with melanoma history. Similarly, the highest quartile of Klotho had 34% lower odds of skin cancer (OR=0.66; 95%CI=0.45, 0.96; P=0.03) than the lower quartile; the odds for melanoma were not significant (OR=0.69; 95%CI = 0.36, 1.32; P=0.26). After adjustment for potential confounders, the relationship between serum Klotho and skin cancer was no longer significant; OR=0.78; 95%CI=0.51, 1.12; P=0.25 for each ng/mL increase in Klotho and OR=0.82; 95%CI = 0.55, 1.23; P=0.33 for the difference between the lowest and highest Klotho quartiles.

Conclusion:
We found that the significant inverse relationship between serum Klotho levels and history of skin cancer disappears after accounting for potential confounders. Our findings suggest that Klotho might not play a significant role in the pathogenesis of skin cancer.

Abstract Title: Medical schools and the HBCU internship program of the Alzheimer's Association and Thurgood Marshall College Fund:

Investigator: Justin Lagbo
Co-Investigator(s): Faven Russom, MS4; Ashley Peterson, MS4; Paul Aravich, PhD. Pathology/Anatomy
Department(s): Pathology and Anatomy

Abstract

INTRODUCTION:
Health literacy is a major contributor to poor health outcomes and health disparities within the African American community. These health disparities have a negative impact on this population's overall health compared to their white counterparts. As a school founded on the principle of community-based care, medical and health profession students in the Eastern Virginia Medical School Chapter of the Student National Medical Association held a community intervention to address health literacy on common health disorders affecting minority populations. This intervention occurred at the 400th Commemoration of the First African Landing in English-speaking North America, held at Fort Monroe in Hampton, Virginia.

METHODS:
For our intervention, we first provided general health information on certain chronic diseases such as diabetes, hypertension, heart disease, and Alzheimer's disease. An IRB-exempt attitudinal and knowledge questionnaire was then administered to assess participants' awareness of these chronic diseases on a 5-point Likert scale (from strongly disagree to strongly agree). Our survey population included 38 participants ranging from ages 18-70. Out of the demographics, 66% of the patients identified as Black/Mixed Race, 94% had at least some college education, and 61% were women.

RESULTS:
One of the major results of this study showed that while 71.1% of respondents agreed/strongly agreed they learned more about heart attacks, less knowledge was gained about Alzheimer's disease (AD) (63.2% agreed/strongly agreed they learned more). Other important findings showed that 71.1% of participants agreed/strongly agreed that they learned more about regular blood pressure checks, while 68% better understood the importance of regular blood sugar checks.

CONCLUSION:
Data suggests a need for extensive Alzheimer's disease education within minority communities. Multiple initiatives by the Alzheimer's Association are aimed at addressing minority awareness, research, and treatment disparities, including their collaboration with the Thurgood Marshall College Fund (TMCF). This multiyear collaboration aims to engage students, faculty, and university leaders from 47 Historically Black Colleges and Universities (HBCUs) to increase awareness of dementia-related disparities in the Black/African American community. We propose that the existing regional HBCU-AD-TMCF internship program could be greatly enhanced by formally partnering with regional medical schools, including SNMA and health profession students as near-peer paid mentors and volunteer faculty with dementia and public health expertise.

Abstract Title: Cementing the Fracture: Comparing Approaches to Percutaneous Vertebral Augmentation

Investigator: Christian Law
Co-Investigator(s): Matt Kang, EVMS Radiology Residency
Department(s): EVMS Radiology Residency

Abstract

Introduction:
Vertebral compression fractures are the most common form of osteoporotic fracture, and usually occur from low-trauma situations such as falling from a standing height or less. These fractures may result in significant back pain, limited physical function and activities of daily living, and can lead to loss of independence, depression, and chronic pain. Vertebral compression fractures are also associated with height loss, neurological impairment, severe thoracic kyphosis, and increased risk of subsequent fracture.

Using interventional radiology techniques, compression fractures can be treated through the injection of bone cement, often under fluoroscopy, into a fractured vertebra percutaneously. The primary goal of this procedure is the improvement of acute pain and patient function, while also being effective in the prevention of further collapse and the preservation of posture.

There are two methods of percutaneous vertebral augmentation procedures: Vertebroplasty and Kyphoplasty. Kyphoplasty differs in that there is an inflatable balloon inserted into the fracture of the vertebral body, creating a low-pressure space for the injection of bone cement. While these procedures are very similar, their efficacy, risk profile, and additional benefits such as patient height restoration are unique. The purpose of this educational exhibit is to familiarize current and future radiologists with these procedures, compare the different surgical approaches (Vertebroplasty vs. Kyphoplasty, unipedicular vs. bipedicular), and to discuss their potential outcomes and complications.

Main Body:
Both Vertebroplasty and Kyphoplasty involve the injection of bone cement percutaneously into a fractured vertebral body under imaging guidance. Kyphoplasty differs in that this procedure utilizes inflatable bone tamps to create a low-pressure space within the vertebral body, into which the bone cement is placed. In theory, this added step allows for improvement of the kyphotic deformity secondary to the compression fracture, through the restoration of the vertebral body's height. Both of these procedures are typically performed in an outpatient setting with sedation or under general anesthesia. The primary short-term benefits of both Vertebroplasty and Kyphoplasty are the improvement of patient-reported pain, while the long-term benefits include the prevention of recurrent pain, avoidance of long-term opioid use, limitation of height loss and spinal deformity, and improved functional capacity. Patient selection is another important consideration in the context of percutaneous vertebral augmentation procedures. These procedures are not indicated for patients who experience mild to moderate pain that is responsive to medical management. For patients with incapacitating pain who are intolerant to oral opioids or unable to taper parenteral opioids, there is evidence to suggest that vertebral augmentation would be beneficial. Vertebral augmentation can have adverse effects, which include extravasation of cement, pulmonary cement embolism, infectious complications, and new fractures. Complications from cement extravasation are usually not clinically relevant unless located in the spinal canal or neural foramina, where damage from heat or pressure on the spinal cord and nerve roots may cause increased pain. Potential long-term complications of these procedures may include local acceleration of bone resorption caused by the treatment itself or by foreign body reaction at the cement bone interface. There is also evidence to suggest that Polymethylmethacrylate (PMMA) cement is not as biologically inert as once thought, and it has been associated with bone necrosis surrounded by fibrotic tissue, foreign body reaction, and neovascularization.

Conclusions:
Percutaneous vertebral augmentation is an effective and safe method for treating vertebral compression fractures resulting from osteoporosis in the elderly. This procedure can avoid potentially severe complications related to back pain and prolonged bed rest, through the immediate pain relief and early mobilization that it allows. There are several different approaches to carrying out the procedure, and the choice is largely dependent on patient anatomy, severity of compression fracture, and the surgeon's preference. While percutaneous vertebral augmentation is a relatively accessible procedure for an experienced interventionalist, it does have complications, primarily associated with cement extravasation and new adjacent fractures.

Abstract Title: Incidental Finding of a Retroperitoneal Liposarcoma

Investigator: Christian Law
Co-Investigator(s): Christian Law, EVMS MD Program; Zaydi Javeed, EVMS Radiology Residency
Department(s): EVMS Radiology Residency

Abstract

Introduction:
The retroperitoneum is the anatomical space posterior to the peritoneal cavity and anterior to the paraspinous musculature. Of the potential neoplasms that may arise within the retroperitoneum, approximately 80% of them are malignant, and the majority of patients who present with a primary extravisceral mass are found to have a sarcoma. These neoplasms rarely produce symptoms unless they grow large enough to invade or cause mass effect on surrounding tissues, so they are commonly discovered incidentally as an abdominal mass on imaging. Compared to soft tissue sarcomas at other anatomical locations, such as the trunk or extremities, RPS have considerably less favorable treatment outcomes. This may be attributable to the fact that RPS often grow large enough before diagnosis that they become anatomically situated where wide-resection would be too dangerous or impossible. Additionally, the surrounding tissues of an RPS, including the liver, kidneys, stomach, intestines, and spinal cord, all have relatively low tolerance for radiation therapy, limiting the options for adjuvant treatments. The most important predictive factor for survival is tumor resectability, followed by its histologic grade of differentiation. In this case report, we discuss a patient who was incidentally found to have a well-differentiated retroperitoneal liposarcoma on an ultrasound evaluation of the kidney, in the context of an acute kidney injury.

Case Information:
Patient is a 58 year old male who was admitted for congestive heart failure (CHF) and acute kidney injury (AKI). Renal ultrasound (RUS) was performed to evaluate the AKI which incidentally revealed a hypoechoic nodule involving the right kidney. The patient denied gross hematuria or flank pain, however he did report right lower quadrant (RLQ) pain that occurred in the morning and improved with standing. In an outpatiet follow-up with his urologist, an MRI of the abdomen with and without contrast revealed prominent right retroperitoneal fat stranding, within which a large nodular density measuring 1.6 x 1.0 cm was found. Suspicious for retroperitoneal sarcoma, a CT-guided core needle biopsy was performed which confirmed the presence of a well-differentiated Grade 1 liposarcoma. This is a very recent case and thus no plan for treatment has yet been enacted nor any outcome achieved, however we will be outlining in detail the general treatment strategies and considerations for retroperitoneal sarcomas in the discussion section below.

Discussion/Clinical Findings:
Given that the most important prognostic indicator for RPS and the choice of treatment is the tumor's resectability, radiographic findings that indicate unresectability are very important in the evaluation of these neoplasms. These findings include extensive vascular involvement, peritoneal implants, distant metastases, involvement of the root of the mesentery, and spinal cord involvement. For patients whose evaluation suggests a high-likelihood of grossly positive margins, preoperative therapies, including radiation therapy and chemotherapy, are appropriate. In cases where an RPS appears resectable, the role of preoperative radiation therapy is controversial. Those who favor the practice argue that patients usually die from local recurrence and not distant disease, whereas its critics contend that the risk for local recurrence is more based on biology than the specific treatment. The use of adjuvant therapy following surgical resection of an RPS depends on the tumor grade and completeness of the resection. For patients that did not receive neoadjuvant therapy and had margin-negative tumor resections, adjuvant radiation therapy is not preferred. It can be considered for patients with high- or intermediate-grade tumors at risk for local recurrence, however these patients are typically just observed over time as adjuvant radiation therapy may be difficult to deliver without causing unfavorable side effects. Long-term follow up for at least 10 years is mandatory in all patients, given that late recurrences are quite common in retroperitoneal sarcomas. According to the National Comprehensive Cancer Network (NCCN), the recommendations for posttreatment follow-up are physical examinations with abdominal/pelvic imaging every 3 to 6 months for 2 to 3 years, then every 6 months for the next 2 years, and then annually.

Conclusion:
This case report provides insight into the diagnosis, treatment, and management of retroperitoneal sarcomas. Clinicians should have a low threshold to proceed with follow up imaging or core needle biopsies in the case of a mass found in the retroperitoneal space.

Abstract Title: A Case of Post-Ictal Psychosis: Identifying Cause of Psychotic Features in the Post-Operative and Epileptic Patient

Investigator: Connor Lemos
Co-Investigator(s):
Department(s): Psychiatry

Abstract

Introduction:
Periods of psychosis are significantly more common in patients with epilepsy in whom they most often occur post-ictally. However, several potential contributing factors to psychosis often occur in an acute clinical setting. We present a case in which a patient with seizure disorder, existing anti-epileptic medication regiment, and recent cranial surgery presents with psychotic features.

Case Information:
This patient is a 64-year-old man with epilepsy who was admitted to our hospital for surgical reconstruction of a calvarial defect of the skull. Twelve hours after surgery, the patient was found having a tonic-clonic seizure, which resolved shortly after anti-epileptic pharmacotherapy. The following night, he began to display features of psychosis – including paranoid delusions, agitation, hallucinations, and confusion – which waxed and waned for about four days until Psychiatry was subsequently consulted. On the date of initial presentation of psychotic symptoms, labs showed no evidence for COVID19 infection, syphilis infection, infection of the blood or urinary tract, hypercalcemia, hypernatremia, Vitamin B12 or folate deficiency. (Freudenreich, 2009).

Significant medical history includes a glioblastoma multiforme, which was found during workup for seizure disorder thirteen years prior to admission. He underwent subsequent surgical removal followed by radiation treatment. Seven years after initial radiation treatment, he underwent surgical excision of squamous cell carcinoma of the scalp and suffered from higher frequency of seizures and chronic open wound of the scalp afterwards. Patient had been prescribed clonazepam 0.5 mg tablets and midazolam 2 mg injections to be taken as needed for seizures. In addition to the patient's described relevant surgical history, he was also diagnosed with adjustment disorder with depressed mood and generalized anxiety disorder. Initial Psychiatric evaluation occurred five days after admission, when patient was uncooperative with mental status exam but exhibited multiple persecutory delusions, stating the hospital staff wanted to take his money and and that he was "trapped and there is no way out". We initiated treatment of psychosis five days after admission with risperidone 1 mg/d taken by mouth at bedtime along with melatonin 3 mg/d nightly, and discontinued sertraline 100mg daily via feeding tube.

Discussion:
As our patient has a history of seizure disorder treated with anti-epileptic medication and was status-post recent craniectomy during his first presentation with psychotic features, specific etiology of his psychosis was initially unclear. After other medical causes were ruled out with medical history and lab results, post-ictal psychosis, post-operative delirium with psychosis, and anti-convulsant induced psychosis were all included on differential diagnosis. After initial Psychiatric consult, our team proposed a working diagnosis of post-ictal psychosis.

Our rationale focused on the timeline of pertinent events including administration of anti-convulsants, surgery, post-operative seizure, and subsequent psychosis. The patient was found to have some anxiety and confusion one night after his initial ictal period followed reported persecutory delusions, agitation and hallucinations the following night. This sequence fits well into the current understanding of post-ictal psychosis which states that psychosis typically follows a relatively lucid interval of 48 to 72 hours after seizure activity and can continue to wax and wane in following days.

Conclusion:
In conclusion, this case demonstrates potential pitfalls in identifying the primary cause of psychosis in a complex patient with surgical history, a large medication list, and a history of seizures. Although multiple factors may contribute to a patient's presentation with psychotic features, establishing a primary diagnosis is critical when formulating a Psychiatric management plan. In this case, the main focus of treatment could vary from cessation or reduction of medication, antipsychotics, epilepsy prophylaxis, or more supportive measures pending the initial diagnosis.

Abstract Title: Profiling immuno-microRNAs present in human breast milk in the context of SARS-CoV-2

Investigator: Danxun Li
Co-Investigator(s):
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Human milk is an established food source however the bioactive elements contributing clinical attributes to the infant are poorly studied. MicroRNAs (miRNAs) are ~22 nucleotide noncoding RNAs that regulate essential cellular processes, ex. immune response. MiRNAs are noted in human milk and can be absorbed by the digestive tract in amounts that have an effect on host gene expression. Specifically, immuno-miRNAs are noted in extracellular vesicles (exosomes) secreted into human milk. Exosomes are resistant to harsh conditions such as that of the infant's digestive tract, raising the question of whether miRNAs in breast milk reflects the mother's immune status, thereby conferring protection to the infant via exosome delivery. We studied this question in the context of COVID-19 and hypothesized that milk collected from mothers recovered from or vaccinated against SARS-CoV-2 reflected the mother's immune status and possessed distinct immuno-miRNA expression profiles. Since banked milk commonly undergoes Holder pasteurization (62.5˚C for 30 min) before public distribution, we also tested how pasteurization impacted RNA stability.

Methods:
Three independent human milk specimens purchased from Innovative Research LLC were collected prior to (December 2019) and during (March 2021; April 2022) the COVID-19 pandemic and stored at -20. Total RNA isolated from 300 uL of each "raw" and pasteurized milk sample was compared. Two methods for milk exosome isolation (serial ultracentrifugation; ExoQuick-TC kit) were analyzed for quality by NanoSight and total RNA yield. Immuno-miRNAs (miR-141, miR-148, *let-7b*) in raw and exosome milk samples were measured by qRT-PCR. Milks were screened by ELISA for human IgA against SARS-CoV-2 spike protein.

Results:
Holder pasteurization decreased total RNA yield by 4- to 13-fold. Exoquick-TC and ultracentrifugation exosome preparations yielded similar ranges of particle sizes, however, Exoquick-TC generated higher exosome concentrations versus ultracentrifugation. Surprisingly, when analyzing immuno-miRNA expression within each milk specimen, we did not find immuno-miRNA enrichment in the milk exosomes when compared to the whole milk fraction, as we had expected to from literature review. The April 2022 milk contained human IgA against SARS-CoV-2 spike protein, indicating this mother's immunity to COVID-19. As predicted, the SARS-CoV-2 IgA-positive milk specimen (April 2022) showed elevated let-7b immuno-miRNA levels in the whole milk RNA fraction and more dramatically in the exosome RNA milk fraction when compared to the Dec 2019 SARS-CoV-2 IgA-negative milk fractions.

Conclusion:
Best practices for milk RNA and exosome isolation were established. let-7b may confer therapeutic protection against COVID-19 infection to the infant and studying its gene targets may lead to better understanding of its mechanism. Future RNAseq screening will provide a more complete picture of milk noncoding RNAs and antiviral response.

Abstract Title: Evaluation of the Patient Global Impression of Symptom Severity (PGISS) Score as a Subjective and Objective Measure of Disease Activity in Chronic Rhinosinusitis

Investigator: Subin Lim
Co-Investigator(s): Daniel Trotier, BA, Department of Otolaryngology and Head and Neck Surgery, Matvey Karpov, MPH, Healthcare Analytics and Delivery Science Institute, Kent Lam, MD, Department of Otolaryngology and Head and Neck Surgery
Department(s): Department of Otolaryngology and Head and Neck Surgery at EVMS

Abstract

Introduction:
Patient Global Impression of Symptom Severity (PGISS) scale is a visual analogue scale that measures patients' subjective symptom severity. SNOT-22 is a validated tool that measures patients' quality of life in chronic rhinosinusitis (CRS). To assess the clinical value of PGISS in relation to CRS, we investigated the correlations between PGISS and SNOT-22 scores and objective measures of CRS disease activity.

Methods:
A retrospective chart review of CRS patients was performed at a tertiary rhinology center. Data on PGISS and SNOT-22 scores, demographics, and treatment interventions were collected and analyzed.

Results:
A total of 150 subjects were evaluated. PGISS and SNOT-22 scores were found to be strongly and positively correlated ($r=.697$, $p< .0001$). Logistic regression models found that when compared to mild scores (0-3), patients with severe PGISS scores (8-10) had higher odds of changing their treatment plan (OR=4.82, 95% CI 2.29-10.14), receiving systematic steroids (OR=3.10, 95% CI 1.22-8.58), surgery (OR = 37.89, 95% CI 4.77-300.94), and imaging (OR=8.11, 95% CI 1.58-41.71). Alternatively, severe scores had decreased odds of receiving no medical intervention (OR=0.26, 95% CI 0.13-0.52). There were no significant statistical associations between PGISS scores and receiving topical steroidal ($p=.104$), biological ($p=.851$), or non-steroidal interventions ($p=.154$).

Conclusion:
The PGISS score can predict patients' subjective symptom severity in CRS patients. It may also be used to predict certain treatment interventions, such as the need for systemic steroids, surgery, and imaging. The PGISS score may serve as a clinically valuable tool that aids clinicians' understanding of disease progression and therapeutic management of CRS patients.

Abstract Title: Blood Transfusion at the Time of Cesarean Section

Investigator: Danielle Long
Co-Investigator(s): Tetusya Kawakita, MD OB/GYN\EVMS; Camille Kanaan, MD OB/GYN\EVMS; Renee Morales, MD OB/GYN\EVMS
Department(s): EVMS OB/GYN

Abstract

Introduction:
Cesarean sections (CS) make up nearly one-third of all births in the United States and have higher rates of obstetric complications than vaginal deliveries, including adverse outcomes such as postpartum hemorrhage (PPH) and blood loss. These risks increase with each subsequent CS. Although ultimately rare, common risk factors for requiring blood transfusions following a CS include preoperative anemia, abruption on presentation and abnormal placentation. Currently, there is no standard of practice at Sentara Norfolk General Hospital (SNGH) for holding blood products nor having blood in the room prior to CS.

Objective:
To identify the incidence of major obstetric hemorrhage requiring blood transfusion at the time CS and propose appropriate revisions to SNGH protocols for blood product requirements.

Methods:
A retrospective chart review of patients aged 18 and older who had CS at SNGH between January 1, 2021 to January 31, 2022 was conducted looking at obstetric history, intrapartum variables and neonatal outcomes. Obstetric history included variables such as maternal demographics; gravity and parity; tobacco, alcohol, or drug use during pregnancy; previous c-sections, vaginal deliveries, and vaginal births after c-sections; as well as previous spontaneous miscarriages or PPH. Intrapartum variables examined included admission hematology labs, maternal co-morbidities, use of intrapartum oxytocin, complications at the time of c-section, and need for blood transfusion. Neonatal outcomes included APGAR scores and adverse outcomes.

Results:
372 charts were reviewed with 346 patients requiring no blood transfusion and 26 patients requiring a blood transfusion. Of the charts reviewed, older patients (30.7 vs 33.2, $p=0.04$) with risk factors such as chronic hypertension ($p=0.02$), placental abruption ($p<0.001$) or placental accreta ($p<0.001$) were more likely to require blood transfusion. There was no significant difference found between the two groups based on race, ethnicity, BMI, previous CS, substance use, insurance status, previous PPH, pre-gestational diabetes, gestational diabetes, preeclampsia with severe features or the number of fetus(es).

Conclusions:
Preliminary data indicates that patients at SNGH are more likely to require a post CS blood transfusion when they are older ($p=0.04$), have a history of alcohol use during pregnancy ($p=0.03$), have chronic hypertension ($p=0.02$), developed preeclampsia without severe features ($p=0.05$), have placental abruption ($p<0.001$) or have placenta accreta ($p<0.001$). Notably, patients with placental abruption and placenta accreta have significantly higher odds of requiring a blood transfusion, with odds ratios of 20.82 and 28.99, respectively. Prior history of PPH was not associated for need to transfusion in subsequent delivery. Currently, we have evaluated 372 charts of 1500 and therefore more data is needed prior to reviewing and implementing changes to our CS protocol for type and cross of blood products.

Abstract Title: Use of Immersive Virtual Reality for Laceration Repairs in the Pediatric Emergency Department

Investigator: Bhavya Malladi
Co-Investigator(s): Anne McEvoy MD, CHKD Pediatric Emergency Medicine; Olivia Vincent MS/CCLS, CHKD Child Life Specialist
Department(s): CHKD Pediatric Emergency Medicine

Abstract

Introduction:
Managing acute procedural pain in pediatric patients is essential to avoid long-term consequences such as fear of needles. Previous research has shown that virtual reality (VR) has the potential to be an effective distraction technique for minimizing pain and anxiety during pediatric medical procedures. The goal of this randomized pragmatic study was to determine if VR goggles can improve patient pain and anxiety scores specifically during laceration repairs when compared to standard passive distraction techniques in the pediatric emergency department (ED).

Methods:
After appropriate consent and assent were obtained, patients aged 6-17 with simple lacerations were randomized to potentially receive immersive VR goggles in addition to the standard of care. During the laceration repair, patients receiving the VR goggles played a game preselected by Child Life staff. Afterwards, the patient, guardian, and provider were surveyed; study data were collected on paper surveys and managed using REDCap electronic data capture. Primary outcomes measured were pain score (assessed by the Wong Baker Faces scale) and anxiety score (assessed by the Children's Fear scale). Secondary outcomes measured were duration of procedure, use of physical holding, adverse effects, and use of pharmacological interventions.

Results:
At the time of data analysis, 41 participants were surveyed, 28 in the 6-11 age group (Group A) and 13 in the 12-17 age group (Group B). Anxiety scores were calculated by assigning numerical values to each "face" on the scale, similar to the pain rating scale. Preliminary analysis was done by calculating average pain scores and anxiety scores obtained from the patient surveys. Within group A, participants using VR had an average pain score of 2.3 and anxiety score of 4, versus a pain score of 2.8 and anxiety score of 3.4 for the controls. Within group B, participants using VR had an average pain score of 1.3 and anxiety score of 1.3, versus a pain score of 4.7 and anxiety score of 4.3 for the controls.

Conclusion:
Although the target number of surveys has not yet been reached, preliminary results show that pain and anxiety levels stayed similar between the control and VR cohorts in the younger age group, but were considerably decreased for the VR cohort within the older age group. Of note, younger patients who received the VR goggles had relatively higher anxiety scores; this may be because these patients knew they were undergoing a procedure and were more nervous when they were not able to see what was being done. Procedure duration for all surveyed participants was also relatively lower when VR goggles were used. These results indicate that VR does show promise to reduce pain and anxiety during simple laceration repairs in the pediatric ED.

Abstract Title: Prevalence of select S. aureus Virulence Factors in Community-associated Infection in Hampton Roads

Investigator: Scott Marston
Co-Investigator(s): Katelyn Cranmer, MS, Department of Microbiology and Molecular Cell Biology \ Laboratory Assistant; Lanay Clark, MS in Biomedical Sciences Research Program \ Graduate Student
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

Introduction:
Staphylococcus aureus is a widespread and successful human pathogen responsible for a variety of infectious states. Despite a recent decrease in the overall prevalence of methicillin-resistant *S. aureus* (MRSA) in the United States, the proportion of community-acquired (CA-MRSA) strains compared to healthcare-acquired (HA-MRSA) strains has increased which is thought to correlate with an increase in infectious capacity of *S. aureus* regardless of methicillin sensitivity. Panton Valentine leucocidin (PVL), a toxin associated with immune evasion, has been implicated in community associated *S. aureus*, specifically in CA-MRSA carrying Staphylococcal chromosomal cassette (SCC*mec*) type IV, making PVL a potential pseudo marker for this gene island and community associated infection. *S. aureus* virulence is driven by an arsenal of virulence factors (VF) that support immune evasion, toxin production/excretion, and adhesion/biofilm formation. The goal of this project is to identify prevalence, commonalities, and differences of various *S. aureus* VFs among community associated infections in the Hampton Roads area to highlight potential therapeutic targets.

Methods:
Community-associated *S. aureus* clinical isolates were obtained from patients of the Children's Hospital of the King's Daughters (IRB#18-05-EX-0109). Genomic DNA was extracted and subjected to Whole Genome Sequencing (WGS) using the Illumina iSeq 100 instrument. The data was assembled and annotated using the Galaxy Project analysis tool and Prokka genome annotation software. Sequence type (ST) and the presence/absence of select VFs were determined using NCBI BLAST and www.MLST.org, as appropriate. SCC*mec* type was identified for CA-MRSA strains using multiplex PCR and gel electrophoresis. Statistical analysis was performed via Chi-Squared test to determine associations among VFs, methicillin resistance, patient locale, and sample type. STs and clonal complexes (CC), a group of STs with similar allelic profiles, represented by ≥2 samples were determined as percent positive occurrence for each VF. The VFs analyzed are associated with 1) immune evasion: pvl, hemolysins a and b (*hla, hlb*), gamma-hemolysin ABC complex (*hlgabc*), staphylococcal complement inhibitor (*scn*), chemotaxis inhibitory protein of *S. aureus* (*chp*), serine-aspartate repeat protein E (*sdre*), and clumping factor A (*clfa*); 2) host cell adhesion and biofilm formation: *sdre* and *clfa*; and 3) skin exfoliation: the exfoliative toxins A and B (*eta* and *etb*).

Results:
A total of 23 isolates were analyzed via WGS for the presence of genes encoding 10 VFs. Of these, 8 were MRSA and 15 were MSSA. 5 samples were obtained from blood, 4 from urine, and 14 from skin/soft tissue (SSTI). A total of 6 samples were from patients residing in the southwest region of Hampton Roads, 11 in the southeast, and 6 in the peninsula. CCs 8, 15, 30, and 45 (n=11, 3, 2, 2) and STs 8 and 30 appeared in ≥2 samples. *clfa* was present in all 23 samples.

Of the MRSA isolates, 7 contained SCC*mec* type IVa, and 1 contained type IVc. These 7 were all of ST8 and CC8, while no trends were observed to MSSA STs or CCs. When comparing the presence of VFs among MRSA and MSSA groups, *pvl* was different (5 vs. 0, p=0.0022) and found only in SCC*mec* type IVa. eta and etb were found exclusively in MSSA samples. *sdre* and *chp* appeared in all MRSA samples, while *hlgabc* and *hlb* were in all IVa samples. All ST8 and CC8 samples contained *hlb* and *hlgabc*, while all ST8 samples contained *sdre* and *chp*. All blood samples had *scn* and *sdre*, and all SSTI samples had *hlgabc*.

There was no significant difference among gene prevalence when compared to infection type or patient locale.

Conclusion:
CA-MRSA were primarily ST8, while CA-MSSA were varied in ST; ST8 was the most prevalent ST overall. The presence of *pvl* differed between MRSA and MSSA isolates, but no other differences were noted in VF presence when categorized by methicillin resistance, patient geography, or infection type. Various commonalities were observed, however, highlighting potential therapeutic targets. While statistical analysis is limited due to sample size, the observed trends are prospects for further investigation. Future plans involve VF expression metrics in a laboratory simulated infectious state as an indication of predicted virulence potential in the host. These trends will become increasingly important to recognize as novel treatment strategies against a broad range of community-associated *S. aureus* are developed.

Abstract Title: #MedTwitter Big Data Analysis: A Machine Learning Approach

Investigator: Nolan Martin
Co-Investigator(s): Lieutenant Commander, Gregory J. Booth, MD; Lieutenant Commander, Henry DeYoung, MD; Lieutenant Trevor Elam, MD; Lieutenant Commander, Scott Hughey, MD; Lieutenant Commander, A. Steven Bradley, MD;
Department(s): Uniformed Services University of the Health Sciences, Naval Medical Center Portsmouth, Portsmouth, Virginia

Abstract

INTRODUCTION:
Twitter has emerged as a powerful platform for engaging physicians, students, and the public in health discourse, professional networking, and medical recruiting. The ubiquity of social media managers for medical conferences and journals indicates a growing awareness of the importance of social media in professional organizations, but quantitative research studying what content attracts healthcare audiences remains limited. We examined the activity of the American Society of Anesthesiologists (ASA) and users associated with ASA on Twitter over a 10-year period to identify methods for exposing the topics and user characteristics that drive user engagement in medical Twitter communities.

METHODS:
We used the Twitter Application Programming Interface to collect all tweets sent by ASA between October 2011 and September 2021 (11,196 tweets). We quantified user engagement for each tweet by dividing the total likes, replies, retweets, and quotes by the number of followers the ASA had at the time of the tweet. Using unsupervised machine learning and natural language processing (NLP), we organized the tweets into topics and used logistic regression to explore associations between topics and engagement. In addition, we tested associations between engagement and concrete variables such as time/date, inclusion of media, and hashtags. We then collected tweets that mentioned @ ASALifeline from January 2020 to September 2021. We compiled a list of every user referenced in each of these tweets and used these connections to calculate each user's eigenvector centrality, a measure of how well-connected each user is to the larger social network. We categorized the 100 users with the highest eigenvector centrality by type (residency program, physician, student, etc.) to understand which types of users were most well connected in this network.

RESULTS:
ASA's hashtags with the highest engagement rate were #MedStudentTwitter, #MedTwitter, #HealthCareHeroes, and #COVID19. NLP analysis identified six topic groupings in ASA's tweets, with the highest engagement associated with: Research, Quality, & Safety; Policy, Advocacy, & Leadership; Outreach & Social Media; and Professional Education. @ ASALifeline was mentioned in association with 17,045 unique users, with 167,169 connections between those users. 42 of the top 100 most connected users were mentioned by the ASA. Tweets that mentioned these highly connected users were more likely to have high engagement than tweets mentioning poorly connected users (35.4% vs. 23.6%, p-value < 0.001). Only four of the top 100 users by eigenvector centrality appeared in the top 100 users by follower count.

CONCLUSION:
Although unsupervised machine learning can be a difficult process to validate, the six topics partitioned by our approach closely aligned with ASA's six Strategic Pillars, suggesting that our model independently identified that ASA's tweets target their Strategic Pillars. Armed with the ability to analyze the content of thousands of historical tweets, medical organizations can use this topical analysis to drive more interest in their platforms. Equally important in driving interest is placing emphasis on attracting the right users. Although it is often assumed that follower count is a meaningful representation of influence, the high engagement associated with users with high eigenvector centrality and the small overlap between top users by follower count and top users by eigenvector centrality suggest that centrality is an important and unique metric to consider when targeting users. Additionally, despite the highest engagement hashtag in our analysis being #MedStudentTwitter, the list of the top 100 users by eigenvector centrality in ASA's network did not include a single medical student or resident. Targeting this massive group of physicians in training remains a significant opportunity for growth. Many students and residents use Twitter as a professional record of discourse and research, and as such, may be reluctant to be active participants in discussion for fear of scrutiny. A successful targeted approach to attract these users will therefore include posting content that engages trainees as well fostering an inclusive culture of professional conversation with awareness of the level of training of each user.

Abstract Title: CRH-mediated microglial activation involves in galectin 3 upregulation and autophagy dysregulation

Investigator: Damian Martinez Pineda
Co-Investigator(s): Kazemi Soheil, Pathology and Anatomy; Yan Cheng, Pathology and Anatomy; Rachael Dempsey, Pathology and Anatomy
Department(s): Pathology and Anatomy

Abstract

Introduction:
Chronic sleep disturbances (CSDs) including insomnia, insufficient sleep time, and poor sleep quality are major public health concerns around the world especially in the developed countries. CSDs are well-known for exaggerating multiple neurodegenerative and neuropsychological diseases. Accumulating evidence suggest that CSDs could activate microglia and increase neuroinflammation which act as driven forces causing neuronal dysfunctions. However, the detailed mechanisms underlying CSDs-mediated microglial activation remain unexplored. Previously we have shown that CSDs could upregulate corticotropin-releasing hormone (CRH) and activate microglia in the brain hippocampus. In this project, we explored the mechanisms underlying CRH-mediated microglial activation in vitro.

Goals:
Identify detailed molecular mechanisms underlying CRH-mediated microglial activation.

Methods:
Cell culture, Western blots, gel imaging, qRT-PCR, and data analysis

Results and Findings:
BV2 cells and primary microglia were cultured and treated with CRH for varying doses (25 - 200 nM) for 6 or 24 hours. At indicated time points, cells were collected for RNA and protein extractions to examine the levels of interested molecules. Our results demonstrated that CRH increased levels of pro-inflammatory mediators including il1β, il6, tnfα, and ccl2 in microglial cells. Meanwhile, CRH increased galectin 3 levels (neuroinflammation marker) in both BV2 cells and primary microglia. CRH also increased the formation of autophagosome formation evidenced by the increased levels of LC3II in microglial cells.

Conclusions:
Galectin 3 upregulation and autophagy dysregulation might be involved in CRH-mediated microglial activation. More experiments are going on for this purpose.

Abstract Title: The Application of Contrast-Enhanced Ultrasound-Guided Core Needle Biopsy in Diagnosis of Indeterminate Hepatic and Renal Lesions: A Series of Three Cases.

Investigator: Robert McCauley
Co-Investigator(s): Tyler Klause, MD\EVMS Department of Radiology; Christopher O'Neill, MD\EVMS Department of Radiology
Department(s): Department of Radiology

Abstract

Introduction:
Contrast-enhanced ultrasound (CEUS) utilizes gas-filled microbubbles stabilized within a lipoprotein membrane. Lumason (Sonovue) is the only ultrasound contrast agent FDA-approved for abdominal imaging.

CEUS offers many advantages over contrast-enhanced computed tomography (CECT) and contrast-enhanced magnetic resonance imaging (CEMRI), namely its safety profile and the benefit of dynamic real-time examinations. Moreover, the ability to eliminate the linear responses from background tissue allows for a purely vascular image with superior visualization of smaller structures, such as septa and mural nodules. We present three cases demonstrating our early experiences with the utility of CEUS.

Case Information:
Case #1: An 85 y/o male with a history of human immunodeficiency virus and hepatitis B virus presented to the emergency department with several months of weight loss, melena, and weakness. CT scan demonstrated a right colonic mass with multiple hypovascular hepatic masses consistent with metastatic colon adenocarcinoma. There were also two indeterminate hyperdense lesions in the left hepatic lobe. CEUS demonstrated multiple early arterial enhancing lesions in the left hepatic lobe with late-phase washout concerning for a malignant lesion. CEUS-guided biopsy was performed and returned positive for metastatic colon adenocarcinoma.

Case #2: A 71 y/o female with a history of cirrhosis was found to have a right hepatic lobe mass on screening ultrasound. Further characterization with MRI was suggestive of hepatocellular carcinoma, but not definitive. She initially underwent CT-guided biopsy of the mass, however, the lesion was not identified. She subsequently underwent CEUS-guided biopsy, which demonstrated the right hepatic lobe mass with a characteristic early arterial enhancement with late-phase washout concerning for malignancy. Biopsy returned positive for hepatocellular carcinoma.

Case #3: A 79 y/o male with a history of left clear cell papillary renal cell carcinoma status-post left nephrectomy and right chromophobe renal cell carcinoma in the lower pole status-post microwave ablation was found to have an enlarging mass in the right mid-kidney demonstrating nodular central post-contrast enhancement on CEMRI. CEUS-guided biopsy was performed demonstrating intralesional enhancement confirming a solid renal mass concerning for malignancy. Biopsy returned positive for clear cell papillary renal cell carcinoma.

Discussion:
CEUS can be used to differentiate benign and malignant liver lesions to reduce the need for biopsy, and it can be used to target the lesion to ensure adequate sampling. In noncirrhotic patients, benign and malignant lesions can be accurately differentiated based upon the pattern of enhancement. In cirrhotic patients, differentiation of benign from malignant lesions cannot be done as accurately, thus a LIRADS (Liver Imaging Reporting and Data System) categorization has been developed to help evaluate hepatic lesions in cirrhotic patients using CEUS. The presence of microbubbles demonstrating intralesional vascularity on CEUS is sufficient to classify a renal lesion as a solid mass which is highly suspicious for renal cell carcinoma. CEUS can then also be used to guide a biopsy of the lesion.

Conclusions:
CEUS provides a safe, more accessible, and efficacious alternative to CECT and CEMRI in patients with contraindications for the detailed evaluation of hepatic and renal masses prior to biopsy.

Abstract Title: Healthcare Perspectives Of Adolescent E-Cigarette Use: Associated Risk Factors And Resources. A Qualitative Study.

Investigator: Noah Meester
Co-Investigator(s): Hannah Savage, Old Dominion University; Ann L. Edwards, EVMS Pediatrics; Jelina Deocampo, Old Dominion University; Kelli England PhD, EVMS Pediatrics; Amy Paulson, EVMS Pediatrics; Natasha Sriraman MD, EVMS Pediatrics; Paul Harrell PhD, EVMS Pediatrics
Department(s): Pediatrics

Abstract

INTRODUCTION:
In the past decade, e-cigarette use has become the most common form of nicotine consumption for adolescents and young adults, and nicotine's addictive, psychoactive, and furtive qualities present health risks that negatively impact younger users. Considering these health implications, healthcare providers may be in an ideal position to intervene when they encounter adolescents who vape, and this investigation seeks to characterize their perception of the risks associated with vaping and the resources necessary to remedy vaping behavior.

METHODS:
Interviews and focus groups were conducted with 13 Hampton Roads healthcare professionals (physicians, inpatient nurses, school nurses, and athletic trainers) who directly interact with adolescents. Using vignettes, opinions were elicited to describe variables that may predispose a teen to vaping, risks attributable to current vaping behavior, and resources to mitigate vaping-associated risk. In this investigation, a given risk can have a bidirectional relationship with vaping. Vignette-based responses were grouped based on the vaping behavior within the vignette, with two vignettes portraying an adolescent who currently vapes, and one vignette portraying an adolescent who has yet to vape. Interviews were conducted via Zoom and transcribed manually. Themes were identified using common language and analyzed for frequencies using Microsoft Excel.

RESULTS:
For adolescents who may not yet have begun vaping, healthcare professionals identified peer pressure as the primary variable promoting vaping initiation. Other variables included personality, proximity to use, and home environment. Resources for adolescents who required preventative interventions were focused on education, social and familial support, and development of social strategies. For adolescents who already exhibit vaping behavior, motivation for use (life event, stress relief or coping mechanism) was identified to be the most prominent factor associated with vaping use. Poly-substance use, social context of use, and detriment to health were also major risk factors. Adolescents who already vape were thought to require education, medical intervention, motivational interviewing, and mentorship.

CONCLUSION:
Healthcare professionals' responses varied based on an adolescent's level of interaction with vaping behavior. Findings contained in this study may help healthcare providers address adolescent vaping prevention and cessation.

Abstract Title: Myeloid Derived Suppressor Cells Modulate Abdominal Aortic Aneurysm Formation

Investigator: William Montgomery
Co-Investigator(s): Craig T. Elder, University of Florida Department of Surgery; Joseph Hartman, University of Florida Department of Surgery; Gang Su, University of Florida Department of Surgery; Guanyi Lu, University of Florida Department of Surgery; Lyle Moldawer, University of Florida Department of Surgery; Philip Efron, University of Florida Department of Surgery; Ashish Sharma, University of Florida Department of Surgery; Gilbert R. Upchurch JR, University of Florida Department of Surgery
Department(s): University of Florida Department of Surgery

Abstract

Introduction:
Myeloid derived suppressor cells (MDSCs) are a heterogenous population of myeloid precursor and progenitor cells associated with potent immune regulatory activity, but their role in the pathogenesis of abdominal aortic aneurysms (AAAs) remains unknown. Granulocytic (G-MDSCs) and monocytic (M-MDSCs), the two main subsets of MDSCs, are phenotypically and morphologically similar to neutrophils and monocytes respectively, and have been associated with trafficking via CXCR2 and CCR2 receptors, respectively, in other chronic inflammatory conditions. The goal of this study was to investigate the role of G- and M-MDSCs in the pathogenesis of AAAs and to establish their trafficking mechanism as well as T cell suppression during aortic inflammation.

Methods:
AAAs were induced in 8- to 12-week old male C57Bl/6, Balb/c, crelox Lyz2-*cebpb*-/-, (deficient in MDSCs), mCXCR2-/- and CCR2-/- mice using topical (0.4 U/mL type 1 porcine pancreatic elastase) treatment or deactivated elastase as control. On postoperative days 3, 7, 14, and 21, aortic diameter was measured using video micrometry prior to harvest. Flow cytometry analysis was performed for the quantification of MDSCs (CD11b+Gr-1+). *In vitro* experiments of mixed lymphocyte reactions using MNCs (mononuclear cells) (3×105) and MDSCs were performed to analyze the phenotypic role of MDSCs in T cell-dependent IL-17A suppression, a pro-inflammatory cytokine linking T cell activation to neutrophil mobilization and AAA pathogenesis.

Results:
A significant increase in aortic diameter was observed in elastase-treated C57BL/6 mice compared to controls on day 7 (-6 ± 3.4% vs 141 ± 20.6%; n=5 vs n=4; p<0.0001) and day 14 (-12 ± 1.4% vs 175 ± 30%; n=5 vs n=14; p<0.0001). Elastase-treated WT mice had a significant increase in CD11b+Gr-1+ MDSC population in the aortic tissue compared to heat-inactivated controls on days 7 (5.8 ± 1.3% vs. 1.8 ± 0.9%; n=6/group) as well as day 14 (12.3 ± 1.2% vs. 5.1 ± 0.4%; n=6/group). However, aortic diameter was significantly decreased in elastase-treated mCXCR2-/- mice compared to elastase-treated WT mice on day 7 (97 ± 14% vs 141 ± 21% dilation; n=4/ group; p=0.02). In addition, aortic diameter in CCR2-/- mice was significantly decreased compared to elastase-treated WT controls on day 14 (122 ± 33% vs 175 ± 30%; n=5 vs n=14; p=0.006). Interestingly, both incidence of rupture and AAA diameters were significantly increased at day 21 in cebpb-/- mice compared to Balb/c controls (4/12 vs 0/10 rupture, p=0.04) (249 ± 120% vs 158 ± 93% dilation; n=12 vs n=10; p=0.02). *In vitro* studies showed that anti-CD3/CD28 activated MNCs had a significant increase in IL-17A secretion, which was attenuated by co-culture with MDSCs (1695 ± 224 vs. 589 ± 95 pg/ml; p<0.05).

Conclusions:
These results suggest that MDSCs play a contributory role in the pathogenesis of AAA via CXCR2 and CCR2-dependent trafficking. The relative contribution of G- and M-MDSC subsets in the immunomodulation of aortic inflammation and vascular remodeling needs to be further delineated in ongoing studies.

Abstract Title: Rural versus Urban PROMs Following Primary TKA

Investigator: Caleb Morgan
Co-Investigator(s): Brian Dykstra, EVMS/ MD 2024; Samantha Elliott, EVMS/ MD 2025; Jonathan Parker, EVMS/ MD 2024; Joseph Gondusky, MD, Jordan-Young Institute, EVMS
Department(s): Jordan-Young Institute

Abstract

Introduction:
Individuals in rural areas have worse healthcare outcomes overall, including increased complication rates following total joint arthroplasty. However, few studies have investigated patient-reported outcomes measures (PROMs) in this population. The aim of this study was to investigate PROMs in rural and urban individuals following total knee arthroplasty (TKA).

Methods:
This was a retrospective, survey-based study investigating PROMs in 96 individuals who underwent primary TKA by one surgeon. Responses were collected a minimum of two years following surgery. Participants were stratified into rural (n=34) or urban (n=62) groups based on the Federal Office of Rural Health Policy designation of their addresses. The knee injury and osteoarthritis outcome score (KOOS Jr.), 10-point visual analog scale (VAS) and subjective outcome data were collected, including access to postoperative resources. Sociodemographics and comorbidities were recorded. Multivariate analysis of variance (MANOVA) and independent t-tests were performed for continuous variables and chi- squared tests for categorical responses.

Results:
MANOVA results indicated no significant differences for PROMs (p=.315). Independent t-tests revealed lower KOOS Jr. scores for the rural compared to the urban group with means of 77.36 and 82.13, respectively (p=.183). Rural individuals had a higher mean VAS pain score of 2.00 compared to 1.73 for the urban group (p=.291). Both groups had similar VAS scores for met expectations and satisfaction, as well as reported access to postoperative resources. Individuals in the urban group were more willing to have the surgery again if needed, 98.4% versus 91.2% (p=.095). The rural group had a significantly higher incidence of depression and anxiety compared to the urban group, 38.2% versus 19.4% (p=.044).

Conclusion:
PROM data comparing urban versus rural TKA patients is lacking. The study reveals lower but not significant PROMs differences for rural patients. Higher-powered studies are needed to determine the significance of the expected differences in outcomes between these groups and we hope to accomplish this as we increase our sample size.

Abstract Title: Developing a Differential Diagnosis of Cystic Lesions in the Abdomen

Investigator: Meghann Muldowney
Co-Investigator(s): Jutras, Lauren MD, Department of Radiology; Elgohary, Dina MD, Department of Radiology
Department(s): Radiology

Abstract

Introduction:
Cystic lesions identified on imaging can be difficult to classify due to significant similarity in appearance and difficulty identifying an organ of origin particularly for large masses. Considerations such as appearance, location, and clinical history are useful in establishing a differential diagnosis.

Case Information:
A 32-year-old woman with a PMH of cystic fibrosis presented to the emergency department for a CF exacerbation, abdominal pain, and fullness. The patient endorsed 5 days of intermittent, dull abdominal pain. Additionally, the patient noted an increase in abdomen size over the past couple of months. On CT angiography (CTA), the patient was noted to have a large intra-abdominal cyst. Follow-up CT scan demonstrated a 16.4 x 30.3 x 33.8 cm homogenous fluid attenuation cystic structure in the anterior abdomen and pelvis with mass effect on all intrabdominal organs. The patient was evaluated by surgery and subsequently scheduled for resection of the mass. A large, right paraovarian cyst arising from the broad ligament was resected and sent to pathology which demonstrated a benign serous cystadenofibroma of the fallopian tube.

Discussion:
The differential diagnosis for cystic lesions identified on imaging is very broad. There are multiple ways to help narrow the differential despite the significant overlap in the appearance of the lesions. The differential of cystic lesions can be narrowed by organ of origin, content of the cyst, presence of locularity, wall thickness, septations, and calcifications. In the case of this patient, the size of the cyst made it difficult to identify the organ of origin. Lack of previous scans also hindered the ability to identify how long the lesion had been present or how quickly it had grown. Based on this the leading differential was a mesenteric cyst, which are simple, thin-walled, unilocular cysts, with no septations or calcifications, consistent with the patient's imaging. Surgical exploration and resection demonstrated a right, paraovarian cyst arising from the broad ligament and adherent to the right fallopian tube. The specimen was sent to pathology which demonstrated a thin-walled cyst filled with clear, watery fluid. TA tubular structure and stretched fimbria were identified on the surface of the cyst leading to the final diagnosis of a serous cystadenofibroma of the fallopian tube.

Conclusion:
This case demonstrates the difficulty in diagnosing cystic lesions arising in the abdomen based solely on imaging due to significant similarities in appearance of multiple lesions. Imaging may be able to help narrow the differential, but it may be necessary for a Pathologist to determine the final diagnosis.

Abstract Title: Anemia Prevalence Time Trends and Disparities in the US Population: Examination of NHANES 1999-2020

Investigator: Adan Naseer
Co-Investigator(s): Yunjoo A Hwang, MD2024; Kripa R Ahuja, MD2025; Syed M Haque, MD2024; George F Jones, MD2025; Oren Shechter, MD2025; Simrah Siddiqui, MD2024
Department(s): Department of Internal Medicine

Abstract

Introduction:
Anemia has significant associations with increased morbidity and mortality and can serve as a valuable indicator of disease processes. Adverse effects associated with anemia are observed in patients with heart failure. Anemia status is also a valuable prognostic indicator in serious diseases. While a rising prevalence of anemia in the United States (US) was reported in older studies, recent data are lacking. There is a dearth of evidence on how the prevalence may differ among various groups in the US, so we investigated the current prevalence of anemia and subgroup trends.

Methods:
Data from the National Health and Nutrition Examination Survey (NHANES) from 1999-2020 was used. Each NHANES survey sampled about 10,000 individuals of all ages and genders with oversampling of persons 60 and older, African Americans, and Hispanics. Hemoglobin levels of participants were used to determine anemia presence using the World Health Organization criteria. Hemoglobin was measured by NHANES mobile examination center. Survey-weighted raw and adjusted prevalence rate ratios (PRR) were determined using generalized linear models for the overall population, and by gender, age groups, race, and household to income poverty threshold ratio (HIPR). Interaction terms were used to examine whether anemia time trends differed among various categories of the sample. All analyses were conducted using Stata 16.1 and a $p<0.05$ was considered significant.

Results:
Complete data on hemoglobin, age, gender, and race was available on 87,554 participants. The mean age is 34.6 years, and women made up 49.8%. The study includes 37.3% whites, 29.8% Hispanics, and 23.7% Blacks. The mean hemoglobin was 13.8mg/dL and HIPR was 2.3.

Anemia prevalence by Race, Gender, Age, and HIPR
In adjusted analyses, anemia prevalence was higher in the elderly than in 26-45 years old (PRR=2.14, 95%CI=1.95, 2.35), in Blacks than in Whites (PRR=3.97, 95%CI=3.63, 4.35), in women than in men (PRR=1.98, 95%CI=1.83, 2.13), and in those with HIPR≤1 than HIPR>4 (PRR=0.68, 95%CI=0.61, 0.75).

Anemia Prevalence Time-Trends
The prevalence of anemia increased from 4.03% during the 1999-2000 survey cycle to 6.49% during 2017-20; the adjusted PRR was 1.61 (95%CI=1.24, 2.09) in the 2011-12 cycle and 1.44 (95%CI = 1.14, 1.82) in the 2017-20 cycle.

Gender Modified Relationship between Anemia Prevalence and Race
Compared to their male counterparts, Black (interaction PRR=1.39; 95%CI=1.20, 1.62), Hispanic (interaction PRR=2.38; 95%CI=1.91, 2.95), and other women (interaction PRR=1.50; 95%CI=1.13, 1.99) had higher anemia prevalence and higher prevalence than white women.

Conclusion:
The prevalence of anemia in the US has risen from 1999 to 2020, although the anemia prevalence plateaued between 2017-2020. The prevalence remains high among the elderly, minorities, and women. Further, the difference in anemia prevalence between men and women is larger in non-whites highlighting undesirable disparities among different races and genders calling for more focused attention.

Abstract Title: Utilizing a Quality of Life (QOL) Tool to Examine the Presence of Fatigue in Subjects with Diabetes Mellitus

Investigator: Catherine Nguyen
Co-Investigator(s): Henri K. Parsons PhD, Jordan Pettaway MS, Elias S. Siraj MD, Carolina M. Casellini ,MD
Department(s): EVMS Endocrine and Metabolic Disorders

Abstract

Introduction:
Prevalence of fatigue in patients with diabetes mellitus (DM) is as high as 50%. Physical, mental, and psychosocial components of fatigue negatively impact quality of life (QOL) and increases morbidity and mortality. Several tools have been developed to address fatigue, but none have been developed specifically for measuring fatigue in DM and its effect on commonly associated complications such as depression and diabetic neuropathy (DN). The aim of this study is to assess the impact of diabetes and neuropathy on fatigue and QOL using the Norfolk QOL-Fatigue (QOL-F) survey, a 35-item validated questionnaire sensitive to physical, cognitive, and emotional aspects of fatigue. We hypothesize that fatigue symptoms will be more prevalent in subjects with diabetes, and more specifically with DN, when compared to healthy controls (HC).

Methods:
Sixty-five healthy participants from Hampton Roads (ages 35 to 79) were recruited and added to previously recruited HC (n=140) and subjects with DM (type 1 or type 2 DM, n=400). All subjects completed the Norfolk (QOL-F), which was administered either on site or online via RedCap survey. Demographics, weight, height, and duration of diabetes were obtained. The QOL-F assessed five domains: physical and cognitive fatigue, subjective fatigue, reduced activities, impaired activities of daily life (ADLs), and depression.

Results:
DM subjects reported significantly higher fatigue scores in all five domains when compared to HC (52.63 vs 33.89, $p<0.0001$). DM subjects with DN were significantly more fatigued than those without DN in all domains (59.72 vs 27.83, $p<0.0001$). Fatigue scores in diabetic patients without DN were similar to HC (27.83 vs 33.89, p= NS). Significant associations were observed between age and fatigue scores with younger participants reporting more fatigue ($r= -0.303$, $p<0.0001$). Female gender was significantly associated with higher fatigue scores in the control group ($p<0.001$), but not in the DM group.

Conclusion:
This study shows that the Norfolk QOL-F questionnaire can potentially identify the impact of chronic diseases such as diabetes on fatigue. Assessing the different components of fatigue is important for clinicians in improving disease management and outcomes. Further investigations are needed to confirm these observations in specific cohorts with other comorbidities.

Abstract Title: mtDNA mutation detection, differentiation of NTER-2 cells with retinoic acid and transfection with siRNA

Investigator: Alexandra Nigro
Co-Investigator(s):
Department(s): Physiology Department

Abstract

Introduction:
Alzheimer's has an association with decreased mitochondrial enzyme activity and therefore decreased mitochondrial metabolic capability. A single nucleotide polymorphism (T9861C) has been shown to be associated with AD brain samples2. This previously identified mutation affects subunit 3 of RC-4 and ultimately mitochondrial function, providing a link between known mitochondrial dysfunction in degenerative brain disease and genetic changes. One goal of this project is to test 18 additional brain samples for the T9861C mutation. A second goal is to identify how knocking down UQCRC1 will affect mitochondrial function. UQCRC1 encodes the core protein of cytochrome c reductase. UQCRC1 is a component of RC-3 and is implicated in Alzheimer's as seen in methylation studies1. If UQCRC1 is knocked down in Ntera-2 cells, then there will be changes to mitochondrial function as seen via pH, ROS, and ATP synthesis.

Methods:
End-point PCR was used in order to amplify the sequence of interest of mtDNA for mutant testing. DNA purification was employed to concentrate the PCR DNA. This DNA was then used in a restriction digest with the Hae III which cleaves mutant mtDNA. These results were analyzed via acrylamide gel electrophoresis. Allele-specific fluorescent qPCR was used as an alternative method to detect this mutation, utilizing different blockers and primers. As a prelude to the siRNA experiments, our lab has treated a human carcinoma NTERA-2 cell line with retinoic acid to initiate differentiation into a neuronal cell line, NT2-N. I am in the process of demonstrating successful differentiation by assessing Nestin mRNA levels by qPCR. I am also assisting in the optimization of the transfection protocol to knockdown UQCRC1 mRNA. This latter experiment will be performed if time permits.

Results:
Results showed no significant mutant DNA in the 18 new brain samples. Transfection was optimized and the next step will be to establish knockdown cell lines for metabolic testing.

Conclusion:
None of the newly acquired brains samples possessed the T9861C mutation. We appear to have identified conditions for successfully achieving a high level of transfection frequency with our NT2 cells. Results of Nestin mRNA levels are to come.

References:
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Abstract Title: COVID-19 Precautions and Their Effect on Influenza Rates

Investigator: Blake Nowakowski
Co-Investigator(s): Joseph Rogers, MD Student
Department(s): Family Medicine

Abstract

Introduction:
Since the beginning of the WHO announcing a new strain of coronavirus on January 9, 2020, the SARS-CoV-2 has fundamentally changed the healthcare landscape. While the virus began to rapidly spread, numerous precautions were taken by the governments and citizens around the world with aims to halt the spread of the growing pandemic. The transmission of influenza and COVID-19 are similar in that both causative viruses are spread person-to-person via respiratory droplets when an infected individual coughs, sneezes, or talks within about six feet of close contact with another individual. It has also been documented that both viruses may be transmitted from an infected person before the individual experiences any symptoms of illness. Considering risk factors, complications, and mechanism of transmission are similar between influenza and SARS-CoV-19, we suspect that precautions taken to mitigate the spread and infectivity of one will subsequently impact the other.

Methods:
A retrospective chart review was used to query patients at the Portsmouth and Ghent Family Medicine practices in Virginia who have tested positive for influenza for the 2019-2020 and 2020-2021 influenza seasons.

Results:
Of the cases queried, during the 2019-2020 flu season, there were 36 positive influenza cases at Portsmouth family medicine and 51 positive influenza cases at Ghent Family Medicine. During the flu season of 2020-2021, there were 0 positive influenza cases at both Portsmouth and Ghent Family Medicine.

Conclusion:
There was a significant decrease in the number of positive influenza cases from the 2019-2020 season to the 2020-2021 season, with a similar trend seen statewide. Three possible explanations for these results include patients with influenza/COVID-like illness being instructed not to present to family medicine practices, driving down the number of positive tests, preventative measures for COVID decreasing the transmission of influenza, and the superinfection exclusion principle, making simultaneous COVID and influenza infection less likely.

Abstract Title: Harnessing Extracellular Vesicle-mediated Immunosuppression Against Breast Cancer

Investigator: Sarah O'Berry
Co-Investigator(s):
Department(s): Leroy T. Canoles Jr. Cancer Research Center

Abstract

Introduction:
Breast cancer is the most common and second deadliest cancer in women. It is now known that both breast cancer cells and non-tumor cells in the tumor microenvironment (TME) release nano-sized, membrane-enclosed vesicles termed extracellular vesicles (EVs) that primarily function in intercellular communication. EVs can promote breast cancer initiation, progression, and metastasis in several ways, such as enhancing angiogenesis and motility, remodeling extracellular matrix, inducing epithelial to mesenchymal transition, creating a favorable pre-metastatic niche, and mediating resistance to chemotherapeutic drugs. By transferring bioactive cargo molecules, EVs are also reported to play the immunomodulation roles in cancer. As the addition of immune checkpoint inhibitors to chemotherapy becomes the standard-of-care treatment for triple-negative breast cancer and in trials for other subtypes of breast cancer, this review summarizes the recent findings on immunoregulatory roles of EVs and discusses their potential clinical applications in breast cancer.

Main Body:
Articles were chosen from the PubMed database for review based on publish date within the last ten years. The body of evidence demonstrates that EVs derived from both tumor cells and other cellular components in the TME contribute to the formation of an immunosuppressive microenvironment through the following mechanisms. First, tumor-derived EVs can suppress anti-tumor immune cells on multifaceted aspects. They can induce T cell apoptosis and inhibit their activation and proliferation, suppress the immunity of NK cells, and block the differentiation and maturation of dendritic cells. For example, breast cancer cells release high levels of EVs expressing PD-L1, which inactivates CD8+ T cells. In contrast, tumor-derived EVs can also activate regulatory or pro-tumorigenic immune cells in different ways. They can enhance the proliferation and functions of Tregs and Bregs, promote the polarization of M2 macrophages, and induce the expansion and functions of myeloid-derived suppressor cells (MDSCs). Studies have shown that PDL1+ EVs activate MDSCs, which release cytokines that decrease T cells and increase M2 macrophages in lung metastasis. Lastly, non-tumor cells in the TME (such as cancer-associated fibroblasts (CAFs), MDSCs, and tumor-associated macrophages) also secrete EVs to contribute to immune escape of tumor cells. For example, CAFs secrete EVs containing tumor growth factor b, which supports tumor growth and suppresses the immune response.

Based on the immunosuppressive roles of EVs in breast cancer, EVs have great potential to help breast cancer management in clinic. First, EVs can be isolated from body fluids, and immune molecular signatures carried in EVs can be used to develop accurate and sensitive assays for noninvasive and real-time assessment of immunotherapy response in breast cancer. Second, new therapeutic strategies based on modulation of the level or function of EVs may help overcome immune escape in breast cancer and improve patient outcomes. One such method includes eliminating cancer-derived EVs in circulation by inhibiting EV biogenesis, blocking EV uptake by target cells, and using antibodies to target and destroy EVs. In addition, tumor-specific antigens can be loaded into EVs and delivered to immune cells, which enables the formation of an immune response against cancer cells. This would allow the possibility of a vaccine to prevent breast cancer.

Conclusions:
In breast cancer, EVs secreted by tumor cells and surrounding non-tumor cells in the TME orchestrate an immunosuppressive microenvironment favorable for tumor development and progression. On the other side, these properties also allow taking advantage of EV-mediated immunoregulatory effects and their unique features to develop innovative anti-tumor therapeutic avenues.

Abstract Title: Imaging Findings in Gestational Trophoblastic Disease: A Case of Metastatic Choriocarcinoma

Investigator: Philip Olivares
Co-Investigator(s): Emily Glavich, MD, Department of Radiology
Department(s): Department of Radiology

Abstract

Introduction:
Choriocarcinoma is a rare tumor on the spectrum of gestational trophoblastic disease that is highly aggressive but also very responsive to chemotherapy. Imaging is important for the diagnosis and staging of this disease.

Case Information:
A previously healthy 24 yo female presented to the emergency department with new onset seizures. Initial head CT was performed which showed a large intraparenchymal hematoma in her left frontal lobe and she was also found to have markedly elevated beta-HCG on labs. A pelvic ultrasound subsequently revealed a markedly enlarged, heterogeneous, and hypervascular uterus suspicious for choriocarcinoma. Follow-up imaging then showed evidence of pulmonary metastases. The patient was admitted and medically stabilized. She underwent further workup followed by biopsy of the left frontal lobe brain lesion which revealed metastatic choriocarcinoma. She was then transferred to a quaternary care center for initiation of chemotherapy.

Discussion:
Choriocarcinoma is a highly aggressive, malignant tumor that is part of the spectrum of gestational trophoblastic disease (GTD) It is suspected in patients with vaginal bleeding and inadequate uterine regression following delivery or is diagnosed via serum B-hCG surveillance in non-symptomatic patients (shaaban et al). Pelvic ultrasound is often the first imaging obtained in the initial work-up and computed tomography (CT) and magnetic resonance (MR) imaging play an important role for staging disease. Metastases occur most commonly in the lung (up to 87%) and vagina (30%), but can occur anywhere, including the liver and brain. Gestational choriocarcinoma is highly sensitive to chemotherapy; patients at low-risk for metastatic disease are treated with single-agent chemotherapy and have cure rates approaching 100% while patients with high-risk for metastatic disease are treated with multiagent chemotherapy with or without adjuvant radiation therapy or surgery have cure rates of 80%-90% (shaaban et al).

Conclusion:
Choriocarcinoma is a rare but highly aggressive malignancy typically affecting reproductive age woman. It has characteristic imaging features and patterns of metastatic disease and imaging play an important role in the diagnosis and staging of this disease.

Abstract Title: Patient Satisfaction Survey Data in the Hofheimer Hall Primary Care Clinic

Investigator: Kristin Olson
Co-Investigator(s): Rajita Kannaparredy, BA (Medical Student, EVMS); Zooha Altaf, MBBS (Research Volunteer, EVMS Dept. of Internal Medicine); Jennifer Ryal, MD (Principal Investigator, EVMS Dept. of Internal Medicine)
Department(s): EVMS Internal Medicine

Abstract

Introduction:
Recent findings suggest that time spent with a provider is a stronger predictor of patient satisfaction than time spent in the waiting room. Patient satisfaction has been associated with better adherence to recommended therapy by patients and better patient outcomes. Examining patient satisfaction is particularly relevant, given that the COVID-19 pandemic has amplified the mass shortage of healthcare personnel across the country. As part of this research study, we surveyed patients in the Hofheimer Hall, Primary Care Clinic to better understand current satisfaction levels.

Methods:
Patients interested in study participation were given a one-page (double-sided) questionnaire. This questionnaire contains demographic and clinical questions followed by validated patient satisfaction questions (VSQ9). No patient identifiers were collected in the questionnaire. Hard copies of the questionnaire were distributed to subjects by IRB-approved research team personnel.

Results:
Of the 289 patients who consented, 102 (35.3%) were Male and 174 (60.2%) were Female. 13 (4.5%) selected "Other or prefer not to say". 139 (48.9%) were White, 131 (46.1%) were African American, and 14 (4.9%) selected "Other or prefer not to say". 14 (5.2%) identified as "Hispanic or Latino". 179 (63.0%) of patients completed "College", while 101 (35.6%) had only completed "High School or GED" and 4 (1.4%) had completed "middle school" as their highest level of education. 100 (34.7%) reported being "Single", 111 (38.5%) are married, 34 (11.8%) are divorced, and 43 (14.9%) are widowed. 88 (31.2%) have Medicare, 75 (26.6%) have Medicaid, 117 (41.5%) have private insurance, and 2 (0.7%) have no health insurance. 90 (32.4%) had an income of less than 25,000, 62 (22.3%) have an income between 25,000 and 50,000, 79 (28.4%) have an income between 50,000 and 100,000, and 47 (16.9%) had an income of greater than 100,000.

209 (73.1%) rated their overall health as "Excellent", "Very Good" or "Fair", while 77 (26.9%) responded either "Fair" or "Poor". 42 (18.2%) had Heart Disease, 160 (69.3%) have High Blood Pressure, 34 (14.7%) had Cancer, 73 (31.6%) had Diabetes, 47 (20.3%) had Asthma, 68 (29.4%) had High Cholesterol, and 15 (6.5%) had COPD. 38 (13.8%) smoke, while 238 (86.2%) are non-smokers.

In response to "How long you waited to get an appointment", 252 (88.1%) selected "Excellent", "Very Good" or "Good", while 34 (11.8%) responded "Fair" or "Poor". In response to "Convenience of the office location", 263 (91.3%) responded "Excellent", "Very Good" or "Good", while 25 (8.7%) responded "Fair" or "Poor". For the question "Getting through to the office by phone", 237 (83.7%) responded "Excellent", "Very Good" or "Good", while 46 (16.2%) responded "Fair" or "Poor". In response to "Length of time waiting at the office", 262 (90.9%) responded "Excellent", "Very Good" or "Good", while 26 (9%) responded "Fair" or "Poor". In response to "Time spent with physician you saw", 281 (98%) responded "Excellent", "Very Good" or "Good", while 6 (1.1 %) responded "Fair" or "Poor". In response to "Explanation of what was done for you", 281 (98.3%) responded "Excellent", "Very Good" or "Good", while 5 (1.7 %) responded "Fair" or "Poor". In response to "Technical skills (thoroughness, carefulness, competence) of the provider you saw", 283 (98.7%) responded "Excellent", "Very Good" or "Good", while 4 (1.4 %) responded "Fair" or "Poor". In response to "Personal manner (courtesy, respect, sensitivity, friendliness) of the person you saw", 284 (99.2%) responded "Excellent", "Very Good" or "Good", while 2 (0.7 %) responded "Fair" or "Poor". In response to "The visit overall", 280 (98.2%) responded "Excellent", "Very Good" or "Good", while 5 (1.8 %) responded "Fair" or "Poor".

Conclusion:
These results are preliminary data points for a larger patient-satisfaction and compassion survey study on clinic staffing models. These early survey results suggest potential areas to increase patient satisfaction. Early survey results also suggest that the primary care population is more educated and has health insurance coverage compared to the overall community in Norfolk, based on the 2020 Norfolk City Census. Further data is needed to achieve our primary study objective to understand how clinic staffing models impact patient satisfaction.

Abstract Title: Modulation of HSP90 and HSP70 Inflammatory Pathway within Acutely inflamed Human Lung Endothelial Cells

Investigator: Michael Osei-Nkansah
Co-Investigator(s): Ruben Manuel Luciano Colunga Biancatelli, Research Assistant Professor, Frank Reidy Research Center for Bioelectrics\Old Dominion University
Department(s): Research Center for Bioelectrics, Old Dominion University

Abstract

Introduction:
Hydrochloric acid (HCl) is a known chemical that evokes inflammation of the respiratory system (Marinova et al., 2019). HCl is used in various settings such as the oil, gas, and steel industries, medical practices, scientific laboratories, and swimming pool maintenance. One single exposure to HCl can lead to mild inflammatory and profibrotic responses within the lungs (Marinova et al., 2019). Furthermore, depending on the concentration and duration of exposure more severe complications such as acute respiratory distress syndrome, pulmonary edema, bronchitis, and even death may arise (Kerger & Fedoruk, 2015). Modulation of pulmonary inflammation using a Heat Shock protein 90 (HSP90) inhibitor and a Heat shock protein 70 (HSP70) inducer could prove beneficial in mitigating the effects of HCl inflammatory damage in Human Lung Microvascular Endothelial cells (HLMVEC) through the restoration of endothelial barrier function.

Heat shock proteins (HSPs) are molecular chaperones that assist in the folding, stabilization, and activity of other proteins (Sevin et al., 2015). HSPs constitute about 5-10% of the total protein content in most cells, being further increased by stressors such as oxidative stress, alcohol, and infection. HSPs are classified into a multitude of families dependent on their molecular weight. HSP90 is the most abundant HSP found in cells. HSP90 plays an essential role in many cellular processes such as cell cycle control, cell survival, and cell signaling (Sevin et al., 2015). It also plays a role in the stabilization of transforming growth factor-β (TGF- β), the leading cytokine in pulmonary fibrosis. Recent research suggests that by disrupting the protein stability of HSP90 and blocking specific cellular responses via an HSP90 inhibitor, anti-inflammatory and antifibrotic effects are observed (Colunga Biancatelli et al., 2022). HSP70, like HSP90, is important for many cellular processes. HSP70 acts as a co-chaperone of HSP90. Research has shown that inhibition of HSP90 with overexpression of HSP70 has a positive effect on endothelial barrier function within cells (Colunga Biancatelli et al., 2022)

Materials and Methods:
Previously harvested HLMVECs were cultured in 100 mm dishes until 90-95% confluency. After cells were deemed confluent, cells were trypsinized to dissociate cells from the dish and centrifuged. The supernatant was aspirated and separated from the pellet. The pellet was resuspended in 6ml of in-house growth media. After resuspension cells were added to a trough containing 24ml of in-house made growth media. HLMVECs were then seeded on an electrode array (96W20idf). Each well contained 300µl of HLMVECs in growth media. Cells were placed in the ECIS-Z theta instrument and endothelial barrier integrity was estimated by the electric cell-substrate impedance sensing (ECIS) technique. Cells were grown in ECIS till stable resistance (>600Ω) After cells reached a stable resistance, wells were treated with different concentrations of 20µl of TAS-116 4 and GGA (4 with 8µm Tas-116, 4 with a 16µm TAS-116, 4 with 8µm TAS-116 + 8µm GGA, and 4 with 8µm TAS-116 + 16µm GGA). After treatment cells were left in the ECIS for 24 hours. After 24 hours the wells were treated with 2µl of .02N of HCl. Four wells acted as experimental controls with 20µl of saline added to them. Another four wells served as negative controls with 20µl of saline + 2µl of .02N HCl added to them.

Results and Conclusion:
Analysis of the results showed a statistically significant difference in membrane resistance between cells treated with TAS-116 + HCl, TAS-116+ GGA + HCl, and cells treated with saline + HCl. No statistically significant difference was found between control cells and cells treated with HSP90 inhibitor and HSP70 inducer. These findings show the effectiveness of TAS-116 and GGA in maintaining endothelial barrier function after exposure to an inflammatory agent such as HCl. Furthermore, no statistically significant difference was found between cells treated with TAS-116, TAS-116+GGA, and control cells showing that these treatments may have the potential to bring endothelial barrier function back to baseline. However, this experiment has some limitations. The long-term effects of TAS-116 and GGA use in chronic inflammatory lung conditions were not investigated.

Abstract Title: Analyzing Demographics and Older Adult's Ability to Master Technology

Investigator: Alim Osman
Co-Investigator(s): Alexandra Nigro, M1; Pavan Suryadevara, M1; Sarah Mayo, M1
Department(s): Internal Medicine: Glennan Center for Geriatrics and Gerontology

Abstract

Introduction:
With the increasing older adult population, previous studies have examined how technology can become an integral part of healthcare for older adults (1). The finding of this systematic review includes studies that report older adults' eagerness to learn technology, involvement of peers, the effectiveness of coaching and timely follow up with novice learners. It is important to assess and understand older adults' ability to learn how to accurately use technology. Furthermore, it is important to account for factors that could enhance or inhibit one's learning experience.

The HealthWise Technology Program was created first as a virtual program to combat isolation due to the pandemic. Eastern Virginia Medical School, Glennan Center for Geriatrics and Gerontology, Senior Services of Southeastern Virginia, PrimePlus Norfolk Senior Centers and Westminster Canterbury on the Chesapeake Bay collaborated to develop the program to support older adults who could no longer attend the centers and programs in person. Senior Services of Southeastern Virginia, the local area agency on aging, now offers HealthWise in its array of services to support health and wellness.

Methods:
HealthWise is now offered for virtual learners and through a newly created in-person course instructed by the HealthWise Technology Program Director. Twenty-five older adult volunteers enrolled in the course at a local recreation center. EVMS student volunteers in Beyond Clinic Walls Community Engaged Learning Initiative serve as teaching assistants for each class. The course began in August and will end in mid-October 2022. Each older adult enrolled in the course received a tablet provided by HealthWise. Participants are required to attend class on a weekly basis for eight weeks, following instructions provided by the class instructor with EVMS students' support. Each participant is given homework to complete on the tablets on a weekly basis. Participants are then asked to fill out a survey each week assessing comfort level, level of social support, and other concerns regarding their learning experience. Their ability to complete their homework is also monitored to gauge retention of skills learned in class.

The purpose of our study is to analyze the effects of socioeconomic status (SES), sex, previous occupation, and social support on older adult's ability to gain comfort in using an electronic tablet. Our hypothesis is multifaceted in its approach: (i) We predict that a higher SES is associated with a higher comfort level; (ii) We predict that male participants will have a higher comfort level due to gender biases as well as previous occupations that required greater use of technology; (iii) We predict that a higher level of social support will have a positive impact on comfort level as well as optimism for future class assignments.

Results:
To date, 25 older adults have participated in three one-hour classes. EVMS students will continue to attend classes offering assistance to the learners and plan to submit an application to the IRB to examine the data related to the hypothesis.

Abstract Title: A rare tumor in an unusual location: myxopapillary ependymoma in the left gluteal subcutaneous tissue

Investigator: Chirag Patel
Co-Investigator(s): Michael Pender, MD EVMS Department of Radiology
Department(s): EVMS

Abstract

Introduction:
Myxopapillary ependymoma (ME) is a benign spinal cord tumor that arises from ependymal glia of the filum terminale. Glial cells or neuroglia are cells that that provide metabolic and physical support to neurons in the central and peripheral nervous system. These cells are thought to arise from the coccygeal medullary vestige or extradural remnants of the filum terminale. MEs account for approximately 1-5% of all spinal neoplasms, 13% of all spinal ependymomas and 90% of all tumors located in the conus medullaris. Due to their rarity, diagnosis of these tumors and subsequent management is debated. Generally, patients diagnosed with a myxopapillary ependymoma have a mean age of onset of 35 years and experience symptoms related to the location and size of the tumor. Patients commonly experience back pain, urinary difficulties, nausea, vomiting and other neurological deficits due to the tumor's proximity with the spinal cord. Treatment of the tumor usually involves surgical excision and subsequent monitoring with imaging for recurrence.

Case information:
This report is of an 11 year-old patient with a past medical history of Ehlers-Danlo and POTS syndrome who presented to the emergency department with concerns for an enlarging mass in the left gluteal region. Patient reports that he noticed the lesion while showering 7 days ago. He denies any pain in the area, constipation, and states that he has daily bowel movements. Review of systems was negative and physical exam showed an engorged and violaceous superficial papules in the left gluteal region that were easily compressible. These papules extended from the anus up to the left aspect of the gluteal cleft. Adjacent to these lesions, there was non-tender subcutaneous nodule measuring 9cm x 4cm. MRI pelvis with IV contrast showed a well-circumscribed, lobulated, septated T2 hyperintense, T1 hypointense, hyperenhancing lesion measuring 8.1 x 5.7 x 8.5 cm (AP, TRN, CC). These characteristics suggested a myxomatous lesion. The mass was surgically resected and intraoperative pathology was consistent with myxopapillary ependymoma.

Discussion/ Conclusion:
This case report aims to highlight the unusual presentation and location of this patient's myxopapillary ependymoma. At baseline, these central nervous system tumors are extremely rare and almost always located within the lumbosacral spine segment, mainly in the conus medullaris and cauda equina regions. We show a myxopapillary ependymoma located in the left gluteal soft tissue in a young patient who denied any symptoms. Thus, it is important for clinicians to recognize that myxopapillary ependymomas can present outside of central nervous system and should be included on the differential for soft tissues masses in the thoracolumbar region.

Abstract Title: Comparing Wrist Arthroplasty Procedures Between Orthopedic and Plastic Surgeons

Investigator: Jason Pham
Co-Investigator(s): Melinda R Lem, The University of California, Irvine Plastic Surgery Department
Department(s): Plastic Surgery

Abstract

Introduction:
Osteoarthritis (OA) is prevalent in up to 56.6% of men and women in the United States. Multiple specialties can treat OA. The purpose of this study is to utilize the American College of Surgeons National Surgical Quality Improvement Program to collect information on patient information to determine if there is a difference between acute clinical outcomes between orthopedic and plastic surgery when performing arthroplasty for the treatment of osteoarthrosis of the hand and wrist.

Methods:
A retrospective cross-sectional analysis was performed by including patients who were diagnosed with osteoarthrosis of the hand and wrist by ICD9 or ICD10 codes and had an associated Current Procedural Terminology code. Surgical specialty was collected, and orthopedic and plastic surgery patients were compared. Univariate analysis including Pearson chi-square and Fischer's exact test were used for categorical variables while a two-tailed Mann-Whitney U test was performed on continuous variables. Multivariate regression analysis was performed on significant complication variables to determine strength of predictors.

Results:
There was a total of 3721 patients queried for those who received arthroplasty for osteoarthrosis of the hand and wrist from the 2007-2020 dataset. Most cases were performed by orthopedic surgeons (82.7%) however, there was an increasing number of surgeries performed by plastic surgeons throughout each year. The majority of cases were performed on the intercarpal or carpometacarpal joints (81.7%). The incidence of acute complications was low (1.9%) with superficial SSI being the most common complication. Univariate analysis found that plastic surgery may result in higher chances of superficial SSI when compared to orthopedic surgery, but multivariate analysis indicated that there were no significant differences between the two groups.

Conclusion:
There were no significant differences on multivariate regression analysis between plastic and orthopedic surgeons, suggesting that both surgical specialties can confidently perform hand osteoarthrosis care without safety concerns.

Abstract Title: Predictors and Acute Outcomes Associated with Ganglion Cyst Surgeries of the Wrist

Investigator: Jason Pham
Co-Investigator(s): James Tran, Huntington Health, General Surgery Residency
Department(s): Plastic Surgery

Abstract

Introduction:
Ganglion cysts account for 60-70% of soft tissue masses in the hand and wrist. Prior to undergoing any surgical procedure, proper preoperative risk stratification should be performed to minimize potential complications. There are many factors that could contribute to complications. Two tools that aggregate potential risk factors are the Charlson Comorbidity Index and the Frailty Index. However, there is a paucity in the literature that reviewed the acute outcomes of excision of ganglion cyst and its potential predictors.

Methods:
We performed a retrospective cross-sectional analysis utilizing the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database from 2005-2020. Our study filtered through patient data to determine if they were diagnosed with ganglion cyst according to International Classification of Diseases (ICD) 9 or ICD10 codes. We subsequently included patients if they received a Current Procedural Terminology (CPT) code that indicated removal of ganglions cysts of the hand or wrist. The Modified Charlson Comorbidity Index (mCCI) and the Modified Frailty Index (mFI-5) were calculated and compared with other comorbidities to determine predictive ability.

Results:
Our study queried approximately 8991 patients from the ACS NSQIP database from 2005-2020. There was an overall complication rate of 1.1%. The most common surgical complications were superficial incisional surgical site infections (SSI) and wound disruption, while the most common medical complication was urinary tract infection (UTI). White patients, ASA classification of 3-Severe Disturbance, and of 4-Life Threatening were statistically significant on multivariate analysis for surgical complications. 4-Life Threatening ASA classification had the strongest association with increased risk of superficial incisional SSI.

Conclusion:
The mCCI and mFI-5 were not found to be accurate predictors for ganglion cyst surgery complications. Increasing ASA classification was found to be the most predictive factor for potential complications.

Abstract Title: Determining Online Patient Reviews and Breast Reconstruction Satisfaction

Investigator: Jason Pham
Co-Investigator(s): Joshua K. Kim, Duke Medical School; Stepehn E Hunt, The University of California, Irvine; Dominique M Willette, The University of California, Irvine
Department(s): Plastic Surgery

Abstract

Introduction:
Breast reconstruction is a life-changing decision that may help restore a sense of identity for women who feel that they have lost a part of their identity after mastectomy. Understanding how patients experience and reflect on their procedures is critical to improving care. RealSelf is an online community that hosts an expansive number of online reviews for cosmetic and reconstructive plastic surgery procedures. The purpose of this study is to analyze patient satisfaction with breast reconstruction procedures from RealSelf to determine factors contributing to a positive or negative patient experience.

Methods:
The breast reconstruction category from RealSelf.com was analyzed using a web crawler-based application built from Python and Selenium. Reviews were collected from May 2009 to November 2021. Information including RealSelf's inherent "Worth It" ranking system, review text, the number of submitted photos, and the number of readers who found the review helpful was captured. The content of the review was then independently reviewed by the authors and was categorized with key factors that determined positive or negative reviews.

Results:
A total of 3451 breast reconstruction reviews were collected. After the authors analyzed each review, 3225 (94.33%) were identified as positive reviews. The most common factors associated with positive reviews were physician demeanor (n=2600, 31.7%), aesthetic outcome (n=1955, 23.8%), or staff (n=1543, 18.8%) while negative reviews were associated with unfavorable aesthetic outcome (n=94, 28.9%), physician demeanor (n=82, 25.2%), or postoperative complications (n=75, 23.1%).

Conclusions:
While there are surveys that analyze patient satisfaction for breast reconstruction, there has not been a study that analyzed a large online review database. Predominating factors in both positive and negative reviews were physician demeanor and aesthetic outcome.

Abstract Title: Perceived Fear, Stigma, and Discrimination During COVID-19 Pandemic – Findings from a Mixed-Methods Study Conducted in 2022 among Chinese Americans in Eastern Virginia

Investigator: Tram Phung
Co-Investigator(s): Timothy W. Liu, BS; Elizabeth C. Li, BS; James Chung, BS; Caitlyn F. Ling, BS; Spencer G. Chee, MS; Tracy Dien, BS; Marc Franco T. Nepomuceno, MS; Jaime Luis D. Almirante, BA; Cynthia C. Romero, MD; Hongyun "Tracy" Fu, PhD
Department(s): Pediatrics

Abstract

Background:
Although the surge in anti-Asian sentiment and hate crime has been widely acknowledged in the U.S., particularly after the outbreak of the COVID-19 pandemic, limited empirical research has been conducted to address this issue in smaller size cities in the United States. We examined the extent to which Chinese Americans (CA) experienced stigma and discrimination and the disparities across subgroups of CA, using data collected from a mixed-methods study in Eastern Virginia.

Methods:
A community health resources and needs assessment (CHRNA) which integrated an online quantitative survey and virtual qualitative interviews, was conducted in April/July 2022 among Asian and Pacific Islanders (APIs) in Eastern Virginia. Survey respondents (N=1,462) were recruited through a range of social media channels and in-person events via the existing AAPI networks in Eastern Virginia, following three sampling criteria: 1) being decedents of Asian and Pacific Islanders; 2) ages 18-85 years, and 3) residents of Hampton Roads and the Eastern Shore. Data from a subsample of CA (N=325) were analyzed, using descriptive statistics and multivariable logistic regression. Key informants (N=23) were recruited through snowball sampling and referrals from Chinese community stakeholders. Semi-structured interviews (30-60 minutes) were conducted virtually via Zoom either in English or Chinese by trained bilingual researchers. An Amazon E-gift card ($25) was provided to compensate for the participant's time. Semantic analysis was conducted to identify the key themes, guided by the grounded theory and the Creswell method.

Results:
The majority of CAs considered that 1) social and mass media reports about COVID-19 created biases against APIs (71%); 2) The U.S. is becoming more dangerous for APIs due to fear of COVID (64%), and APIs are more likely to lose their jobs (52%). Significant proportions of CA reported experiences of being treated with less courtesy (44%), less respect (43%), received poorer services (41%), considered dishonest (33%), being called names or insulted (30%), being threatened/harassed (26%), and being abused verbally/physically (16%), and being followed around in stores (15%) by someone in the past year. The odds of experiencing stigma and discrimination are higher among those who were older, had lower education, worked in blue-collar professions, and did not speak English fluently. While the results from qualitative interviews revealed similar patterns of findings, they showed the protective effects of having good family support and living in a close-knit neighborhood against stigma and discrimination.

Conclusions:
Findings revealed high levels of experience with stigma and discrimination among CA living in small size cities in Eastern Virginia, highlighting the urgent need for targeted interventions to combat Racism against Chinese Americans to protect their health and wellbeing rights.

Abstract Title: Echocardiography Follow-up after Mitral Valve Surgery

Investigator: Fletcher Pierce
Department(s): Sentara Mid-Atlantic Cardiothoracic Surgeons

Abstract

INTRODUCTION

Mitral valve regurgitation is divided into two broad etiological categories. Primary mitral valve regurgitation refers to intrinsic issues with the mitral valve apparatus. Causes of primary regurgitation include, though are not limited to, myxomatous degeneration, Barlow's disease, and endocarditis. Secondary mitral valve regurgitation, often called functional regurgitation, refers to regurgitation caused by left ventricular remodeling, as seen in the context of ischemic cardiomyopathy. Surgical treatment of mitral valve regurgitation involves either repair or replacement of the incompetent valve. Echocardiography is the gold standard for determining the severity of the regurgitation, as well as the success of the surgical treatment. Despite the widespread use of echocardiography, there is limited echocardiography data from which surgeons are able to compare their treatment results for various etiologies of mitral disease. Publishing echocardiography results categorized by etiology of mitral regurgitation requires careful patient evaluation, follow-up, and chart review. This study reviews the outcomes of all mitral valve surgeries for mitral valve regurgitation completed at Norfolk Heart Hospital by Sentara Mid-Atlantic Cardiothoracic Surgeons between June 1st 2019 and December 31st 2022. Surgical results are broken down by surgeon and etiology and evaluated based on echocardiographic scoring methods.

METHODS

Echocardiography measures the severity of mitral regurgitation using regurgitation volume (RV), in milliliters, and regurgitation fraction (RF), in percentage. This study scores the severity of regurgitation based on the following standardized values: 0 (RV:0, RF:0), 1+ (RV: <30, RF: <30), 2+ (RV: 30-44, RF: 30-39), 3+ (RV: 44-59, RF: 40-49), 4+ (RV: ≥ 60, RF: ≥ 50). These scores (0-4) are referred to, respectively, as none, trivial, mild, moderate, and severe regurgitation. Using chart review in EPIC, etiology and echocardiography data was collected for all mitral regurgitation patients treated with open surgical valve repair or replacement between June 1st, 2019 and December 31st, 2021. Each patients' echocardiography scores were collected at four different time intervals: pre-operative transesophageal echocardiogram (TEE), post-operative TEE, discharge transthoracic echocardiogram (TTE), and 6-8 week follow up TTE. By comparing these four scores, four values were calculated that quantify patients' improvement in mitral valve regurgitation:

1. Total improvement: (6-8 week follow-up TTE) - (pre-operative TEE)
2. Intra-operative Improvement: (post-operative TEE) - (pre-operative TEE)
3. Discharge Improvement: (discharge TTE)- (post-operative TEE)
4. Follow-up Improvement: (6-8 week follow-up TTE) - (discharge TTE)

RESULTS

168 patients and 7 surgeons were included in this study.

Echocardiography outcomes by surgeon:

- Number of surgeries completed by surgeon ranged from 3 to 76.
- Average total improvement of patients, divided by surgeon, ranged from 3.03 to 3.33.
- Average total improvement for all patients is 3.167 with a standard deviation of 0.866.

Echocardiography outcomes by etiology of disease:

- Primary mitral regurgitation includes 107 patients.
- Average total improvement for this group is 3.121.
- Primary mitral regurgitation includes myxomatous degeneration, Barlow's disease, and endocarditis. Average total improvement scores in these groups are 2.969, 3.235, 3.385, respectively.
- Secondary mitral regurgitation includes 23 patients.
- Average total improvement for this group is 3.360.
- Secondary mitral regurgitation includes ischemic cardiomyopathy and non-ischemic cardiomyopathy. Average improvement in improvement scores for these two groups are 3.133 and 3.625, respectively.

CONCLUSION

Regardless of the operating surgeon or disease etiology, on average, patients' regurgitation improved by at least 3 points and surgery resulted in less than trace regurgitation at 6-8 weeks. Outcomes between surgeons vary minimally; the variability in outcomes between disease etiologies is greater. The greatest average improvement is seen with non-ischemic cardiomyopathy and the smallest average improvement is seen with myxomatous degeneration.

Abstract Title: Trochlear Dysplasia and Anterior Knee Pain after ACL Reconstruction: A Sex-Based Comparison

Investigator: Emily Pilc
Co-Investigator(s): Maria Velasquez Hammerle, MD, Massachusetts General Hospital/Department of Orthopaedic Surgery; Miho Tanaka, MD, Massachusetts General Hospital/Department of Orthopaedic Surgery; Sean Hazzard, PA, Massachusetts General Hospital/Department of Orthopaedic Surgery; Peter Asnis, MD, Massachusetts General Hospital/Department of Orthopaedic Surgery
Department(s): Massachusetts General Hospital, Department of Orthopaedic Surgery

Abstract

Introduction:
Trochlear Dysplasia (TD) is defined as a congenital morphological abnormality of the trochlear groove of the femur characterized by a shallow sulcus angle (>145°) [1]. Historically this abnormality has been associated with patellofemoral instability, defined as one or more episodes of patellar dislocation [2]. More recent attention has been given to the association between TD and ACL tears. Chen et al. and Ntagiopoulos et al. found that the presence of TD was significantly higher in patients with torn ACLs compared to control groups [1][3]. Chen et al. determined that the incidence of TD in their ACL injury group was 30.7% compared to 14.4% in their control group ($p<0.001$) [1]. The increased incidence of TD in ACL injury could be explained by the altered orientation of the ACL in knees with trochlear dysplasia. Al-Assam et al. found an association between TD and more vertical sagittal and anteromedial ACL angles, which have been implicated in ACL failure [4]. TD tends to be more predominant in females compared to males [5], but a sex-based comparison of TD and ACL tears and the effect on postoperative anterior knee pain has yet to be investigated.

Methods:
We used an institutional database to identify 288 patients who had an ACL reconstruction and received magnetic resonance imaging (MRI). Of those patients, 175 completed Kujala Scores at the one year postoperative mark to assess knee function with special focus on anterior knee pain. Trochlear Dysplasia was assessed by measuring the bony sulcus angle. TD was considered present if the angle measured 145° or higher.

A chi square test was used to analyze the different rates of TD in males compared to females. A linear regression analysis was performed between the sulcus angles and Kujala scores in the overall cohort and in the male and female groups to determine the significance of the relationship between TD and postoperative anterior knee pain.

Wilcoxon rank-sum tests were used to determine if there was a significant difference in mean Kujala scores in males or females with TD compared to without TD. Finally, chi square analysis was performed on individual Kujala questions including pain, walking limitations, and swelling at one year postoperatively to determine if there was a significant difference between the dysplastic and normal groups of males compared to females.

Results:
Of the 288 patients who presented with a torn ACL and underwent surgical repair, 132 (45.8%) identified as male and 156 (54.2%) identified as female. The mean age of the patients was 32.2 years. Of the 132 males, 15.2% has TD while of the 156 females, 34.0% had trochlear dysplasia. Using a chi-square test, it was determined that there was a significant difference in the incidence of TD between the males and females with ACL tears ($p=0.00025$), however without a control group we cannot determine if there is a higher incidence of TD in females with ACL tears.

The median one-year postoperative Kujala Score for males with TD was 96 and without TD was 96. In females the median scores were 95 and 94 with and without TD respectively. According to the linear regression analyses, there was no significant difference in the one year postoperative Kujala Scores between the normal and dysplastic knees in the overall cohort nor in either gender category ($p>0.05$).

Wilcoxon rank-sum tests did not find a significant difference in mean Kujala scores in males or females with TD compared to without TD ($p>0.05$). Chi square analysis did not find a significant difference in pain, walking limitation, or swelling between males vs females with and without TD ($p>0.05$).

Conclusion:
Previous data has shown that TD occurs at higher rates in patients with ACL injuries and that TD is more predominant in females [1][3][5]. Our data shows that females with ACL tears have significantly more incidence of TD than their male counterparts. However, without a healthy control group we cannot determine that TD is a risk factor for ACL injury. We did not find a significant difference in the rates of postoperative anterior knee pain between the normal and dysplastic groups or differences in other markers of knee function for normal and dysplastic groups between the two gender cohorts. This study should be repeated with more subjects, a control group, more markers of TD rather than just sulcus angle, and with more outcome data in addition to patient-completed surveys in order to ensure the accuracy of our data.

Abstract Title: Early indicators of early childhood mental health concerns in toddlers

Investigator: Dustin Platter
Co-Investigator(s): Morgan Shelton; M3 at EVMS
Department(s): Psychology, Psychiatry, Pediatrics

Abstract

Introduction:
Approximately one in ten preschool children experience emotional behavioral difficulties (Egger, 2006). As of 2022, the American Academy of Pediatrics (AAP) recommends annual social-emotional screening for all children to promote identify children at risk, as well as caregiver mental health screening early in life (AAP, 2022). Rapid synaptogenesis and developmental changes during early childhood provide an opportunity for effective early intervention (Tierney, 2009).

The Brief Early Childhood Screening Assessment (B-ECSA) is a validated screen to identify mental health concerns in children 18-60 months. Previous validity studies included children from the full 18-60 month rage range, so a limited number of 18-month-olds (Fallucco, 2017).

This study expands the validity of the B-ECSA with a focus on 18-month-old children, examines the association between caregiver stress and depression and child/caregiver factors, and explores a predictive model for the B-ECSA using clinical and demographic factors.

Methods:
A retrospective chart review was performed via CHADIS on 1416 patients with a completed B-ECSA at 18 months old. The review analyzed concurrent social determinants of health, demographics, responses to the Family Assessment of Safety and Stress Survey (FASS), discipline strategies via the Conflict Tactics Scale (CTS) and the Ages and Stages Questionnaire-3, a questionnaire used to assess early childhood developmental domains.

Results:
The B-ECSA demonstrated convergent validity with clinical factors such as low income, food insecurity, any developmental delay before 18 months, children of color, and caregiver education less than a college degree. Linear regression identified 4 significant factors (early developmental delay, caregiver stress, harsh punishment, and corporal punishment) that together explained 15.4% of variance in B-ECSA scores. The data also suggested that caregiver stress and depression have differential associations regarding to child and caregiver factors.

Conclusion/Discussion:
This study demonstrates the validity of the B-ECSA in early childhood mental health screening. It also identifies important demographics and child/parent factors related to child mental health symptoms. Addressing these factors early could reduce the risk of childhood mental health difficulties.

Abstract Title: Heavy Metal Trauma: Severe Mercury Toxicity from Gunshot Wounds - A 28-Year Case Review and Current Management Guidelines

Investigator: Timothy Putnam
Co-Investigator(s): Adin Tyler Putnam II, University of Massachusetts Baystate, General Surgery, Surgical Critical Care
Department(s): Pathology and Anatomy

Abstract

Introduction:
We review the case of a police officer shot seven times with hollow-point mercury-filled bullets. Systemic mercury poisoning is extremely rare, and this case represents the only known example of gunshot wound-related severe mercury toxicity.

Case Information:
A 35-year-old male deputy sheriff was shot at close range with 7 mercury-filled 45 caliber hollow point bullets. The victim received wounds to the abdomen, buttocks, perineum, knee, and thigh. No initial evidence of mercury contamination was noted, and no bullets were recovered during initial emergent surgery. Suspicion arose when postop plain films revealed abdominal wall stippling of a radiopaque substance; the assailant then reported mercury bullets. Serum and urine mercury levels were obtained on post-op day one and serially thereafter. Mercury-contaminated soft tissue, bone, and four mercury-tipped bullets were excised during multiple operations. 3 courses of D-penicillamine were completed during the hospitalization.

Serum mercury levels were initially 300 mcg/dl (normal < 5 mcg/dl). Initial urine mercury excretion was 2 mcg/dl (normal < 10 mcg/dl). Mercury urinary excretion was > 1000 mcg/dl after the third course of D-penicillamine therapy. All excised tissue contained very high levels of mercury (acetabulum fragment > 26,000 mcg/gm). Surgery and chelation therapy rapidly decreased the patient's mercury load prior to discharge (LOS-60 days). Serum mercury levels at 6-year follow-up evaluation were < 5 mcg/dl and remained low during his life.

The patient was followed closely for a 6-year period with serial exams/mercury level testing and then followed as needed. Serial clinical psychological testing was normal during follow-up, and the patient worked as a police officer for 10 years after injury. He died from neurological disease (brain tumor) 28 years after the initial toxicity.

Discussion/Clinical Findings:
Metallic mercury poisoning, as opposed to organic or inorganic mercury toxicity, is rare and a review of the literature reveals only 53 cases of metallic mercury poisoning, with five deaths reported. Most of these cases include accidental subcutaneous injection or metallic mercury use in suicide attempts. There have been no previously reported cases of 'traumatic" metallic mercury poisoning resulting from gunshot wounds.

Although there have been 45 documented cases of serious lead poisoning from retained bullets, similar reports do not exist for mercury poisoning from gunshot wounds. The use of mercury in bullets has only been rumored by ranchers, criminals, soldiers in the Vietnam conflict, and in popular culture (Hollywood), but the absorption of injected subcutaneous mercury by the body tissues and resultant mercury toxicity is well documented. The subsequent management of such mercury toxicity requires an initial high index of suspicion, prompt recognition, and early aggressive intervention.

Conclusion:
To better understand the diagnosis and treatment of traumatic subcutaneous, intraperitoneal and intraosseous poisoning leading to systemic mercury toxicity, we have presented the first case study of mercury bullet wounds.

This case demonstrates how metallic mercury can be readily absorbed in tissue and corroborates previous reports of subcutaneous metallic mercury toxicity. A high index of suspicion in the gunshot victim and prompt medical and surgical treatment was required for a favorable outcome. The unpredictable nature and limited experience with mercury toxicity requires long term monitoring to include serial blood testing and psychological evaluation.

Successful diagnosis and treatment of this rare case of severe, systemic mercury toxicity resulted in a 28-year survival after injury. Current literature review recommends rapid removal of gross contamination, chelation, hemodialysis/plasmapheresis, and supportive therapy with long-term monitoring for sequelae.

Abstract Title: Itching to find a solution for Alpha-Gal's Pain

Investigator: Mahiar Rabie
Co-Investigator(s): Manasa Vallabhaneni/MD 2023; Dhanveer Singh, MD/Department of Internal Medicine; Jody King, MD/Department of Internal Medicine
Department(s): EVMS Department of Internal Medicine

Abstract

Introduction:
Alpha-gal syndrome (AGS), also known as mammalian meat allergy, refers to a hypersensitivity reaction between IgE and galactose-alpha-1,3-galactose which is found on glycolipids and glycoproteins of all mammals, except primates. Tick bites primarily induce these IgE antibodies, but Trombiculidae Mites and Parasites have recently been implicated as well. The most common presentation of AGS is a delayed reaction, typically 3 to 6 hours, following meat ingestion that commonly includes urticaria, gastrointestinal upset, or anaphylaxis. This is a case of AGS which highlights the presentation, causative agents, and the complexity in management.

Case Information:
A 45-year-old African American female with a past medical history of AGS and hypertension presented to the emergency department with a severe, acute onset headache with associated emesis, photophobia, and phonophobia. Head CT revealed a subarachnoid hemorrhage, and she was subsequently transferred for neurosurgical evaluation. CT Angiogram was completed which showed an anterior communicating artery aneurysm and the patient subsequently underwent endovascular coiling. Low molecular weight heparin (LMWH) was commenced for DVT prophylaxis and acetaminophen as needed for headache and back pain. During the hospital course, the patient developed diffuse itching and was given diphenhydramine. Notably, the patient also reported poor pain control and was given oxycodone. Due to the patient's continued pruritus, it was hypothesized that meat derivatives in her LMWH, acetaminophen, and oxycodone were the culprit. After identifying alternative meat-derivative free medications, LMWH was first replaced with enoxaparin, followed by discontinuation of acetaminophen, and then replacement of oxycodone tablets with Lehigh Valley liquid oxycodone. Following these stepwise medication adjustments, the patient's pruritis improved with each change.

Discussion:
AGS has become increasingly prevalent in recent years. Given that this condition precludes standard management, it is important to identify symptoms and signs that may suggest a diagnosis of AGS. Our patient was initially prescribed LMWH and acetaminophen which contain meat derivatives in most formulations. Given these active ingredients, our patient experienced diffuse pruritus. When the patient was started on oxycodone tablets due to poor pain control, she continued to have pruritus because many oxycodone formulations contain meat derivatives, such as glycerin and stearic acid. However, when the patient's DVT prophylaxis was adjusted to enoxaparin, her symptoms improved. When the patient's acetaminophen was discontinued and her oxycodone tablets were replaced with Lehigh Valley liquid oxycodone, her pruritus resolved.

Conclusion:
Given the rising number of AGS cases, it is important for to understand which medications can be used. This, in turn, directly impacts patient care and satisfaction. Clinicians need to be familiar with AGS which will allow them to consider it as a differential diagnosis and to tailor their management accordingly. This case is intended to serve as a guide for patients with AGS who are seeking pain relief, and who are incurring allergic reactions to many common medications.

Abstract Title: The Effect of the Teen Health 360 Academy on Sexual Health Knowledge among High-School Students in Hampton Roads

Investigator: Samra Rashid
Co-Investigator(s): Hongyun "Tracy" Fu, PhD, MA, Department of Pediatrics, Community Health and Research Division; Rebecca J. Slimak, Program Coordinator, Department of Pediatrics, Community Health and Research Division; Brady Goggins, MPH 2023; Danielle Long, MD 2025; Rose Dever, MD 2025; Janvi Agrawal, MD 2026; Amil Ahsan, MD 2025; Katherine Johnson, MD 2025; Taylor Wallace, MD 2023; Amy C. Paulson, BS, MPH, Department of Pediatrics, Community Health and Research Division; Kelli J. England, PhD, MS, Department of Pediatrics, Community Health and Research Division; Matthew C. Herman, MPH, BS, Brock Institute for Community and Global Health
Department(s): Department of Pediatrics, Community Health and Research Division

Abstract

Introduction:
Although high rates of teen pregnancy and sexually transmitted infections (STIs) have been consistently reported in Hampton Roads, access to comprehensive sex education (CSE) for school-age youth is limited in this region due to a range of socioeconomic, cultural, and structural barriers. The Teen Health 360 program at the EVMS Pediatrics Department adopted the Get Real Comprehensive Sex Education That Works (Get Real) curriculum for implementation as academy sessions among school-age youth. This study examined the effect of the Teen Health 360 academy on sexual health knowledge among high school program participants.

Methods:
Participants were recruited between May 2021 and June 2022 through online and in-person promotion channels. Parents/guardians were invited to register their children via an opt-in form. Academy sessions were delivered either in person or virtually via zoom by trained health educators. Participants who completed the sessions were awarded a certificate of completion and a $35 incentive. A range of data was collected using pre- and post-assessments, student feedback forms, parent feedback forms, and program fidelity logs. Descriptive statistics and regression analysis were performed to examine differences in sexual health knowledge between pre- and post-assessment, and differential effects between virtual and in-person program models.

Results:
The average age of participants (N=160) was 15.4 years old (Std=0.09); 41.4% were White, 27.6% African American, 24.8 % Asian, and 6.2% Latino. Regarding gender identity, 33.8% self-identified as boys, 54.5% as girls, and 11.7% as transgender/unsure. Regarding sexual orientation, 61.4% self-identified as heterosexual, 22% as non-heterosexual, and 16.6% as unsure/not-known. The vast majority (79%, 127/160) attended the virtual sessions, the rest (21%, 33/160) attended in-person sessions. Of the attendees, 91% (145/160) completed the pre-assessment, and 71% (114/160) completed the post-assessment. Knowledge about STIs significantly increased from pre- to post-assessment, with the magnitude of change slightly larger among in-person participants (Beta:1.18, P<0.001), relative to virtual participants (Beta:1.16, P<0.001). However, the increase in knowledge about sexuality was slightly larger among virtual participants (Beta:0.28, P<0.04), relative to in-person participants (Beta:0.23, P=0.17).

Conclusion:
Findings indicate that both virtual and in-person Teen Health 360 academy sessions are effective in improving sexual health knowledge among high-school students in Hampton Roads.

Abstract Title: Low-Volume Resuscitation with Polyethylene Glycol-20k increases Survival after severe Splanchnic Artery Occlusion shock in Swine

Investigator: Aref Rastegar
Co-Investigator(s): Jad Khoraki, Virginia Commonwealth University Department of Surgery; Ru Li, Virginia Commonwealth University Department of Surgery; Caitlin Archambault, Virginia Commonwealth University Department of Surgery; Loren Liebrecht, Virginia Commonwealth University Department of Surgery; Martin Mangino, Virginia Commonwealth University Department of Surgery
Department(s): Virginia Commonwealth University Department of Surgery

Abstract

Introduction:
Post Traumatic hemorrhagic shock (HS) is a leading cause of preventable death in civilian and combat trauma. The current gold standard therapy involves a balanced transfusion of red blood cells, plasma, and platelets, but prehospital logistic constraints limit the availability of blood products soon after injury when early effective resuscitation is key to survival. Low-volume crystalloid solutions containing hypertonic saline or polymers have shown suboptimal clinical results. Consequently, there remains a need for a safe and effective resuscitation solution that is stable, abundant, and transportable in the prehospital setting. Ischemia in splanchnic organs caused by HS plays a significant role in increasing the mortality of patients. Hence, this study investigates the effectiveness of isotonic crystalloid [lactated Ringer's (LR)] containing 10% polyethylene glycol 20,000 (PEG-20k) in an acute swine model of severe splanchnic ischemia caused by superior mesenteric artery occlusion mimicking HS outcomes.

Methods:
Traumatic critical illness was simulated in new splanchnic shock model in 35 kg swine (n=4/group). After anesthesia using isoflurane, a midline abdominal incision was made to expose the superior mesenteric artery. A vascular clamp was used to completely occlude the SMA for 30 minutes. The occlusion was verified by directly visualizing mucosal capillary flow in the distal ileum using orthogonal polarization spectral imaging (OPSI). After 30 min of occlusion, shock was induced by reperfusion of the SMA. This is time zero. Ten minutes after release, swine were randomized to receive a low volume resuscitation (6.8 ml/kg, IV, over 5 minutes) of either LR solution (control) or PEG-20k IV solution dissolved in LR. Macro-hemodynamics (mean arterial pressure, heart rate, cardiac output, SVO2, pulmonary artery pressure) were continuously measured along with mucosal capillary blood flow of the distal ileum via OPSI every hour after shock. Arterial blood gases were determined every hour and metabolic panels were determined every 2 hours after shock. Swine were allowed to stay in the shock state after SMA release for up to 8 hours or until their blood pressure reached 30 mm Hg, at which time they were euthanized.

Results :
These data demonstrate that under these conditions, 30 minutes of global ischemia to the small bowel produces SAO shock as seen by cardiovascular and metabolic outcomes and death within 4.5 hours from time of the release of SMA in the control group. The PEG-20k swine survived to study endpoint of 8 hours with preserved cardiovascular and metabolic outcomes. The functional trends after PEG-20k treatment suggest an increase in tissue perfusion (lactate) and a paying back of the oxygen debt in the intestinal tissues since the cardiac output increased above normal after reperfusion and returned to control about the time the lactate returned to baseline. This rapid repayment of debt in tissues is necessary for regaining function and arresting continued ischemia after reperfusion due to a swollen microcirculation.

Discussion and Conclusion:
In traumatic HS, inadequate tissue oxygenation and loss of cellular bioenergetics reduce energy-dependent cell volume control mechanisms including the NA+/K+ ATPase pumps. This results in metabolic cell and tissue swelling that compresses the microcirculation, which further hinders organ perfusion and exacerbates ischemic injury. The resulting "no-reflow" phenomenon is further exaggerated by crystalloid overloading with sodium and water, which promotes a vicious cycle. Due to unique molecular properties, PEG-20k exerts a hybrid impermeant-oncotic effect targeting the ischemic cell-swelling by moving isotonic fluids out of the cells and to the intravascular compartment. This decompresses the microcirculation, reloads the capillaries, and restores local tissue perfusion which allows the NA+/K+ ATPase pumps to function. In this study we have demonstrated that early restoration of tissue perfusion with PEG-20k IV solution will delay, attenuate, or abrogate the development of intestinal reperfusion injury and the follow-on systemic shock. This is an important mechanism in surgical trauma and secondary critical illness, which can be treated by targeting the small intestinal and splanchnic circulation by maintaining capillary perfusion during the reperfusion and resuscitation period.

Abstract Title: ABC294640, a Selective Sphingosine Kinase-2 (SK2) Inhibitor, also inhibits Complex I Respiration

Investigator: Aref Rastegar
Co-Investigator(s): Jennifer Bradley, Virginia Commonwealth University Department of Surgery; Ria Fyffe-Freil, Virginia Commonwealth University Department of Physiology and Biophysics; Ru Li, Virginia Commonwealth University Department of Surgery; Martin Mangino, Virginia Commonwealth University Department of Surgery
Department(s): VCU Department of Surgery

Abstract

Introduction:
ABC294640 is an orally active selective inhibitor of sphingosine kinase-2 (SK2), which is currently used clinically for its activity against solid tumor cancers (those of the liver and prostate) and as a laboratory research tool. However, we have shown that this compound has cellular targets other than SK2; namely, mitochondrial complex I proteins.

Methods:
HepG2 cells were treated with ABC294640 for 24hrs, then the drug was removed and replaced with fresh medium for 15min and 24hrs. High-resolution respirometry was utilized to measure electron transport chain (ETC) activity in HepG2 cell lines (Oxygraph-2k by Oroboros, Vienna, Austria). Substrates and inhibitors for complexes I - IV were delivered and the resulting change in oxygen consumption was recorded. Complex I respiration was calculated by subtracting oxygen flux following rotenone injection from the flux following complex I specific substrates and ADP injection.

Results:
ABC294640 acts as a potent and selective inhibitor of complex I of the mitochondrial ETC. ABC294640 is long-acting as its effects were still seen after 24hr washout (Figure). In other experiments using ABC294640 in liver preservation injury to block SK2, the drug was universally fatal after transplantation, completely destroying liver graft function.

Conclusions:
A novel mechanism of the clinically relevant SK2 inhibitor ABC294640 has been discovered. This long-acting inhibitory action of the drug on complex I of the ETC is an important dual mechanism of action to consider when designing clinical trials as well as using ABC294640 as a research tool.

Abstract Title: Racial Disparities in Maternal Cardiovascular Disease

Investigator: Sruthie Rathnam
Co-Investigator(s): Dr. Jerri Waller, Maternal Fetal Medicine; Dr. Lindsay Robbins, Maternal Fetal Medicine
Department(s): EVMS Maternal Fetal Medicine

Abstract

Introduction:
The United States has the highest maternal mortality rate among developed countries and the rate of maternal mortality has more than doubled over recent decades from 7.2 deaths per 100,000 live births in 1987 to 17.4 deaths per 100,000 live births in 2018. Social determinants of health such as race and ethnicity, marital status, and maternal age can contribute to an increased risk of gestational hypertension, the primary predictor of maternal morbidity and mortality. Examining the health disparities among women with cardiovascular disease in Virginia will allow for the identification of strategies to combat these disparities and improve maternal and neonatal outcomes at the community and state level.

Methods:
A retrospective chart review evaluating 450 women with cardiovascular disease who delivered a child between 1/1/2011-2/1/2021 at the Sentara hospital system was performed. Maternal demographics such as maternal age, race, insurance status, and drug and alcohol use were noted. The primary outcome was a composite of Severe Maternal Morbidity (SMM), which is defined as unexpected outcomes of labor which lead to negative consequences to a woman's health. The secondary outcomes were composites of SMM 30 days, 6 months, and 1 year following hospitalization. Neonatal outcomes such as Apgar score or NICU admission were noted.

Expected Outcomes:
According to previous studies on maternal mortality rates, it is hypothesized that Black women compared to White women will have increased maternal morbidity and mortality rates and worse neonatal outcomes. Demographic characteristics, maternal outcomes, and neonatal outcomes between Black and White women will be compared and differences will be considered statistically significant at a p-level of less than 0.05.

Abstract Title: Characterization of Glycosylated Cargos on Extracellular Vesicles for Human Breast Cancer Subtyping

Investigator: Morgan Rouse
Co-Investigator(s): Caleb Smack, MD student/EVMS
Department(s): Microbiology and Cell Biology

Abstract

Introduction:
Breast cancer is a highly heterogenous disease with many subtypes that differ in pathological features, treatment response, and clinical outcome. However, current tissue-based diagnostic routines simplify the inherent complexity of breast biology and provide limited information for patient-tailored treatment decisions. Extracellular vesicles (EVs), as means of cell-to-cell communication and with great potential in liquid biopsy, have been shown to promote tumor progression and therapy resistance. While acknowledged that EVs like their parent cells are heavily glycosylated, little is known about their glycosylated cargos and their representativeness of known cancer characteristics. Here, we characterized the glycosylated molecules (proteins and RNAs) in EVs released by different breast cancer cell lines to define subtype-specific signatures that can be used to improve breast cancer diagnosis and subtyping non-invasively.

Methods:
We used an azido-modified bioorthgonal chemical reporter to metabolically label sialylated molecules in 3 subtypes of human breast cancer cells - MDA-MB-231 (triple negative), SK-BR-3 (HER2-enriched), and BT-474 (ER-positive). EVs were isolated from conditioned media using differential ultracentrifugation and quantified by Nanoparticle Tracking Analysis. Labeled molecules were further tagged via copper-free click chemistry (DBCO reagent) on living cells. Immunofluorescence (IF) was performed at the cellular level to confirm the location and efficiency of label incorporation. Western Blot (WB) and Northern Blot (NB) were used to evaluate labeling effects on glycoproteins and glycoRNAs, respectively.

Results:
If results showed the incorporation of labeled sialic acid into cell surface glycoconjugates of human breast cancer cells. The specific cell-surface sialoglycoprotein signals were detected by WB. Optimal metabolic labeling (24 hr incubation with 25 uM analog sugar) and click reaction (1 hr incubation with 100 uM DBCO at RT) conditions were determined through a series of experiments. Importantly, the abundance of cell-surface sialoglycoproteins correlated with the aggressiveness of each subtype and EVs inherited sialoglycoprotein patterns from their parent cells.

Conclusion:
In this project, we've shown the feasibility to characterize glycosylated proteins on parent cells and their vesicles in multiple breast cancer subtypes by combining metabolic labeling and click chemistry. Future studies aim to further characterize subtype-specific glycoRNAs and profile these glycosylated biopolymers in these cells and their secreted vesicles via proteomics and RNAseq. Ultimately, our findings will provide potential complemental diagnostic biomarkers for breast cancer subtyping and risk stratification.

Abstract Title: Associations Between Cutaneous T-cell Lymphoma and Dermatological Comorbidities Using the National Inpatient Sample

Investigator: Ryan Saal
Co-Investigator(s): Dustin Platter, MS, MD Class of 2025; Mahlete Yared, BS, MD Class of 2025; Waleed Adawi, MS, MD Class of 2024
Department(s): Department of Dermatology

Abstract

Introduction:
Cutaneous T-cell lymphoma (CTCL) is the group of malignancies that result from the monoclonal proliferation of T-cells involving the skin. These diseases typically present with erythematous plaques or patches that can progress to painful and pruritic widespread cutaneous involvement or nodular tumor growth. Several studies have associated hemato-oncological, infectious, cardiovascular, respiratory, and gastrointestinal comorbidities with CTCL, but investigation regarding dermatological diseases associated with CTCL patients is lacking.

Methods:
The 2016 - 2019 National Inpatient Sample, a de-identified patient database accounting for 20% of all U.S. hospitalizations, was analyzed for adult patients with and without CTCL (including mycosis fungoides). Using a multivariable logistic regression adjusting for demographic variables, associations of CTCL with 23 dermatological diseases were determined against the general inpatient population.

Results:
In this study, 12,675 CTCL patients were identified out of 121,074,975 hospitalizations. CTCL was more likely to affect males and white patients. In multivariable logistic regression models controlling for age, sex, race, and insurance type, CTCL was associated with having any dermatological condition (adjusted odds ratio [aOR] 3.73, 95% CI: 3.557 - 2.353). Specifically, CTCL was associated with 16 of the 23 dermatological conditions, with pigmented purpuric dermatosis (aOR: 34.78, 95% CI: 14.44 - 83.76), lichen simplex chronicus (aOR: 14.323, 95% CI: 9.67 - 21.22), and dissecting cellulitis (aOR: 9.035, 95% CI: 5.44 - 15.00) having the greatest association with CTCL.

Conclusion:
Research regarding CTCL and associated dermatological conditions has been previously limited. Our study supports further investigation into CTCL associated comorbidities, due to its intricate pathogenesis.

Abstract Title: Evaluating the Need for a Medical Arabic Program

Investigator: Fatima Sabti
Co-Investigator(s): Sarah Sabti, MD 2025; Dr. Alexandra Leader, CHKD/EVMS; Lydia Sa
Department(s): EVMS, CHKD

Abstract

Introduction:
Cultural competency in healthcare provision is essential to improve health outcomes and dismantle barriers to healthcare access. Efforts to integrate cultural competency training for medical professionals fall short concerning Arab immigrants in the US. Lack of representation, research, and data available about Arab immigrants perpetuates cultural incompetency amongst healthcare professionals, and related health disparities. This research aimed to study and address this population's unique healthcare needs.

Methods:
A literature review identified quantity and types of research conducted on Arab immigrants nationwide, using specific immigrant-related keywords including: assimilation status, recency of arrival, English-competency, country of origin, religious status, etc. Geographic factors, such as states and cities with the largest populations of Arabic speakers, were identified by US census data and the Arab American Institute Foundation. To understand the local Arab population profile, partnerships with resettlement agencies were leveraged.

Results:
In general, Arab immigrants represent disproportionately recent arrivals into the US when compared to other immigrant populations. Two of the biggest barriers to healthcare access were cost and linguistic barriers. Arab immigrants were found to have lower rates of health literacy compared to US-born Arab Americans, partly due to limited English proficiency. Discrimination against this group correlated with higher rates of mental illness, isolation, and worsening health outcomes/practices. One barrier to language learning efforts in healthcare was bias/implicit discrimination, resulting in a lack of culturally competent care that further alienated Arabic patients. Several gaps in the data were established: a lack of a unified database of Arabic-speaking providers, sparse medical Arabic curricula nationwide, research that was insensitive to differences among immigrants due to country of origin, and lack of data about immigrants in rural areas. The Virginia Department of Health provides recommendations for on-site translation services/written vital documents in Arabic throughout several counties, but their data is pulled from the US census and is non-comprehensive due to a lack of MENA (Middle East and North Africa) racial/ethnic category. Among the unmet needs and barriers to healthcare access, linguistic differences presented as particularly impactful.

Conclusion:
Future efforts should focus on providing culturally competent medical Arabic education to healthcare professionals.

Abstract Title: Developing A Medical Arabic Curriculum for Non-Arabic Speakers Using Translation and Transliteration

Investigator: Sarah Sabti
Co-Investigator(s): Fatima Sabti/MD 2025
Department(s): EVMS

Abstract

Introduction:
The United States is home to 1.2 million Middle Eastern immigrants, 40% of whom have limited English proficiency (LEP). LEP is identified as a leading cause for isolation, depression, anxiety, and helplessness, an effect which is amplified in the healthcare setting and leads the community to seek out Arabic-speaking physicians. Thus, there is a need for a program that teaches medical Arabic. To our knowledge, no such program exists, even in the Middle East where medicine is often taught in English and where research shows a gap between the language of the physician and that of the patient.

Methods:
A pilot-ready medical Arabic curriculum for medical students was developed to respond to the growing need for Arabic-speaking physicians. The backwards design model was utilized to establish six curriculum aims: cultural humility, diversity, active learning, medical vocabulary, clinical skills, and service/immersion. Assessment methods were designed according to these aims. Lessons, worksheets, and quizzes were incorporated for asynchronous active learning. Transliteration and incorporation of various widely-used Arabic dialects supported medical vocabulary and diversity aims. Several lessons were dedicated to cultural humility and culturally specific clinical practices. Volunteering and partnership with community stakeholders supported the service/immersion aim.

Results:
Anticipated results include improved knowledge of Medical Arabic vocabulary, familiarity with culturally sensitive clinical practices, and improved student ability to take a patient history in Arabic. Anticipated challenges include sustained engagement in a demanding extracurricular course, and integration of students with diverse and demanding academic schedules.

Conclusion:
This project represents an unprecedented approach to medical Arabic training by using the English alphabet and supports the goal of addressing needs of Arabic-speaking patient communities in the U.S. by building capacity for culturally and linguistically competent care among medical trainees.

Abstract Title: An awareness of availability bias in the COVID era

Investigator: Christina Santana
Department(s): EVMS Infectious Diseases

Abstract

Introduction:
We present a case that highlights the importance of maintaining a broad differential throughout the diagnostic evaluation of a patient presenting with progressive dyspnea, hypoxia and interstitial lung changes on imaging. The prevalence of COVID related information experienced by both the general public and the scientific community, prompts it to be at the forefront of our minds. We hope that this case will aid in diagnostic strategy by preventing premature closure that can be due to the availability heuristic all clinicians are currently being exposed to.

Case Information:
A 40-year-old man with no significant past medical history was brought to the emergency department (ED) with complaints of fatigue and progressive dyspnea. At the time of presentation, he reports the shortness of breath has been progressively worsening over the past week to the point that he is unable to walk to the restroom comfortably. He had also been experiencing loss of appetite and a couple episodes of emesis in this past week. He noted a change in his weight, estimating that he has lost approximately 40 pounds in the last two weeks. EMS noticed the patient's oxygen saturation was 82% on room air. Notably, his four children tested positive for COVID about a month prior, he and his wife had been caring for them and assumed they were positive as well. After his 14-day isolation the patient returned to work, on returning is when he noticed he was very weak and short of breath.

On exam, patient was a thin appearing male on oxygen supplementation with the only pertinent findings being bibasilar crackles and faint course breath sounds. A portable chest film revealed bilateral lower lobe pulmonary opacities 'would be consistent with suspected diagnosis of Covid pneumonia', along with an elevated CRP led to consideration of COVID-19 as the diagnosis and he was subsequently given a dose of steroids. After his COVID reverse-transcriptase polymerase chain reaction (RT-PCR) resulted negative, he was empirically treated with antibiotics for a bacterial pneumonia, however his oxygen requirements continued to rise.

Pulmonology was eventually consulted. After multiple negative COVID tests, >20 days since last exposure, two negative capsid antibody results and a single negative spike protein antibody, it was concluded that his current symptoms are most likely not due to COVID pneumonia. His imaging was also potentially suggestive of a hypersensitivity pneumonitis or other interstitial pneumonia. A subsequent autoimmune workup was unrevealing.

Further testing revealed a reactive HIV-1 antigen/antibody assay, with a CD4 of 17 (1%). His bronchoscopy revealed cytology that was significant for positive pneumocystis jiroveci pneumonia (PJP) PCR from the bronchioalveolar lavage. His infection was treated with Trimethoprim/Sulfamethoxazole and adjunctive steroid protocol, and he was eventually discharged with instructions to follow up with Infectious Diseases for antiretroviral therapy initiation (ART).

Discussion:
In this specific case it was not unreasonable to suspect the patient was presenting with COVID pneumonia, recent known exposures in combination with other clinical aspects led to a lag in revealing the true cause of this patient's condition, but in hindsight the lag might've been an example of anchoring bias. Although a definitive diagnosis is made with the use of reverse-transcriptase polymerase chain reaction (RT-PCR), however this lab work may not result immediately in some settings. For that reason, around this hectic period of crowded emergency departments, it was common to see a working diagnosis based on chest imaging results noting 'findings seen in COVID pneumonia' or 'suspect COVID pneumonia' as part of the single sentence summary.

The radiographical findings of COVID pneumonia may appear similar to those of other etiologies. One single blinded study to evaluate the performance of radiologists in differentiating CT scans of patients with COVID pneumonia versus patients with atypical pneumonis. [4] The radiologists differentiated between COVID-19 and non-COVID-19 pneumonia with an overall accuracy, sensitivity, and specificity of 88%, 79%, and 90%, respectively. A lower performance was observed in the early and late stage of COVID 19 pneumonia. [4]

Conclusion:
As a result of the COVID-19 pandemic, it is most likely one of the first things to pop into a clinician's mind when evaluating a patient such as this one. This case demonstrates the importance of maintaining a broad differential diagnosis in the setting of an illness of unknown etiology. A screening HIV test on admission would help to maintain a broad differential from the start, something some hospitals have made part of their standard admission protocol. By maintaining an awareness of alternative pathologies, a broad differential can be constructed in order to make an accurate diagnosis and not further delay appropriate treatment.

Abstract Title: Comparison of anesthesia recovery times after initiating a standardized sleep endoscopy protocol

Investigator: Colleen Schinderle
Co-Investigator(s): Dr. Cristina Baldassari, MD; CHKD ENT
Department(s): CHKD ENT

Abstract

Introduction:
Drug induced sleep endoscopy (DISE) is an otolarygology procedure used to study patients with obstructive sleep apnea. In March 2021, CHKD implemented a standard anesthesia protocol for children under 13 undergoing DISE based on an expect consensus statement from the American Academy of Otolaryngology. This new protocol involves administration of IV dexmedetomine, an a2-adrenoceptor agonist, in a sequential, dosed amount. Dexmedetomine has a slower metabolism than other comparable sedatives, leading to concern that dexmedetomine may lead to longer wake times in post-DISE recovery. Prior to March 2021, CHKD had no standard anesthesia protocol for DISE. This study is a preliminary investigation of whether the new protocol impacted patient recovery time in the Post Anesthesia Care Unit (PACU). We hypothesized that there would be no significant time increase.

Methods:
We performed a retrospective review of patients under 13 who underwent DISE between March 2020 and March 2022 using electronic medical records. Patient information collected included age, sex, race, co-morbidity, and time spent in the PACU for each patient. Descriptive statistics included median and interquartile range (IQR) to compare recovery room times between the two cohorts.

Results:
Fifty-eight patients were identified, 29 in the pre-protocol cohort and 29 in the post-protocol cohort. Patient population was similar for male to female ratio but not for age or race.
Two subgroups were then identified, DISE-only (n=9) and DISE-airway (n=49). Median time spent in the PACU was identical when comparing all patients pre-and post-protocol (59 minutes). In DISE-only, post-protocol patients spent 90 minutes less in the PACU. DISE-airway spent five less minutes in the PACU post-protocol. However, IQR for the post-protocol group in the PACU was four minutes longer.

Conclusion:
Preliminary data on PACU times for pediatric patients undergoing DISE shows similar median recovery between the pre- and post-protocol cohorts. IQR demonstrates a marginally longer recovery time for the post-protocol cohort. The impact of this increased PACU time could potentially translate to increased costs and congested OR schedules. Further study will be needed to elucidate this significance.

Abstract Title: Enterococcus Faecalis-Induced Infective Endocarditis: An Unusual Source of Infection and A Rare Clinical Presentation

Investigator: Robert Seby
Co-Investigator(s): Christine Kim, MS4; Dr. Mahmoud Khreis, EVMS Department of Infectious Disease; Dr. Khaldoun Khreis, University of Pecs (Hungary), Department of Internal Medicine
Department(s): Department of Infectious Disease, EVMS

Abstract

Introduction:
Enterococcus faecalis (E. faecalis) is the third leading cause of infective endocarditis. The genitourinary (GU) tract is the traditional source of infection in patients with infective endocarditis caused by *E. faecalis.* However, *E. faecalis* is also part of the natural gut flora and has the potential to translocate from the gastrointestinal (GI) tract to the heart and cause infective endocarditis. Furthermore, because infective endocarditis has a high mortality rate, it is imperative to perform a screening test with 100% sensitivity to rule out infective endocarditis, known as the DENOVA screening test.

DENOVA assesses the duration of symptoms, embolization, the number of positive blood cultures, unknown origin of bacteremia, prior heart valve disease, and auscultation of a heart murmur. The DENOVA scoring system is used to determine whether to perform transesophageal echocardiography (TEE) if there is high clinical suspicion for infective endocarditis in a patient with enterococcal bacteremia. Additionally, acute coronary syndrome (ACS) develops in only 1% to 3% of patients with infective endocarditis, making this a rare clinical presentation. We present a case report of a patient with infective endocarditis due to *E. faecalis* with a known source of infection from the GI tract who developed ACS likely secondary to their infective endocarditis.

Case Information:
A 69-year-old woman was airlifted to the emergency department (ED) after awakening with angina, diaphoresis, and shortness of breath. In the ED, review of systems was positive for diaphoresis, chest pain and shortness of breath. The patient's medical history was negative for cardiac disease. Physical examination was unremarkable. An electrocardiogram revealed ST-elevation myocardial infarction. Cardiac catheterization was performed which demonstrated 100% occlusion of her left anterior descending (LAD) artery, corrected with aspiration thrombectomy. Urinalysis and urine culture were unremarkable. Blood cultures confirmed *E. faecalis bacteremia.* Our team used DENOVA to determine whether transesophageal echocardiography was warranted to investigate for infective endocarditis. The patient's transesophageal echocardiogram showed a large vegetation on her mitral valve. Given the presence of infective endocarditis in the absence of known coronary artery disease, we determined that the patient had likely developed ACS from a septic embolus originating from her mitral valve vegetation. Further investigation for the source of the bacteremia revealed a perforation 20 cm from the anal verge at the rectosigmoid junction. After perforation repair, the patient became hypoxic and tachycardic with diffuse abdominal pain, guarding, rebound tenderness, and loss of pulse. Exploratory laparotomy revealed air in the mesentery consistent with extraperitoneal perforation of the rectum, and an end-colostomy was performed. Unfortunately, the patient subsequently died.

Discussion:
Our case was unique for two distinct reasons. First, our patient likely developed myocardial ischemia from a septic coronary embolus at the level of her LAD artery. Second, the importance of this patient's clinical presentation is that if a patient has enterococcal bacteremia with an unrevealing urinalysis and urine culture, imaging and/or colonoscopy of the GI tract should be considered to rule out a GI source of *E. faecalis* as a potential cause of the patient›s enterococcal bacteremia.
The main clinical dilemma that we encountered in the management of this patient was when to order TEE to rule out *E. faecalis* bacteremia-induced infective endocarditis. Currently, the most effective clinical scoring system with which to address this question is DENOVA. Our patient›s score was 3, warranting the use of TEE to investigate for infective endocarditis. DENOVA should be known by all clinical providers who encounter patients with enterococcal bacteremia to rule out infective endocarditis.

Conclusions:
E. faecalis bacteremia due to translocation from the GI tract must be on the clinicians' list of differential diagnoses when considering *E. faecalis* as a potential cause of infective endocarditis. Additionally, if a patient presents with ACS-like symptoms, infective endocarditis should be on the differential diagnosis. Finally, clinicians should use the DENOVA scoring system to decide whether to perform TEE to investigate potential infective endocarditis in patients with enterococcal bacteremia.

Abstract Title: Retrograde Pyloric and Proximal Duodenal Intussusception Secondary to Gastrostomy Tube Migration

Investigator: Robert Seby
Co-Investigator(s): Blair Dodson, MD, Northwestern Feinberg School of Medicine, Department of Radiology; Jennifer Rush, DO, Children's Hospital of the King's Daughter, Department of Radiology
Department(s): Northwestern Feinberg School of Medicine, Department of Radiology

Abstract

Introduction:
Maintaining adequate nutrition is essential for all patients, particularly for the pediatric population. However, a subsection of the pediatric population is unable to achieve adequate oral nutrition due to numerous etiologies. This subsection of the pediatric population relies on enteral feeding through gastro-enteric (GE) tubes to supplement their daily nutrition. Gastrostomy tube (G-tube) related intussusception is a well-known complication. However, retrograde pyloric and proximal duodenal intussusception in the pediatric population is an extremely rare clinical diagnosis, with only two other cases reported in the literature. Here we present a case of a 5-month-old term infant male who developed gastrostomy tube-related retrograde pyloric and proximal duodenal intussusception.

Case Information:
A 5-month-old term male with a past medical history of acute renal failure, hypoxic ischemic encephalopathy, and multiple spontaneous ileal perforations with ileostomy takedown and G-tube placement presented in the neonatal intensive care unit (NICU) with persistent emesis. An abdominal ultrasound (US) was performed with the pylorus unable to be identified due to G-tube balloon shadowing. The following day, an upper gastrointestinal (GI) series was performed which showed no passage of contrast through the gastric outlet, likely indicating that the G-tube balloon was obstructing the gastric outlet. Esophagogastroduodenoscopy was performed the next day which demonstrated intussusception of his pylorus and duodenum through the pyloric channel. The patient was initially managed conservatively with observation and decompression. However, after three days, the patient's abdominal X-ray continued to demonstrate gaseous dilation of the stomach with some progression of air into the distal bowel. A pyloric US was performed the following day which demonstrated an inverted pyloric channel with the gastric antrum along the outside of the pyloric channel and the duodenum within the intervertebral pyloric channel. An exploratory laparotomy was planned for the following day.

Exploratory laparotomy revealed a firm, circumferential ring within the distal stomach confirming the presence of the intussusception. The surgeons applied gradual antegrade pressure which resulted in reduction of the intussusception and complete restoration of normal anatomy to the distal stomach and pyloric region. The procedure was performed without difficulty and with no complications. The patient had no further complications with his G-tube.

Discussion:
Currently, GE tube-related intussusception has been described in the literature as occurring in 16-20% of children, most of whom are young males. Intussusception can present days to years after tube placement as either abdominal pain with bilious vomiting or with no appreciable symptoms. Specifically, retrograde intussusception of the pylorus and proximal duodenum into the body of the stomach is very rare, with only two other case reports identified in the literature.

Often, retrograde intussusception from G-tube placements occur due to migration of the G-tube with the G-tube acting as the lead point, as in our patient's case. The initial operative note for our patient's G-tube placement had a recorded insertion length of 35 cm. However, later notes found the G-tube length to be 30 cm, indicating that the G-tube had likely migrated through the pyloric channel, creating a lead point for the pylorus and proximal duodenum through the pyloric channel. This theory was later confirmed via exploratory laparotomy operative findings.

Conclusion:
The importance of this case is that it is imperative for each clinician to compare the initial operative G-tube length with the recorded current G-tube length to identify any discrepancy. If one exists, then clinical suspicion should be raised for potential G-tube migration and possible intussusception. As mentioned previously, an intussusception can be present in an asymptomatic patient and can occur anywhere from days to years post-G-tube placement. Therefore, if there is clinical suspicion for a potential intussusception in a patient with known G-tube length discrepancies, further imaging work-up is a valid course to follow.

Abstract Title: Successful treatment of Schizoaffective Disorder with Akinetic Catatonia in the Setting of Past SARS-CoV-2 (COVID-19) Infection

Investigator: Robert Seby
Co-Investigator(s): Steven Forte, EVMS MD2023; Dr. Sameer Yousuf, EVMS Psychiatry and Behavioral Science; Dr. Nana Cudjoe, EVMS Psychiatry and Behavioral Science
Department(s): EVMS Psychiatry and Behavioral Science

Abstract

Introduction:
The prevalence and relationship of COVID-19 and neuropsychiatric sequelae is not fully understood. Several cases of COVID-19-induced catatonia have been reported. We present a case of late-onset akinetic catatonia with successful treatment.

Case Information:
A 39-year-old married African-American woman with a past medical history of COVID-19 infection and no psychiatric history presented to the emergency department (ED) with paranoia and delusions. In the ED, she endorsed the recent onset of recurring headaches and a feeling that her email had been hacked by her upstairs neighbors. She also stated that she had contracted COVID-19 five months prior. During the interview, the medical provider noted that she became less talkative and more withdrawn when specifically asked about her delusions, appearing catatonic. Physical exam was unrevealing for any neurological abnormalities. Her catatonia improved with lorazepam. However, her delusions persisted during her hospitalization. We performed an extensive work-up for any organic etiology for her psychosis which was negative. Additionally, a urine drug screen performed at the time of admission was negative.

The therapeutic alliance was built and she shared that she was a Jehovah's witness and that she had an "order of protection filed against her husband." Hearing this, we became concerned about the possibility of Intimate Partner Violence (IPV). After detailed exploration and discussion, we began to understand that this was a delusion. She later shared that the "order of protection was actually from Jehovah." Due to the vulnerability of all patients experiencing IPV, we decided to hold a family meeting. Throughout the family meeting, she continued to make odd statements regarding her marital status, such as "marriages can change day to day" and that she was not comfortable going home with her husband when she was deemed psychiatrically stable. Throughout this, her husband denied any IPV and thought her comments were secondary to her psychotic state.

Out of concern for the patient and to further understand her psychopathology, additional collateral was obtained from the patient's aunt. Her aunt, one of her closest confidants, refuted IPV. Her aunt noted that the patient began behaving bizarrely two months prior to her hospitalization. Her aunt, who lived in a different state, recalled the patient informing her that she would be leaving her husband and moving in with her, which was uncharacteristic of her. Following this conversation, the patient's aunt reported that the patient had abruptly stopped calling her because she thought her "phone was being hacked."

This collateral and the patient's clinical presentation lead us to identify this was either unspecified psychosis or a brief psychotic episode with catatonia, in the setting of her recent COVID-19 infection. Her catatonia resolved with lorazepam and her delusions and paranoia resolved with haloperidol.

Post-hospitalization, the patient was diagnosed with schizoaffective disorder. She was unaware during her hospitalization but she has a family history of schizophrenia (father, brother) as well as type 1 bipolar disorder in her mother. She has had no recurrence of her paranoia or delusions since her hospitalization.

Discussion:
There have been increasing reports of psychosis after COVID-19 infection. We demonstrated one of the first reports and treatment regimens of late-onset akinetic catatonia as a possible sequela of COVID-19. This case also highlighted the importance of treating the symptoms in the absence of a complete clinical history.

Conclusion:
Late-onset akinetic catatonia after COVID-19 infection is a possible sequela of COVID-19 infection. We recommend lorazepam as a first-line treatment for this presentation.

Abstract Title: Exploring Subcutaneous Encapsulated Islet Cell Transplantation as a Treatment for Type 1 Diabetes

Investigator: Oren Shechter
Co-Investigator(s): KaLia S. Burnette, Department of Microbiology, Comprehensive Diabetes Center, The University of Alabama at Birmingham, Birmingham, AL; Joseph M. Feduska, Department of Microbiology, Comprehensive Diabetes Center, The University of Alabama at Birmingham, Birmingham, AL; David Schartung, Department of Microbiology, Comprehensive Diabetes Center, The University of Alabama at Birmingham, Birmingham, AL; Kalin C. Wallis, Department of Microbiology, Comprehensive Diabetes Center, The University of Alabama at Birmingham, Birmingham, AL
Department(s): Microbiology, University of Alabama at Birmingham

Abstract

Introduction:
According to the JDRF, over 1.6 million persons living in the United States live with Type 1 Diabetes (T1D) as of 2020. Current protocols utilize the liver as a transplant site in patients undergoing islet cell transplantation as a treatment for Type 1 diabetes (T1D). However, the need for an alternative and more accessible site is evident with only 50% of patients maintaining insulin independence one year after transplantation. In this study, we set out to evaluate whether transplantation of non- and (PVPON/TA/CTLA-4-Ig)-encapsulated islets can restore normoglycemia to streptozotocin (STZ)-treated diabetic NOD.SCID mice when transplanted into a prevascularized subcutaneous space.

Methods:
We took seven mice that were previously implanted with a nylon catheter subcutaneously in order to induce a foreign body response and increase vascularization. After four weeks, these mice were then administered a dose of 190 mg/kg of STZ in order to induce diabetes. All of the mice were confirmed to be diabetic by a blood glucose value of more than 300 mg/dL. Three mice were transplanted with 500 non-encapsulated islets while the remaining four were transplanted with 500 islets that were encapsulated with a poly (N-vinylpyrrolidone (PVPON)/Tannic acid (TA)/ CTLA-4-Ig nanolayer coating. Blood glucose values were then taken from the tail vein of each mouse to assess whether normoglycemia could be restored.

Results:
Normoglycemia was restored in five out of the seven mice (71.4%) one day after transplantation. Of the two mice (28.6%) in which normoglycemia was not restored, one mouse (14.3%) had an adverse reaction to the STZ treatment and did not survive 24 hours post-transplantation. The other mouse (14.3%) was not engrafted with islet cells and remained diabetic.

Conclusion:
Transplantation into a prevascularized subcutaneous pocket using both non-encapsulated and encapsulated islet cells was found to restore normoglycemia in NOD.SCID mice. This therapy for T1D presents an alternative option to the current protocol and should be further explored in future studies. Future studies may make use of other techniques such as encapsulation with PD-L1 (CD274) in order to further diminish the T-cell response and facilitate islet cell survival.

Abstract Title: Evidence for estrogen biosynthesis in the rat kidney suggests sex differences.

Investigator: Leah Shelton
Co-Investigator(s): Victoria Nasci, Division of Nephrology, Vanderbilt University Medical Center; Eman Y. Gohar, Division of Nephrology, Vanderbilt University Medical Center
Department(s): Division of Nephrology, Vanderbilt University Medical Center

Abstract

Introduction:
Premenopausal women exhibit protection against cardiorenal diseases. RNA sequencing of rat renal inner medulla, previously performed in the lab, revealed predicted increased activation of the estrogen biosynthesis pathway in females compared to males; in particular, *Cyp19a1,* which encodes for aromatase, the rate-limiting enzyme in estrogen synthesis, was upregulated in females. Given that extragonadal estrogen synthesis has been demonstrated in bone, brain, and adipose tissue, we hypothesized that the kidney is capable of estrogen biosynthesis, and this intrarenal machinery is upregulated in females compared to males.

Methods:
Kidneys from male and female Sprague Dawley rats were flushed with saline and either sectioned by region (cortex, outer medulla, and inner medulla) and frozen or fixed and frozen for whole tissue slices for imaging. Kidney tissue was assessed for the expression of different key components of the estrogen biosynthesis pathway using mass spectrometry, Western blotting, and RT-qPCR techniques.

Results:
Mass spectrometry imaging of frozen kidney sections revealed that cholesterol, the initial substrate of steroidogenesis, was significantly higher in females than males, driven by differences in the outer medulla (21.01 x 105 ± 2.2 x 105 vs 7.21 x 105 ± 0.56 x 105 avg. peak intensity, n = 4/group, p = 0.0008). Females elicited higher mRNA expression levels of HMG-CoA reductase, the key enzyme in cholesterol biosynthesis, in the renal outer medulla compared to males (254.4 ± 50.5 vs 100.0 ± 14.4 relative expression, n = 6/group, p = 0.0148). Steroidogenic acute regulatory protein, which transports cholesterol to the inner mitochondrial membrane, displayed a trend towards higher expression in the outer medulla of the female kidney that did not reach statistical significance (190.7 ± 45.8 vs 100.0 ± 22.7 relative expression, n = 5-6/group, p = 0.0938). No sex-related differences were demonstrated in the outer medullary abundance of cytochrome P450 family 11 subfamily A member 1, which converts cholesterol to pregnenolone (p = 0.5145). In addition, females elicited greater outer medullary mRNA expression of hydroxysteroid 17-β dehydrogenase, which converts androstenedione to testosterone, the precursor for estradiol (603.4 ± 161.0 vs 100.0 ± 17.9 relative expression, n = 6-7/group, p = 0.0062). Furthermore, aromatase elicited a trend towards higher abundance in the outer medulla of the female kidney that did not reach statistical significance (169.0 ± 25.8 vs 100.0 ± 25.1 relative abundance, n = 6/group, p = 0.0843).

Conclusion:
The data suggest the presence of estrogen biosynthesis machinery in the rat kidney that is in part more highly expressed in females compared to males. These findings have implications for a potential source of cardiorenal protection in premenopausal women.

Abstract Title: A Rare Case of Traumatic Supra- and Infra-tentorial Extradural Hematoma at an Acute Inpatient Rehabilitation Facility

Investigator: Caitlin Shi
Co-Investigator(s): Dr. Alfred Schupp, Physical Medicine and Rehabilitation\Penn State Health; Dr. Justin S. Hong, Physical Medicine and Rehabilitation\Penn State Health
Department(s): Physical Medicine and Rehabilitation

Abstract

Introduction:
Traumatic Supra- and Infra-tentorial Extradural Hematomas (TSIEDHs) account for only <2% of all extradural hematoma (EDH). Their clinical presentation differs from other types of EDHs, and thus it is important to understand the course and steps to diagnose and treat TSIEDHs. This report presents a case of TSIEDH in the setting of an acute inpatient rehabilitation facility in order to add to the existing literature of the presentation and course of TSIEDH.

Case Description:
A 59-year-old male with a history of hypertension presented with lethargy following 2 syncopal episodes earlier that morning. Initial on-scene Glasgow Coma Scale (GCS) score was 6 presenting as right-sided gaze, gurgling with respiration, and minimal responsiveness to noxious stimuli. At the emergency room, there was concern for Cushing's Reflex given hypertension (Systolic Blood Pressure > 220mmHg), bradycardia, and respiratory instability.

Computed Tomography (CT) scan of the head revealed a large biconvex extra-axial hemorrhage over the left occipital and cerebellar convexities with severe mass effect on the cerebellum and effacement of the 4th ventricle and left tonsillar herniation. He underwent emergent left occipital/suboccipital craniectomy and hematoma evacuation. Post-operative course was uncomplicated. The patient's acute rehabilitation course was significant for central nausea, balance impairment, and anxiety. Ten days later, he was discharged to home at a supervision-modified-independent level.

Discussion:
TSIEDH is a rare clinical entity with relatively scant literature existing on its presentation and treatment. Compared to EDHs not located in the posterior fossa, TSIEDH tend to have a longer asymptomatic "lucid" period followed by a more sudden and dangerous deterioration presenting as headaches, nausea, vomiting, and decreased level of consciousness.

TSIEDH are caused by acceleration-deceleration forces such as traffic accidents and falls. The gold standard for neuro-imaging and treatment is a non-contrast CT (NCCT) and suboccipital craniectomy/craniotomy with hematoma evacuation respectively. For TSIEDH less than 3cm without co-occurring hematomas in the posterior fossa, non-operative management is an option. There are multiple protective factors that influence the prognosis of TSIEDH such as acute hydrocephalus, a midline shift <5mm and initial GCS score, of which a higher initial GCS greater than 9 may be the most influential on a better prognosis.

In our case, the patient presented with TSIEDH and an admittance GCS <9, severe mass effect with a hematoma spanning both the supra- and infratentorial spaces and ventricle effacement, which predisposed the patient to a worse prognosis. The patient had a prompt NCCT and craniotomy with hematoma evacuation and was discharged about 2 weeks after admittance with a relatively good prognosis. The patient did experience the noted common symptoms of swelling and pain in the area of the PFEDH, occipital fracture, headaches, nausea, and vomiting. Our case reports an additional case of TSIEDH and supports the current literature in terms of factors that lead to better prognosis. The patient had several factors that are associated with a severe TSIEDH, but prompt NCCT and emergent craniectomy with hematoma evacuation may have led to a better outcome.

Conclusions:
TSIEDH is a rare form of EDH. Given their vicinity to the brainstem and longer lucid period, early diagnosis and treatment is imperative. Clinical suspicion is important to promptly recognize and manage TSIEDH in order to maximize outcomes. This case provides support to the current literature's suggestion for the diagnosis and treatment of TSIEDH.

Abstract Title: Medical Students Combat Health Disparities Within Their Community Through Oral Health Surveys

Investigator: Namrata Singh
Co-Investigator(s): Jonathan Light, MS3; Joshua Edwards, Assistant Director, Community-Engaged Learning; Rohan Dod, MS3; Ayesha Abdullah, MS3
Department(s): Pathology & Anatomy

Abstract

Background:
Oral disease predisposes to systemic morbidities such as cardiovascular disease, reversible if diagnosed early on. Public water supplies often contain regulated levels of fluoride as a preventative measure for dental caries. Local water fluoride levels in Suffolk, VA were found to exceed EPA standards in many areas. These high levels of fluoride can cause enamel fluorosis, predisposing to dental caries as well as skeletal fluorosis, which mimics osteoarthritis. Clinicians often must make a diagnosis early to avoid systemic morbidities, but direct training regarding oral health in many medical schools is limited. The purpose of this study is to identify medical students' knowledge gaps regarding enamel/skeletal fluorosis and implement additional training to reduce common dental disease.

Methods:
A 15 question REDCap survey was sent to the 300 EVMS students involved in the HOPES student run clinic to identify knowledge gaps in dental and skeletal fluorosis. Students were asked questions about their awareness and familiarity regarding oral health screenings and related pathologies. They were then asked how comfortable/confident they were in conducting an oral health exam and their knowledge pertaining to fluoride and fluorosis. A reminder was sent out two weeks after the initial administration of the survey.

Results:
Of the 43 total respondents, 38 (89.4%) were medical students and five (11.6%) were physician assistant students. Approximately 60% of respondents indicated that oral health training is important or extremely important to their future career path. Moreover, respondents indicated a lack of familiarity of oral health curriculum, with 89% reporting no knowledge of signs of dental caries; 53% reporting less than somewhat familiarity of caries prevention strategies; and 67% reporting they have no or minimal familiarity with the causes and prevention of general oral conditions that affect overall health. Additionally, confidence levels in identifying oral health pathologies on physical exam were determined. Specifically, 61% of responses reported no comfort level and 19% reported only slight comfort in properly conducting an exam. Finally, fluoride toxicity awareness was also minimal for our respondents with 88% having never seen and/or heard of a case of fluorosis in the community, 91% having no knowledge of the amount of fluoride that can be safely ingested by an individual, and approximately 95% having no confidence in making a diagnosis of dental fluorosis.

Discussion:
Our findings indicate that EVMS medical and physician assistant students generally view oral health training as important in their careers. However, they lack knowledge in recognizing common oral conditions and were not comfortable conducting an oral health exam. Responses also indicated a lack of awareness of fluoride toxicity and its clinical presentation despite its prevalence in the community. Given the high rates of fluoride in community drinking water in the area and the lack of knowledge possessed by students, it may be beneficial for additional oral health curriculum to be implemented in health professions students' training.

Next steps:
Implement the Smiles for Life curriculum within the HOPES clinic to facilitate interprofessional oral health training specific to the needs of the community

Abstract Title: Beyond Skin Deep: Identifying Stage 1 Pressure Injuries in Dark Pigmented Skin

Investigator: Jennifer Smith
Co-Investigator(s): Christian Sanchez, School of Medicine \ Eastern Virginia Medical School; Marissa Galicia-Castillo, MD, MSEd, CMD, FACP, AGSF, FAAHPM, Glennan Center for Geriatrics and Gerontology \ Eastern Virginia Medical School
Department(s): Glennan Center for Geriatrics and Gerontology

Abstract

INTRODUCTION:
Pressure-induced skin injuries (PrI's), also known as pressure ulcers or decubitus ulcers, comprise a significant portion of U.S. health care costs, estimated around $26.8 billion in 2020. In addition to age and medical comorbidities, race and ethnicity play a role in the incidence and prevalence of PrI's. Epidemiological studies have shown a higher prevalence of PrI's patients with darker skin tones, particularly at higher stages. Studies suggest Stage 1 PrI's, which forecast irreversible injuries, are underdiagnosed in darker skin, necessitating more concrete visual descriptions and diagnostic methods beyond the gold standard of visual assessment. This study seeks to identify the most common descriptions of Stage 1 PrI's in dark pigmented skin, and propose alternative reliable and cost-effective detection techniques, to improve their early detection in patients with dark skin tones, most specifically Black Americans, and address a significant racial disparity contributing to morbidity and mortality within long-term care.

METHODS:
A comprehensive Boolean search of PubMed, MEDLINE, EBSCO, CINAHL, and Google Scholar (*(Stage I OR Stage 1) AND (pressure injury OR pressure-induced skin injury OR pressure ulcer OR decubitus ulcer AND (Black OR African-American OR African American OR dark pigmented)*) was performed according to PRISMA guidelines. Studies were included if they were case reports, case series, cohort studies, or cross-sectional studies specifically describing PrI's on individual patients with dark pigmented skin. These descriptors were compared to the NPUAP definition of Stage 1 PrI's. Two independent reviewers (JS and CS) examined all articles in careful detail, and relevant information on PrI appearance and alternative diagnostic tools were extracted.

RESULTS:
Out of 529 records identified through database search, 23 were eligible for inclusion in the study. Visual descriptions of Stage 1 PrI's varied; the most common descriptors included blue-grey, maroon, purple, and "bruise-like", with few matching the NPUAP definition of "erythematous and non-blanchable," and others described as difficult to visualize. The most common tactile descriptors included edematous, indurated, tense, and taut, with few describing temperature extremes.

CONCLUSIONS:
Visually, Stage 1 PrI's present differently in darker skin compared to lighter skin, and may often be mistaken for bruising or hyperpigmentation, suggesting visual assessment alone may be insufficient. The tactile changes describe subepidermal inflammatory changes that manifest before visual changes, making them important markers of incipient PrI's. Of all alternative diagnostic techniques, ultrasonography and skin conductance were the most promising and cost-effective methods to identify subclinical Stage 1 PrI's, although both require additional research to compare them to the gold standard. Finding a reliable and cost-effective diagnostic strategy for incipient Stage 1 PrI's will help address an important racial disparity in long-term care by addressing a reversible injury, reducing cost burden, and improving patient quality of life.

Abstract Title: A Novel Form of Acellular Dermal Matrix for Local Nitroglycerin Delivery to Improve Flap Survival in Implant-Based Breast Reconstruction

Investigator: Jennifer Smith
Co-Investigator(s): Christopher Campbell, MD, Department of Plastic Surgery \ University of Virginia; Patrick Cottler, PhD, Department of Plastic Surgery \ University of Virginia
Department(s): Department of Plastic Surgery, University of Virginia

Abstract

INTRODUCTION:
Topical nitroglycerin (NTG) is a vasodilatory agent well-known to improve skin flap survival in animals. In human patients undergoing mastectomy with breast reconstruction, topical NTG ointment significantly reduced the incidence of flap necrosis. The acellular dermal matrix (ADM) used in breast reconstruction may serve as a potential vehicle for local delivery of NTG. Previous studies note ADM's utility as a delivery vehicle for interleukin-4 (IL-4) to drive IL4-mediated angiogenesis. This study compared skin perfusion and cellular and vascular ingrowth between surgical sites containing subcutaneous ADM implants and ADM implants infused with NTG.

METHODS:
5mm diameter ADM samples were soaked in 1mL solutions containing 10, 50, or 100µg NTG overnight. Nine female C57BL/6 mice were randomly assigned to each NTG dose group (n=3) and received bilateral subcutaneous 5mm ADM implants. One side received the ADM loaded with NTG (NTG-ADM), and the contralateral side was an unloaded control. Skin perfusion of each implant site was serially measured (pre-op, post-op, POD1, 2, 3, 7, and 21) using laser Doppler imaging. At POD21, ADM samples were harvested for histological analysis of cellular and vascular ingrowth.

RESULTS:
Post-operative cutaneous blood perfusion decreased across all groups to 33.8%-51.0%. The 10µg and 50µg NTG-ADM did not demonstrate increased perfusion on POD1, but exhibited 19-20% increased perfusion on POD2-3 compared to controls. The 50µg NTG-ADM yielded 9% increased perfusion on POD2 and 21% increased perfusion on POD3. The 100µg NTG-ADM showed a 40% increase in skin perfusion on POD1, a 53% increase on POD2, and a 12% increase on POD3. Additionally, markers of vascular growth (smooth muscle, vimentin, and CD31) increased in all treatment groups, with the most marked increase observed in the 10µg treatment group.

CONCLUSION:
Initial findings support ADM as a controlled local NTG drug delivery device to implant sites in breast reconstruction. The nitric oxide radical forms a covalent bond to the thiol side chain of cysteine via S-nitrosylation, promoting slow release. Future research may examine NTG-ADM placed under an L-shaped epigastric flap to assess flap survival. With this and other considerations, NTG-ADM shows promise in increasing blood perfusion, reducing skin flap necrosis, and leading to improved healing and biointegration of the ADM.

Abstract Title: Use of a gene expression test in the diagnosis of vulvar melanoma in situ in a 36-year-old female.

Investigator: Nathanael Smucker
Co-Investigator(s): Dr. Alice Roberts, Department of Dermatology
Department(s): Department of Obstetrics and Gynecology

Abstract

Introduction:
Vulvar melanomas make up about 5% of all vulvar/vaginal cancers and less than 1% of all melanomas. The prognosis of vulvar melanoma is poor with a median overall survival of 43 months, due to presentation late in the disease process. Melanoma is most frequently diagnosed following histological examination of a biopsied lesion. Other techniques, such as immunohistochemistry and molecular characterization can be used to confirm a diagnosis for a histologically ambiguous lesion. Emerging gene expression tools like the myPath Melanoma test are used to determine the likelihood that a lesion is malignant or benign and are scored along a continuum. We report a case of an incidental discovery of a diagnostically challenging melanocytic lesion during an IUD removal and the use of a myPath Melanoma 23 gene expression signature test.

Case report:
Ms. X was a 36-year-old G4P2 with undesired fertility, currently managed by an intrauterine device (IUD) and preferring bilateral tubal ligation (BTL) instead. She presented to the operating surgeon for her preoperative appointment. Following her preoperative visit, which did not include a pelvic exam, the patient presented to the hospital and underwent a laparoscopy with bilateral salpingectomy and removal of the IUD. Her surgery was uneventful and after the laparoscopic portion of her surgery was completed, attention was turned to the vulva to remove the IUD. At that time, multiple areas of hyper and hypo pigmented lesions were noted. At 4 o'clock on the left vulvovaginal junction, a well circumscribed, fingerlike, hyperpigmented projection was noted that crossed into the vaginal mucosa and appeared darker compared to other hyperpigmented areas. This darker area was biopsied, and the patient and her husband were informed post-operatively of the biopsy and surgeon's remote concern for an atypical melanocytic process, possibly vulvar melanoma.

Ten days later, the pathology of the vulvar biopsy revealed an ATYPICAL MELANOCYTIC NEOPLASM, MART1: POSITIVE, SOX-10: POSITIVE. The initial pathology report described "a melanocytic neoplasm composed of single melanocytes, many of them with prominent dendrites which extend into the upper levels of the epidermis...an early melanoma in situ cannot be excluded."

Our institution's dermatology department was consulted and independently reviewed the slides. The tissue was sent for further evaluation using genetic analysis by CASTLE MYPATH. This genetic analysis came back "suggestive of a malignant neoplasm" and the combination of histologic, immunohistochemical stains (IHC), and CASTLE MYPATH were felt to be consistent with an early evolving melanoma in situ.

The patient underwent re-excision by wide local excision by gynecologic oncology which showed margins free of lesional cells.

Discussion:
In this case, the lesion was detected incidentally during the removal of an intrauterine device. Biopsy of the lesion allowed early detection of a melanoma in situ (MIS), a lesion that not infrequently will remain undetected until it evolves into invasive melanoma. The MyPath melanoma panel is a 23 gene panel which uses reverse transcription-PCR technology to categorize lesions as either benign (-16.7 to-2.1), intermediate (-2.1 to -0.1), or malignant (0.0 to 11.1). The score for this lesion was 7.0, placing it solidly in the malignant category, supporting a diagnosis of MIS. The myPath melanoma panel has a sensitivity of 90-94% and a specificity of 91-96%.
The myPath Melanoma panel has also been shown to improve diagnostic certainty in histologically ambiguous cases when measured against clinical outcomes. By increasing diagnostic certainty, outcomes are improved by avoiding late detection of melanoma. Increasing diagnostic certainty may also serve to prevent overdiagnosis, thus enabling reduced margins of surgical removal or reduced unnecessary vulvectomies in cases when melanoma is excluded by a gene expression panel. Indeed, partial vulvectomies can be associated with harmful side effects such as urinary incontinence and loss of sexual function.

Conclusion:
Our case highlights the benefits of using a gene expression study in a diagnostically uncertain case, especially in an area where unnecessary radical surgery could pose harm to the patient.

Abstract Title: Venous Malformation of the Tongue in a 26-year-old woman.

Investigator: Christopher Sommer
Co-Investigator(s): Taylor Pate, MD/EVMS Department of Radiology; Mitchell Wangsgard, MD/Medical Center Radiologists
Department(s): EVMS Department of Radiology

Abstract

Introduction:
As a whole, vascular and lymphatic malformations affect approximately 1% of the population and can occur either sporadically or as a part of various genetic syndromes. Vascular malformations outside of the central nervous system are less common and can pose significant risk to the patient if allowed to rupture. Typically, venous malformations are present at birth and grow with the patient throughout life, often unrecognized until childhood or later. When affecting the tongue, these lesions can produce significant discomfort for patients, with a propensity to bleed, ulcerate, or interfere with speech and swallowing. We present a case of a large venous vascular malformation affecting the lateral tongue and lower lips in a 26-year-old female.

Case Information:
A 26-year-old female presented to the interventional radiology clinic at our institution with complaints of low volume bleeding from the lower lip and tongue. The patient had previously received an MRI of the face showing a venous malformation involving the tongue but had never received treatment for this condition. She had recently noted increased frequency of bleeding and cracking of the affected tissues, as well as intermittent pain throughout the area, which prompted her visit. Physical exam was notable only for swelling of the tongue and lower lip. The patient's past medical history and review of symptoms were unremarkable. Another MRI of the face was obtained, which demonstrated a 5 x 2 x 3 cm T2 hyperintense, enhancing lesion with small internal flow voids extending from the lateral tongue to the mandibular alveolar ridge. This lesion was enlarged when compared to the MRI documented in 2018. The patient discussed possible sclerotherapy with the interventional radiology department, but deferred treatment until after the conclusion her current pregnancy.

Discussion:
Venous malformations are the most common subtype of vascular malformations and are most often found in the head and neck. Diagnosis using MRI provides excellent resolution of these low flow vascular malformations, with high signal intensity seen on T2-weighted imaging. This is especially important in tongue lesions, where visualizing the entire malformation may be impossible without imaging. Treatment of vascular malformations of the tongue is challenging, as there is minimal tissue volume to allow for surgical resection. The advent of interventional radiology has provided an alternative option through percutaneous ethanol sclerotherapy.

Conclusion:
Venous malformations of the tongue are a relatively unusual clinical finding with limited treatment options. Symptoms can lead to considerable discomfort for patients, and rarely, significant hemorrhage. MR imaging is an integral tool in determining both the extent of the lesion and for pre-procedural planning. We believe clinicians will benefit from familiarizing themselves with the diagnostic and therapeutic options for patients suffering from this condition.

Abstract Title: The Perils of Primary Hyperparathyroidism

Investigator: Charles Springer
Department(s): Internal Medicine

Abstract

Introduction:
Hypercalcemia presents in many forms, and accurate diagnosis in a patient with complex history can prove challenging. Detailed knowledge of the manifestations and causes of hypercalcemia can promote early recognition and improved clinical management.
Case Information:

A 63-year-old female arrived via ambulance to the Emergency Department with altered mental status, dark urine, dehydration, dizziness, and weakness. She had a history of hypertension, hyperlipidemia, coronary artery disease, smoking, cocaine and alcohol abuse, and unprotected intercourse with several strangers. The patient's daughter reported the patient stopped leaving home and participating in activities of daily living for seven days prior. She had not used cocaine during these seven days, despite doing so daily for 15 years.

Medications included lisinopril 40mg daily, carvedilol 6.25mg twice daily, atorvastatin 10mg daily, and aspirin 81mg daily; however, she had not adhered to her regimen for one month. Surgical history included triple-vessel CABG in 2004.

Clinical Findings:
Vitals were within normal limits aside from initial blood pressure of 167/118. Physical exam showed thin female with sarcopenia. Cardiac and pulmonary examinations were unremarkable. Lactated Ringer was immediately given for rehydration. At admission, hemoglobin was 20.1g/dL with an MCV of 90fL, and calcium was 13.8mg/dL. After rehydration, her calcium remained elevated at 12.2mg/dL, while hemoglobin dropped to 15.3g/dL. Her phosphate was 1.3mg/dL, and 25-hydroxy-vitamin D was 5.8ng/mL. Fluids, intramuscular calcitonin, and phosphate were administered. Antihypertensive medications were resumed, and she received 50,000U vitamin D2.

Additional testing included urine drug screen showing cannabinoids. STI testing yielded normal RPR titer but positive syphilis IgG and TP-PA, suggesting prior resolved infection. Blood cultures found no growth through five days. EKG showed left ventricular hypertrophy and atrial premature complexes. Urinalysis showed urine protein 30mg/dL, ketones 5mg/dL, urobilinogen 4mg/dL, and 15-20 hyaline casts/HPF. Serum protein electrophoresis was negative for monoclonal spike. Chest X-ray was unremarkable, while cervical spine X-ray showed multilevel degenerative spondyloarthropathy. CT scan of the head showed moderate small vessel ischemic disease. No metastatic bony lesions were noted.

Parathyroid hormone level was elevated at 137pg/mL suggesting primary hyperparathyroidism. Neck ultrasound showed no parathyroid masses; CT scan of the neck found a 10mm enhancing nodule inferior to the left thyroid lobe. She was diagnosed with combined primary hyperparathyroidism and vitamin D deficiency. She received one dose of Zoledronate 4mg intravenously. At discharge, her mental status was at baseline and her appetite and strength had returned. She was discharged with otolaryngology and endocrinology follow-up.

Conclusion:
Primary hyperparathyroidism manifestations may be subtle or suggestive of other disease states. While dehydration is a common result of hypercalcemia, sudden and drastic changes in behavior are not expected. Timely surgical intervention can lead to permanent relief of symptoms and cure; thus, it is imperative to keep a broad differential when evaluating unusual presentations.

Abstract Title: Determining Capacity of Sexual Consent for Long Term Care Patients with Dementia

Investigator: Hannah Stamos
Co-Investigator(s): Nealy Minson, Doctor of Medicine Program; Dr. Kanishk Sharma, MD, MBBS, EVMS Internal Medicine Geriatrics Fellow
Department(s): Internal Medicine: Glennan Center for Geriatrics and Gerontology

Abstract

INTRODUCTION:
As the population ages, it is critical to assess how healthcare structures support a high quality of life in advanced age. The natural desire for physical intimacy does not cease with age and sexually active older adults report a higher quality of life, improved well-being, and better cognitive functioning. For older adults residing in long-term care (LTC) facilities, it is estimated that 16% of males and 10% of females engage in sexual activity. In the case of older adults who have dementia and are living in LTC facilities, this topic posits a clinical and ethical dilemma. A delicate balance must be struck between fostering individual autonomy and quality of life while protecting vulnerable individuals from harm. A central component of this topic necessitating adequate policy and protocol is consent. In this case, a well-known model was applied in a novel way to assess the decisional capacity to consent to physical intimacy between two LTC patients with dementia.

CASE INFORMATION:
Patient Description An 86-year-old male and a 90-year-old female, both with a history of dementia, were observed showing signs of affection in a LTC facility. One afternoon, the patients were found alone in the male patient's room with their pants off, but still wearing their undergarments. Neither of the patients could recall the events that lead to their situation. The medical staff proceeded to help the patients get dressed.

History and Physical Examination Results The male patient had a Saint Louis University Mental Status (SLUM) score of 17. Upon physical exam, he was alert and oriented to person and place. The female patient had a SLUM score of 10. Upon physical exam, she was alert but not oriented to time or place. She was able to state her name.

Diagnostic Procedures and Results The facility did not have a policy or procedure in place to address the sexual activity of the patients. The medical team determined that using the U-CARE model to determine decision-making capacity was appropriate and prepared to conduct separate interviews. The patients were asked questions that assessed whether they understood their medical diagnoses and the limitations that were associated with their mental and physical health. It was assessed if they were able to understand and consistently express their desire to engage in physical intimacy. In addition, the patients were asked to reason through and develop a plan for a scenario where either themselves or their partner needed help.

Treatment Plan and Outcome After the interviews concluded, it was determined the male patient met the U-CARE criteria to have the capacity to consent to sexual intimacy while the female patient did not. It was determined a safety risk for the female patient to be left alone unmonitored. The patients were encouraged to maintain their relationship in common areas.

DISCUSSION:
This case demonstrated an effective and timely response toward two patients with dementia expressing the desire for sexual intimacy. It is important to distinguish capacity, which is a medical assessment that helps answer a specific question versus incompetence, which is a legal status that pertains to judgment. Currently, there are no formal practice guidelines to assess the capacity to consent to sexual activity. The U-CARE Model provides a framework to determine the capacity to consent to sexual activity.

CONCLUSION:
Clinicians, caregivers, partners, and even patients often incorrectly conflate the diagnosis of dementia with the loss of the competency to provide consent for sexual activity. Dementia does not equate to global incompetence and it is important that domain-specific capacity is accounted for. The U-CARE model offers a solution for the determination of decisional capacity, allowing those with dementia to have their autonomy and well-being promoted while protecting them from harm.

Abstract Title: Multiple decrements in switch task performance in female rats exposed to space radiation

Investigator: Samuel Stephenson
Co-Investigator(s): Aiyi Liu, Department of Radiation Oncology; Ashley Blackwell, Department of Radiation Oncology; Richard Britten, Department of Radiation Oncology
Department(s): Radiation Oncology

Abstract

Introduction:
Switching attention between two different cognitive rule sets, task switching, is a complicated process involving diffuse frontoparietal neurological activation. Switching tasks has a performance decrement in which response times or accuracy are impaired following the changes in cognitive attention, known as a switch cost. Task switching has been shown to be affected by space radiation when animals are fully trained to complete the task. When astronauts travel to Mars, they will be subject to this same radiation. When mission anomalies arise, astronauts need to draw upon their prior training which often involves rapidly switching tasks to a skill not practiced in a while. The mission to Mars will also involve longer mission lengths with astronauts needing to complete larger volumes of mission critical work. In behavioral economics terms, the behavioral price goes up. To the best of our knowledge, the effects of space radiation on motivation through behavioral economics and the effects on task switching, have never been studied. These are crucial aspects to future interplanetary missions and we set out to model these situations with rodents.

Methods:
28 Female Wistar rats: 13 Shams, 9 He4 exposed rats, and 6 Galactic Cosmic Radiation spectrum simulation (GRCsim) exposed rats were trained to complete the same touchscreen switch task as previously used (Stephenson & Britten 2022). The rats were trained to complete this task by focusing on one side of the screen while increasing the economic demand, the number of responses per food reward, before switching sides. This enables us to examine a rat's motivation and drive while also their switch task performance the first time they need to switch tasks. The switch task was a single sensory modality utilizing two sets of lights. Rats were trained to activate the trial by pressing a center light then were presented with a light stimulus on one side of the screen. They had to choose the appropriate response, as fast as possible, to receive an intermittent food reward. This was completed in random blocks of 4-8 trials on one side before switching to the other side. The switch trials were the first trial after switching stimulus-response sides and the repeat trials were all subsequent trials on each side of the screen before switching and data was collected for the first day the rats reached criterion on the switch task.

Results:
10/13 (77%) sham rats, 5/9 (56%) He4 exposed rats, and 3/6 (50%) GCR exposed rats completed the switch task training and proceeded to the switch task. These differences were significant (P=0.0001). There was no pattern or significant differences in regards to how many responses were required when the different animals failed. In the switch task itself, the sham rats averaged 52.2% correct, the He4 exposed animals averaged 31% correct, and the GCRsim exposed animals averaged 33.9% correct ($p<0.05$). The sham rats had a switch cost (average switch trial response time/ average repeat trial response time) of 0.13s, the He4 exposed rats had a switch cost of 0.01s, and the GCRsim exposed rats had a switch cost of 0.54s ($p>0.05$).

Conclusions:
Rats exposed to GCRsim radiation have altered accuracy the first time they are required to switch tasks. Rats exposed to both GCRsim and He4 space radiation have decreased motivation as demonstrated by economic demand. Astronauts on the journey to Mars will be exposed to similar radiation which is especially problematic if they are affected in the same way. When life or death situations occur, task switching is often necessary to utilize previously learned training. Task switching and behavioral economics have also been shown to be affected by many stressors that astronauts will be exposed to such as stress and sleep. If these other stressor effects interact with those induced by space radiation exposure, the astronaut's performance could be impaired at the most critical moments of the mission. It would be useful to add both a switch task and a measure of behavioral economics into NASA's cognitive test battery to monitor this potential performance decrement during spaceflight to prevent potential disasters.

Abstract Title: Advanced Machine Learning Approach to Increase Diagnostic Accuracy in Atypical Alzheimer's Disease Cases

Investigator: Molly Sternick
Co-Investigator(s): Ahmed Temtam, Vision Lab Department of Electrical and Computer Engineering\ODU; Erica Cruz, Vision Lab Department of Electrical and Computer Engineering, ODU; Hamid R. Okhravi, Geriatrics\EVMS 4. Daniel Strok, EVMS\MD program; Khan M. Iftekharuddin, Vision Lab Department of Electrical and Computer Engineering\ ODU
Department(s): Geriatrics

Abstract

Introduction
The early diagnosis of Alzheimer's disease (AD) and other types of dementia is essential in clinical practice. Up to 50% of patients with any form of dementia may remain undiagnosed during their lifetime and the diagnosis of AD may often be inaccurate. In assessing patients, accurate diagnosis based on only clinical data and structural (MRI or CT) imaging is suboptimal in a subset of patients with atypical presentation. Although amyloid PET imaging and CSF biomarkers can provide incremental benefits, numerous obstacles preclude their wider use in clinical practice. In this work, a parametric study was performed to create a machine learning (ML) model to accurately diagnose hard-to-detect cases of AD, to mitigate the need for more expensive or invasive testing such as amyloid imaging or spinal tap.

Methods
Data from 173 participants (MCI and mild dementia), including 105 patients (60%) with AD and 68 (40%) Non-AD patients, were included from our memory clinic. The dataset for each participant included pertinent history, AD risk factors, scores on a neuropsychological testing battery, functional status, and MRI volumetric studies. Participants were divided into two groups: Group I (easy-to-detect) with a high probability of AD diagnosis based on clinical data (subjective and objective amnestic presentation) and volumetric studies (hippocampal and medial temporal lobe atrophy). Group II (hard-to-detect), who did not fit into the first group and the diagnosis was confirmed with either amyloid imaging or CSF analysis. The distribution of diagnosis by group: 1- Easy to detect (43 AD, 29 Non-AD),2- Hard to detect (62 AD, 39 Non-AD), a total of three experiments with different combinations of groups were conducted, 1- All Groups (Exp.1.), 2- Hard to detect (Exp.2.), 3- Easy to detect (Exp.3.). In all experiments, Leave-One-Out cross-validation technique was performed.

Results
A total number of 132 features utilized, by employing feature selection approach, 13 features were selected. Our model attains the highest accuracy of 87.27% on classification of Exp.1., 83.28% on Exp.2. and 95.80% on Exp.3.

Conclusion
We investigated discrimination of AD from Non-AD on hard-to-detect cases using ML. The proposed method obtains competitive performance and achieves improved accuracy results.

Abstract Title: The effect of sterile vs clean gloves on rates of chorioamnionitis and postpartum endometritis in term labor at Sentara Norfolk General Hospital

Investigator: Samantha Strohm
Co-Investigator(s): Charles Springer, MD 2023; Hannah James, MD 2024; Dr. Stacy Slat, Obstetrics & Gynecology
Department(s): Obstetrics & Gynecology

Abstract

Introduction:
Chorioamnionitis, also called intraamniotic infection (IAI), affects 5-12% of term pregnancies and is an indication for delivery. Postpartum endometritis is a complication up to 30x more common after cesarean-sections (c-sections) than spontaneous vaginal deliveries (SVD), and patients with scheduled c-sections are usually given prophylactic antibiotics. Sterile vaginal exams (SVE) assess the cervix during labor and are typically performed with sterile gloves, however, gloves lose sterility when coming into contact with the vagina. Therefore, the glove type used during SVE should not impact IAI or postpartum endometritis rates. This randomized control trial examines the effect of glove type (sterile vs. clean) on infection rates in term laboring patients with intact amniotic membranes on admission.

Methods:
Participants are prospectively randomized to SVEs with either sterile or clean gloves under EVMS IRB #21-09-FB-0206. Deidentified patient data, including demographic information, intrapartum, and postpartum courses, is stored in EVMS REDCap. Participants must begin labor with the intention of SVD. Recruitment is ongoing.

Results:
To date, 166 participants have completed the study with 3 being excluded for not meeting inclusion/exclusion criteria. O the 163 participants included, 55% were randomized into the clean glove group and 45% were randomized into the sterile control glove group. SVD occurred for 80% of participants and 20% were delivered by unscheduled c-section. The average time from rupture of membrane to delivery was 6.76 hours in the clean group and 7.34 hours in the sterile group. In both groups, there was an average of 6 SVEs per participant, with IAI rates of 5.4% in the sterile group and 4.5% in the clean group. There was no significant difference in IAI rates between sterile versus clean glove groups ($p = 0.7902$). Of the participants with IAI, 75% delivered by c-section in both clean and sterile glove groups. Additionally, postpartum endometritis rates were 2.2% in the clean glove group and 1.4% in the sterile glove group. There was no significant difference int he rate of postpartum endometritis between the two groups ($p=0.6741$). Of the participants who were diagnosed with postpartum endometritis, none (0 of 2) delivered by c-section in the clean group and all (1 of 1) delivered by c-section in the sterile group.

Conclusion:
Glove type likely does not impact rates of IAI or postpartum endometritis in term laboring patients with intact amniotic membranes. Given the low rates of infection found in this set of participants, a sample size of 18,000 would be needed to show superiority of one glove type with the current incidence rates. Analysis is ongoing to determine if a noninferiority analysis is possible or if further recruitment is needed. At Sentara Norfolk General Hospital, switching from sterile to clean gloves could reduce the cost per unit by up to 92.4%, saving the institution over $20,000 annually.

Abstract Title: Bilateral thalamic masses demonstrating corpora amylacea in a 62-year-old male: case report

Investigator: John Szymanski
Co-Investigator(s): Lauren Jutras, EVMS Radiology
Department(s): EVMS Radiology

Abstract

Introduction:
Corpora amylacea (CA) are collections of hyaline glycoprotein-rich aggregates that accumulate in the central nervous system (CNS) as part of natural aging but also in increased quantity in neurodegenerative diseases. Recent research on CA has postulated their role in waste-removing cellular processes within astrocytes. Typically, the main causes of bilateral thalamic abnormalities include tumor, ischemia, and venous thrombus. We report a rare case of bilateral thalamic masses with radiologic features typical of glioma in a 62-year-old male presenting with confusion and worsening of his chronic, baseline tremor found to be due to obstructive hydrocephalus secondary to accumulation of CA without tumor.

Case Information:
A 62-year-old Caucasian male with a past medical history of resting tremor presented to the emergency department with increasingly frequent episodes of disorientation and worsening of his baseline tremor. On physical exam the patient was afebrile, hypertensive to 166-202 systolic and 73-90 diastolic, but was otherwise vitally stable, fully alert and oriented, and in no acute distress. He had an evident resting and action tremor but had otherwise benign physical and neurological exams. Laboratory results were within normal limits. Non-enhancing computed tomography (CT) of the head revealed a large, heterogeneous infiltrative mass in the bilateral thalamic region resulting in moderate hydrocephalus.

Follow up with magnetic resonance imaging (MRI) of the head with and without gadolinium confirmed the presence of bilateral nonehancing thalamic masses with bilateral central cystic components as well as mass effect on the third ventricle causing abnormal dilatation of the lateral ventricles with transependymal resportive edema in adjacent white matter. The thalamic masses appeared mildly T1 hypointense and mildly T2 and FLAIR hyperintense.

Patient was discharged, monitored closely, and admitted 3 weeks later for septum pellucidotomy, endoscopic biopsy, and ventriculoperitoneal (VP) shunt placement. Analysis of the biopsy specimen showed normal ependyma, mild gliosis with CA, and no evidence of tumor. Post-operatively the patient steadily recovered and was discharged after six weeks to a long-term care facility. His final nonehancing head CT before discharge showed marked improvement of ventriculomegaly status post VP shunt and stable thalamic masses.

Discussion:
The thalami are a pair of deep gray matter structures that lie along the inferolateral border of the third ventricle. Among the neoplastic processes affecting the bilateral thalami, primary glioma, a diffuse low-grade astrocytoma, is one of the biggest contenders. Typically presenting with gait and movement disorders and behavioral changes, BTG appears as symmetrical enlarged masses protruding from both thalami, often with hydrocephalus secondary to mass-effect on the adjacent third ventricle. The masses are best characterized by MRI in which they appear hyperintense on T2-weighted images and iso/hypointense on T1-weighted images.

This patient's bilateral thalamic masses possessed an imaging profile in line with low-grade glioma. This combined with the patient's clinical presentation greatly increased our clinical suspicion for BTG; however histologic investigation of a biopsy revealed the masses were constituted of normal-appearing brain tissue with mild gliosis alongside concentrically laminated, basophilic deposits typical of CA, and thus were not cancerous. This patient's benign gliosis which was likely secondary to CA accumulation presented nearly identically to a low grade thalamic glioma. Cases of CA-containing gliotic tissue masquerading as low-grade glioma are scarcely documented in the literature.

Unfortunately, thalamic gliomas continue to carry a poor prognosis even with modern therapies. To our knowledge, this is the only reported case of CA-gliosis masquerading as BTG. Thus, while uncommon, benign CA-induced gliosis should be considered when presented with a patient with bilateral periventricular masses with high index of suspicion for glioma.

Conclusion:
CA are naturally occurring glycoproteinaceous aggregates that accumulate within the CNS during aging. To our knowledge, this is the first reported case of symptomatic bilateral thalamic masses due to extensive gliosis with accumulation of CA. Given the low incidence of bilateral thalamic masses, clinicians should be aware of CA and its ability to accumulate within periventricular structures to the point of causing obstructive hydrocephalus, closely mimicking low grade gliomas. We hope this report may encourage further investigation and reporting of CA-containing lesions and will contribute to the elucidation of its biomolecular nature and role in CNS pathophysiology.

Abstract Title: What hurdles might we expect with COVID-19 vaccination in infants and children aged 6 months to 4 years?

Investigator: Austin Temple
Co-Investigator(s): John Harrington MD, CHKD; Evelyn Schendler, Penn State/undergrad
Department(s): CHKD

Abstract

Introduction:
With vaccination rollouts for children aged 6 months to 4 years set for July 2022, a plan to gauge parental/guardian vaccine hesitancy was implemented within the CHKD GAP clinic. Vaccination rates have been steadily decreasing by each age group with only 29.5% of individuals aged 5-11 fully vaccinated as of July 2022. Even though most infections are mild or asymptomatic within the younger age groups, infants still experience higher hospitalization rates and pose as vectors of spread in the community.

Methods:
A 23-question survey was provided to individuals with children aged 6 months to 4-years who presented to the CHKD GAP clinic between May 31st and July 5th 2022. The survey assessed parental/guardian readiness and motives for/against vaccination. Data gathered from completed/consented surveys were entered into REDCap for analysis.

Results:
204 out of 375 eligible subjects completed surveys. Responses showed equal representation of age groups within the 6 months to 4-year range with a racial mix of (65% African American, 20% Caucasian, 5% Hispanic, and 5% multi-racial and Asian) and most with a yearly income under $50,000. 2/3 of individuals were hesitant to vaccinate (N=129) versus likely to vaccinate (N=60), and with an equal distribution across age groups. For hesitant individuals, 78% (101/129) needed more information, 43% (55/129) would like to see more children immunized, 30% (39/129) believed vaccination was more likely to harm than help, and 26% (33/129) wanted to discuss further with their physician. Half of 'unlikely to vaccinate individuals' believed that the vaccine was not safe at all (63/126 or 50%). 62% (80/129) of 'unlikely to vaccinate' individuals were not concerned or a little concerned about their child catching COVID-19 while, a majority of these individuals would allow vaccination if it meant protection of their child's health (66/131 or 50%). Hesitant individuals were also less likely to trust established government/healthcare (p=0.003).

Conclusion:
We would recommend healthcare providers target a perceived lack of patient knowledge regarding vaccine safety and efficacy. Supplemental information on where to find current and correct vaccine news can be provided. Health risks and benefits of vaccination versus non vaccination could also be discussed.

Abstract Title: Aristolochic Acid Injury Changes Resident Memory CD 8 T Cell Expression in Male and Female Mice

Investigator: John Thurber
Co-Investigator(s): Kyle Moore, PhD, Department of Surgery, University of Alabama at Birmingham
Department(s): Department of Surgery, University of Alabama at Birmingham

Abstract

Introduction:
Sex differences in protection from kidney injury have been well documented. Specifically, estrogen has been shown to have a protective effect in ischemia-reperfusion injury models. In turn, it should follow that in other models of chronic kidney disease (CKD), such as aristolochic acid (AA), female mice should be better protected than males. Additionally, the aristolochic acid model of chronic kidney disease is unique because of the infiltration of T cells, as opposed to macrophages and other immune cells, into injured kidneys. Importantly, this model of CKD resembles its clinical counterpart remarkably well. In our study, utilizing flow cytometry to quantify T cells and serum creatinine to monitor kidney injury, we examined the differences between male and female mice to elucidate how protected females are from kidney injury. We hypothesized that female mice would have significantly less kidney injury and significantly less T cell infiltration than males.

Methods:
Female mice were injected intraperitoneally with aristolochic acid at a dose of 2 mg/kg for 5 consecutive days. Serum creatinine and weight were recorded each day mice were injected and at 2 and 4 weeks after injection. Their kidneys were then harvested at 4 weeks post-injection. We generated a single cell suspension and then lysed red blood cells. Flow cytometry was performed with fluorescently labeled antibodies. A small cohort of male mice from a prior study was used for comparison. One-Way ANOVAs were run to compare means for each group.

Results:
Female mice demonstrated no detectable injury, based on no increase in serum creatinine, from aristolochic acid ($p>.05$). In contrast, males had a significant increase in creatinine when injected with aristolochic acid ($p<.05$). However, the proportion of T cells and the proportion of various subpopulations of T cells, including CD 8 resident memory T cells (CD103 marker) significantly increased in all populations injected with aristolochic acid, including females who had no clinically noticeable injury ($p<.05$). These data demonstrate that aristolochic acid elicits an immune response in the kidney even if there is no clinically detectable or significant change in creatinine.

Conclusion:
Resident memory T cells increasing in all populations injected with aristolochic acid is intriguing as it shows the potential for a permanent injury in the kidney. Resident memory T cells take up permanent residence in tissues, so they theoretically could influence transplantation rejection. Regarding this specific study, they may play a role in aristolochic acid injury and further studies should elucidate the mechanism of injury to better understand kidney disease.

Abstract Title: Implementation of Orthopaedic Patient Educational Materials at a Student-Run Free Clinic

Investigator: Reagan Treadwell
Co-Investigator(s): Nathanael Smucker, MD2025; Rachel Shulmister, MD2025
Department(s): Portsmouth Naval Hospital Orthopaedics

Abstract

INTRODUCTION:
The Health Outreach Partnership of Eastern Virginia Medical School Students (HOPES) Orthopaedic Clinic exists to meet the needs of under and uninsured people in the Hampton Roads area. For a patient to be an active participant in their treatment and recovery, the patient must be able to comprehend and engage with their physician and remember the steps of rehabilitation. Informational handouts and print resources have been shown to augment patient recall; however, providing a written resource at a literacy level that is comprehensible by all patients presents a challenge.

METHODS:
A group of staff members at HOPES sought to implement the use of informational handouts in the orthopaedic clinic. An online search of current orthopaedic patient informational handouts was conducted to compile a list of existing handouts pertaining to the following most common orthopaedic diagnoses: Bursitis, Carpal Tunnel Syndrome, Flat Foot, Hip Osteoarthritis, Knee Osteoarthritis, Shoulder Osteoarthritis, Rotator Cuff Problems, Tendonitis, Wrist Pain, Low Back Pain, Plantar Fasciitis. The reading level of each handout was determined using the Flesch-Kincaid Grade Level tool, The SMOG Index, and the Automated Readability Index. Holistic analysis of handouts was performed using the Agency for Healthcare Research and Quality's (AHRQ) Patient Education Materials Assessment Tool (PEMAT) guide. Patient handouts found to have an average reading level less than 7.0, as is recommended by the AHRQ, and a PEMAT score greater than 70% were included in handout selection. Handouts were developed for the remaining diagnoses whose existing materials did not meet stated criteria. All informational handouts were translated into both English and Spanish to promote health care equity, given that many HOPES patients are Spanish speaking.

RESULTS:
Analysis of existing handouts
Online search for handouts related to the eleven topics yielded a total of 57 handouts from ten different sources. Of these, nine articles met reading level criteria, while only six articles also met PEMAT criteria; those articles regarded the following diagnoses: pes planus, plantar fasciitis, and low back pain. 16 handouts from eight different sources were found that discussed osteoarthritis. The average reading level of these articles was 8.6, and none were below 7.0. There were 10 handouts regarding low back pain from four different sources with an average reading level of 7.2. Four low back pain handouts had reading levels below 7.0, and these were from two sources. Seven handouts were identified for both rotator cuff pathology and generic tendonitis, with average reading levels of 8.9 and 9.3, respectively. Neither of the sections had text below a 7.0 reading level. The remaining topics were carpal tunnel syndrome with 6 handouts (average 8.6 reading level, 63% PEMAT), generic bursitis with 5 (average 8.0 reading level, 67% PEMAT), plantar fasciitis with 4 (average 7.0 reading level, 72% PEMAT), and pes planus with 2 (average 6.5 reading level, 67% PEMAT).

Development of remaining handouts
Appropriate handouts were created for the remaining topics and underwent multiple rounds of reading level analysis and editing prior to being formatted and scored using PEMAT. Developed handouts had an average reading level of 6.1 and a PEMAT score of 77%. The PEMAT score of these handouts could be improved by adding more illustrations; however, for brevity's sake, only one or two illustrations of the anatomy and pathology were included per handout. Developed handouts were then translated into Spanish.

CONCLUSION:
The readability of existing orthopaedic informational handouts available online for clinical use is, on average, above the recommended reading level for patient educational material, and formatting of existing handouts does not always follow easy-to-read handout guidelines. Handouts were developed for the HOPES orthopaedic clinic patients that met both readability and formatting criteria to augment patient recall and participation in treatment and recovery.

Abstract Title: Imaging Spectrum of Ectopic Pregnancy

Investigator: Adam Trusty
Co-Investigator(s): Dr. Tyler Klause, Diagnostic Radiology Residency; Dr. Christopher O'neill, Diagnostic Radiology
Department(s): Diagnostic Radiology

Abstract

Introduction:
The leading cause of hemorrhage & mortality in the first trimester of pregnancy is ectopic pregnancy, a gestational sac with an abnormal implantation site. With an incidence of 2% across all pregnancies and 18% amongst patients with first trimester bleeding, it is among the more commonly encountered pathology observed in the emergency room setting. Ultrasound often serves as the first line imaging modality and plays a pivotal role in diagnosis. While 95% of ectopic pregnancies occur within the fallopian tubes, it is essential that radiologists and emergency room physicians be familiar with and proficient in recognizing the other less common types of ectopic pregnancies to include cervical, cesarean scar, interstitial/cornual, ovarian, abdominal, and heterotopic pregnancies. We present several cases of ectopic pregnancy to demonstrate the spectrum of imaging findings that may be encountered.

Case Information:
Case #1: A 42 y.o. Gravida (G)6 Para (P) 4014 female presented to the Emergency Department (ED) with spotting in the setting of pregnancy. Patient underwent obstetric (OB) ultrasound (US) which demonstrated an extrauterine gestational sac along the margin of the right ovary with estimated gestational age of 6 weeks 5 days by crown rump length (CRL). She underwent subsequent laparoscopic right salpingectomy with pathology resultant as right tubal ectopic pregnancy.

Case #2: A 31 y.o. G5P2113 female presented to her obstetrician pregnant with complaints of nausea and vaginal bleeding. In office ultrasound was concerning for interstitial ectopic and the patient was subsequently referred to the ED. OB US demonstrated an eccentrically located gestational sac in the right cornua of the uterus, consistent with interstitial ectopic pregnancy. She underwent subsequent right cornual wedge resection & right salpingectomy with pathology consistent with right interstitial ectopic pregnancy.

Case #3: A 38 y.o. G1P0 female presented to the emergency room with abdominal pain, fever, sepsis, severe anemia in the setting of an unknown pregnancy. She underwent subsequent computed tomography (CT) of the abdomen & pelvis and was observed with a fetal skeleton with partially collapsed calvarium within the peritoneal cavity. She underwent an exploratory laparotomy, right salpingoopherectomy, and resection of a mummified, degenerated 2nd trimester fetus free in the abdomen, adhered to small bowel, mesentery, and omentum.

Discussion:
The fallopian ampulla, infundibulum, and isthmus are the most common implantation sites for ectopic pregnancies. Specific imaging features favoring tubal ectopic include the tubal ring sign and ring of fire sign. Interstitial ectopic pregnancy occurs with implantation in the interstitial or intramyometrial segment of the fallopian tubes and has a high rate of maternal hemorrhage and mortality given the proximity to the arcuate vasculature. The main imaging finding is an abnormally eccentric gestational sac with a thin surrounding endomyometrial mantle. Abdominal ectopic pregnancy often occurs secondary to undetected tubal or ovarian ectopic rupture and extrusion to the peritoneal cavity. Implantation can occur anywhere in the peritoneum or abdominal viscera and is associated with considerable maternal morbidity and mortality. Imaging is characterized by an intraperitoneal gestational sac with thick surrounding margins.

Conclusions:
Given that there are no specific clinical signs or laboratory tests to alert clinicians of the uncommon presentations of ectopic pregnancy, radiologists play a critical role in diagnosing this spectrum of disease. It is imperative that radiologists be familiar with and proficient at identifying these cases to facilitate diagnosis and prompt early management.

Abstract Title: Pseudopathologic Enhancement of Brain Parenchyma

Investigator: Chuka Ukekwe
Co-Investigator(s): Tyler Klause, Radiology\EVMS
Department(s): Radiology

Abstract

Introduction:
Multidetector computed tomography (CT) is commonly used in follow-up for oncologic imaging. Intravenous iodinated contrast is often utilized to provide better visualization and delineation of soft tissue findings. While CT soft tissue neck is often acquired during a venous phase of imaging, contrast can be visualized in the vasculature, allowing for limited evaluation of these structures. As a radiologist, it is important to be familiar with and able to identify vascular abnormalities and artifacts which may mimic pathology. We present a case of a patient with vascular artifacts related to a right-sided venous injection resulting in a striking pattern of abnormal enhancement simulating pathology. A search of the literature revealed only two previously reported similar cases.

Case Information:
A 90 y.o. female was initially found with a right neck mass, biopsied by FNA as poorly differentiated carcinoma, suspected as small cell lung cancer. This neck mass was noted encasing the right carotid and subclavian artery as well as a portion of the right subclavian and innominate vein. Subsequent CT chest and PET/CT demonstrated a 3.7 cm hypermetabolic right upper lobe lung mass with hypermetabolic activity within the right neck mass and lymph nodes. She underwent treatment with combination radiation and chemotherapy with dramatic decrease in the size of the right neck mass.

The patient presented for routine follow up contrast enhanced imaging of the head, neck, and chest with contrast. The patient was injected with 60 cc of Omnipaque 350 at the right antecubital fossa. The CT soft tissue neck, acquired 45 seconds after injection, demonstrated a grossly abnormal pattern of enhancement with extensive visualization of the jugular veins, extensive hyperdense parenchymal enhancement of the cerebellar hemispheres along their inferior margin, medulla & inferior pons bilaterally, and venous & arterial enhancement within the right cerebral hemisphere. There was little to no enhancement observed within the left cerebral hemisphere. Concurrently performed CT head, acquired 4-5 minutes after injection, demonstrated an unremarkable pattern of enhancement without asymmetry.

Discussion/Clinical Findings:
We suspect this abnormal pattern of enhancement is related to functional and/or structural narrowing of the right brachiocephalic vein, likely related to prior disease or post treatment changes. There are extensive superficial right sided venous collaterals, which may have preferentially filled following right sided injection. Within the intracranial circulation, it is possible that right hemispheric and posterior fossa cortical veins may have filled via these collateral vessels and caused retrograde flow through the capillary beds, producing the subsequent abnormal pattern of enhancement we observe. The asymmetric enhancement of the right carotid artery is less clearly explained, though both intracranial carotid arteries appear to enhance on the delayed CT head acquisition. Detailed evaluation of the vasculature is also somewhat limited in this patient in the absence of dedicated angiographic imaging.

Conclusion:
While pseudo-pathologic enhancement of the brain parenchyma is a rare phenomenon, knowledge of its existence and familiarity with such angiographic artifacts is useful for radiologists who may encounter these findings in practice and may allow them to distinguish artifactual findings from vascular abnormalities.

Abstract Title: A Comparison of Obesity Prevalence, Demographics and Clinical Features in HOPES Clinic and Clinica Comunitaria Esperanza

Investigator: Chuka Ukekwe
Co-Investigator(s): Kelly Hogan, MD 2025\EVMS; Kenyone King, MD 2025\EVMS
Department(s): Global Health

Abstract

Introduction:
The HOPES (Health Outreach Partnership of EVMS Students) Clinic was founded in 2011 to address the lack of healthcare options available to uninsured patients in the Hampton Roads area. In 2016, the clinic expanded to include Clinica Comunitaria Esperanza, the student-run free clinic intended for uninsured Spanish-speaking members of the local community. While patients of both clinics share a lack of health insurance as a barrier to receiving proper care, the two patient communities have not yet been studied to identify if there are differences in the prevalence of certain medical conditions across both populations. The purpose of this study is to evaluate the two clinic populations to identify and analyze differences in the prevalence of obesity and associated demographic features.

Methods:
This is a retrospective study of patient data from both HOPES Clinic and Clinica Comunitaria Esperanza. Patient charts were standardized in the Practice Fusion EMR and a REDCap is being created to export relevant data to be analyzed. Specific data points that will be extracted and analyzed for the purpose of this study include obesity prevalence rates, body mass index (BMI), age, sex, comorbidities, and medications. If possible, data regarding change of BMI over the course of treatment at the respective clinic will additionally be studied.

Results:
Patient data has been standardized in the Practice Fusion EMR utilized in both clinics. A REDCap survey is being utilized to extract patient-specific data from the EMR to be analyzed by Chi-square analysis.

Conclusion/Discussion:
If this study demonstrates that disparities exist between the prevalence of obesity and associated demographic and clinical features in HOPES Clinic and Clinica Esperanza patients, quality improvement interventions related to disease screening, disease management, health education, and patient follow-up may be undertaken to address disparities and advance health equity in this community.

Abstract Title: Effects of Air Pollution on Categories of Cardiovascular Disease: A Review and Analysis

Investigator: Manasa Vallabhaneni
Co-Investigator(s): Tarek Zagade, EVMS\MD2023; Aditya Gaddipati, EVMS\MD2023; Timothy Liu, EVMS\MD2023
Department(s): EVMS Medical Education

Abstract

Introduction:
Heart disease continues to be the leading cause of death in America due to many contributing factors such as poor diet and lack of exercise. However, one overlooked factor is pollution. Air pollution is a significant contributor to overall heart health in addition to pathological conditions such as arrhythmias, heart failure, and vascular disease. These effects are typically propagated over time. However, it is essential to explore the short-term and long-term consequences of exposure to harmful air pollutants on cardiovascular disease. The goal of this review is to present the current understanding of the relationship between air pollution and various categories of cardiovascular disease.

Main body:
Using clinicaltrials.gov, trials were identified using the keywords "air pollution" and "cardiovascular disease". We included all trials that were listed as "complete". A total of 14 trials were included. Each trial was analyzed to assess study aim, patient population, demographics, primary outcomes, and results from associated publications. Trials were further categorized and analyzed by category. The categories used to stratify the trials were acute coronary syndrome (ACS), arrhythmia, heart failure, and vascular disease. With these categories in place, we completed a summative, qualitative analysis with the studies that were found.

Studies on ACS have shown an increased risk of occurrence with increased sulfur dioxide, ozone, nitrogen, and particulate matter. In addition, industrial areas with increased concentrations of air pollution and diesel exhaust have demonstrated an increased risk for acute coronary syndrome.

Studies on arrhythmias have shown air pollutant particles including diesel exhaust, wood smoke, ozone, concentrated ambient particles, engineered carbon nanoparticles, and high ambient levels of air pollution do not increase risk of short-term arrhythmia in healthy individuals. However, in high-risk patients, such as those who have experienced previous MIs with implantable cardioverter defibrillators or have required cardiac resynchronization, particulate matter 2.5 and 10 both have shown increased risk of ventricular tachycardia and ventricular fibrillation. Gaseous pollutants, other than nitrogen dioxide did not have significant correlations with arrhythmia.

Studies on heart failure have demonstrated diesel exhaust to decrease walking distance and arterial stiffness in heart failure patients compared to their healthy counterparts. Heart failure-related hospitalizations and deaths are higher in cities with increased carbon monoxide, sulfur dioxide, and nitrogen dioxide. There is also a dose-dependent increase in the incidence of heart failure with air pollution in with a component of genetic susceptibility.

Studies on vascular function have shown diesel exhaust to decrease vasodilatory function in vessels. Regular vasodilators such as bradykinin, acetylcholine, and verapamil have been shown to be less functional in patients exposed to diesel exhaust, increasing the likelihood of thrombus formation.

Conclusions:
In conclusion, our review provides a novel insight into current clinical trials from clinicaltrials.gov demonstrating deleterious effects of air pollution on various categories of cardiovascular disease. This emphasizes the importance of further investigation into air pollution's effects on cardiovascular health, as well as the need for increased environmental regulation.

Abstract Title: Improvements in Understanding, Empathy, and Self-Efficacy in Caregivers of Dementia Patients through the Use of Virtual Reality

Investigator: Mark Velasquez
Co-Investigator(s): Lauren Alexis Walters, Christopher Newport University; Hamid Okhravi, MD, EVMS Glennan Center for Geriatrics and Gerontology; Bahar Niknejad, MD, EVMS Glennan Center for Geriatrics and Gerontology; Matthew Bourcier, PA-C, EVMS Glennan Center for Geriatrics and Gerontology; Daniel Cohen, MD, EVMS Neurology; Carrie Elzie, Ph D, EVMS Pathology & Anatomy
Department(s): EVMS Pathology & Anatomy

Abstract

Introduction:
Caregivers for individuals with dementia have been found to be under significantly more stress than non-dementia patients, which can result in depressive symptoms, physical difficulties, financial issues, as well as a variety of other problems. Psychosocial interventions specifically aimed at understanding and empathy have been found to be effective in treating these issues in caregivers but often fail due to an assortment of barriers. Virtual reality is a promising intervention that circumvents these barriers while improving understanding and empathy in caregivers.

Methods:
Participants were caregivers of dementia patients experiencing different stages of dementia at the EVMS Memory Consultation Clinic. Participants were recruited by physicians to engage in a virtual reality simulation lasting less than 30 minutes produced by Embodied Labs, Inc. where they embodied a person with progressive Alzheimer's Disease, seeing situations from the perspective of someone with Alzheimer's and experiencing their symptoms. Afterwards, they completed a post-simulation interview, a demographics survey, a survey regarding the VR experience specifically, and a survey measuring caregiver experiences. The data was collected and organized via Redcap.

Results:
38 caregivers participated in the simulation while only 37 completed the surveys and post-simulation interview. In the post-simulation survey, 97% of participants "agreed" or "strongly agreed" that the simulation had a personal impact on them. 97% "agreed" or "strongly agreed" that the simulation gave them a better understanding of the biological impacts of dementia. 94% "agreed" or "strongly agreed" that the simulation gave them a better understanding of what their loved one is experiencing. 94% "agreed" or "strongly agreed" that the simulation gave them a better understanding of how to deliver better care. 100% "agreed" or "strongly agreed" that the simulation was a valuable experience and 89% "agreed" or "strongly agreed" that they felt better prepared for what is going to happen in the future.

Conclusion:
The virtual reality simulation was well-received as an intervention and revealed to be a valuable experience. It provided informal caregivers with an increased level of understanding and empathy for the person they were caring for.

Abstract Title: Diabetic Ketoacidosis and Acute Mesenteric Ischemia in Adults: An Underreported Association

Investigator: Gina Vivino
Co-Investigator(s): Nicole Crofton, MD 2023
Department(s): Internal Medicine

Abstract

Introduction:
Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes mellitus. Acute mesenteric ischemia (AMI) is a less common, but potentially fatal, complication of DKA. This association has been reported among pediatric patients, however, it has been rarely reported in the adult population. We report a case series of two adult patients who presented in DKA whose course was complicated by AMI.

Case Information:
Case 1: A 60-year-old male with a history of type II diabetes mellitus presented to the emergency department (ED) after he was found in an altered mental status at home. He reported two days of non-bloody diarrhea, nausea, and vomiting. His vitals were notable only for tachycardia. He was confused but calm and intermittently followed commands with no focal neurological deficits. Labs were consistent with DKA, showing severe hyperglycemia and a high anion gap metabolic acidosis.

After initiation of DKA treatment, he developed acute respiratory failure and sepsis. Computed tomography angiography (CTA) of the chest, abdomen, and pelvis showed superior mesenteric artery (SMA) occlusion. He underwent subtotal colectomy with ileostomy and SMA stenting and had a good recovery.

Case 2: A 41-year-old male with a history of type I diabetes mellitus presented to the ED after he was found unresponsive at a bus station. His vitals were notable only for tachypnea. Examination showed Kussmaul breathing. His eyes opened spontaneously, and he occasionally followed commands. Labs were consistent with DKA, with severe hyperglycemia and a high anion gap metabolic acidosis.

He progressed to sepsis despite fluid resuscitation and insulin therapy and developed acute respiratory distress requiring intubation. Computed tomography (CT) scan of the abdomen showed a significant amount of free fluid in the abdomen and multiple loops of small bowel with pneumatosis. He underwent small bowel resection and had a complicated post-surgical course. He was discharged to a skilled nursing facility with need for enteral feeding due to his malnutrition.

Discussion:
Acute mesenteric ischemia is associated with diabetic ketoacidosis. However, many of the cases have been reported in pediatric patients. Our case series is unique because we highlight two adult patients with DKA complicated by AMI. There have been reports of pediatric patients in DKA who developed non-occlusive mesenteric ischemia thought to be secondary to the hypovolemia that can occur in DKA3,4. There are some older reports describing adult patients with DKA who were also found to have AMI5,6, but there are not many cases in the recent literature.

Diabetes mellitus has been well-researched as a hypercoagulable state, and diabetic ketoacidosis also promotes a prothrombotic state2,1. The clot-activating factors in DKA, along with the abnormal vascular endothelium seen in diabetes, are associated with increased risk of thrombotic events. While acute mesenteric ischemia is typically due to vessel occlusion, non-occlusive ischemia may develop in low-volume states due to decreased perfusion7. Our first case demonstrated AMI due to SMA occlusion, but it is also important to consider a non-occlusive etiology for patients with hypovolemia secondary to DKA, as seen in Chan-Cua and DeMeglio's cases3,4.

As seen in the literature and the cases presented here, patients in DKA may initially present with ischemic bowel or it may develop after beginning treatment of DKA. AMI often presents with abdominal tenderness, which may be hard to distinguish in the setting of DKA. If fluid resuscitation and resolution of acidosis in DKA do not improve abdominal symptoms, then it is important to consider ischemic bowel because it is a life-threatening condition. Computed tomography angiography is a first-line imaging choice given that it is fast, noninvasive, and highly accurate8. Treatment is aimed at re-vascularization of the ischemic tissue and resecting the necrotic bowel7.

Conclusion
In this case report, we describe two adult patients with unresolving diabetic ketoacidosis who were subsequently found to have acute mesenteric ischemia. Acute mesenteric ischemia should be considered in patients with DKA who have unresolving acidosis or unresolving abdominal pain. Early identification of mesenteric ischemia is critical to improve outcomes, and clinicians should have a low threshold to perform imaging as it can make a huge difference in bowel salvage.

Abstract Title: Feasibility of using wearable technology to monitor agitation and sleep in patients with Alzheimer's dementia: Lessons learned

Investigator: Lavinia Wainwright
Co-Investigator(s): Hamid R. Okhravi, Glennan Center for Geriatrics; Ajay Gupta, Department of Computer Science, Old Dominion University; Shubham Jain, Department of Computer Science, Stony Brook University; Kurt Maly, Department of Computer Science, Old Dominion University; Christianne Nesbitt, Glennan Center for Geriatrics; Shreyas Gujjar, Department of Computer Science, Old Dominion University; Thrupthi Narayana Murthy, Department of Computer Science, Old Dominion University; Diamond King, EVMS
Department(s):

Abstract

Introduction:
Individuals with Alzheimer's dementia (AD) often go through a period of significant behavioral and psychological symptoms including agitation. This can lead to impaired daily functioning, prolongation of hospitalization, early institutionalization, and higher mortality. The integration of biomedical data acquisition systems and information technology enables continuous real-time monitoring of physiological data in daily life.

Method:
This feasibility study is part of a clinical trial that examines the effects of THC-free CBD oil on agitation in patients with AD (NCT04436081), involves caregiver/care-recipient dyads and the use of technology to capture agitation during a 14-week period. Participants are given 2 Fitbit versa 2 (each includes a 3-axis accelerometer and an optical heart rate monitor), a smartphone, a tablet, and a digital timer. Participants' Fitbit are paired with their smartphone, while the caregivers' FitBit is paired with their tablet. Participants include males/females over 50 years old, with the diagnosis of AD, a MMSE score ≤28 & >4, and agitation measured with an NPI agitation/aggression sub score >3. Each dyad completes 24 forms/questionnaires throughout the study electronically via provided apps. Caregivers are instructed to send a real time electronic alert when agitation episodes happen.

Results:
So far, we have enrolled 26 dyads. For this report we have collected data on 22 participants with 140 million data points for limb movement and heart rate, and 969 nights of sleep data records. Overall compliance with wearable use was 77% of the time, with 82% in 11 participants, 65% in 8 participants and 32% in 3 participants. Compliance with electronic form/questionnaire completion was 87%. Electronic alert for agitation episodes were recorded by the caregivers only 50% of time.

Conclusion:
This study explores the feasibility and acceptability of using technology (wearables, electronic form data completion and submission, sleep, and real time agitation episode collection) for a 16-week period in AD patients with agitation and their caregivers. We found high acceptability of wearing the Fitbit by AD patients with agitation. The primary issues interfering with data collection and device compliance were device battery life and memory, remembering to wear the device after charging, and technical fault in capturing the data.

Abstract Title: Delayed Diagnoses in Patients with Dizziness In the U.S. Commonwealth of Virginia and the Tidewater Region

Investigator: Kendra Walker
Co-Investigator(s): Kevin M. Guy M.S. Otolaryngology, EVMS MS4; Peter G. Volsky M.D. EVMS Otolaryngology
Department(s): ENT

Abstract

Introduction:
Vestibular disease and dizziness are common causes of impairment. Correct diagnosis is necessary to provide appropriate management using available healthcare resources. The purpose of this study is to address a regional public health need for accurate and timely diagnosis of dizziness and vestibular disease.

Methods:
This cross-sectional study includes all patients in the Tidewater region of Southeastern Virginia (estimated population 1,764,298) diagnosed with dizziness or vestibular disease between 2010-2020 at a Sentara Healthcare facility. Prevalence data for dizziness symptom diagnoses and "delayed" diagnoses of vestibular disease or non-vestibular disease were collected and analyzed.

Results:
During the study period, 31,670 diagnoses of dizziness were rendered; 18,390 were later followed with a dizziness related non-vestibular diagnosis, 930 were followed with a vestibular disease diagnosis, and 12,350 were not followed by a diagnosis to explain the dizziness symptom. The proportion of patients diagnosed with vestibular disease (3%) after receiving a dizziness diagnosis in the region is far below expected norms (25-34%) in the general population. There were greater proportions of delayed diagnoses of labyrinth dysfunction (OR 4.8, $p<0.0001$), superior semicircular canal dehiscence (OR 3.1, $p=0.0023$), otolith disease (OR 3.1, $p=0.0023$), among others, and a decreased proportion of delayed diagnosis of benign paroxysmal positional vertigo (OR 0.56, $p<0.0001$).

Conclusion:
Approximately 40% of patients with dizziness do not obtain a specific diagnosis. The discrepancy between expected and observed prevalence in our region indicates that vestibular disease is likely underdiagnosed, resulting in lost opportunities to access rehabilitation and medical management and suggests the need for increased referral to specialists for more thorough evaluation.

Abstract Title: Usefulness of mock residency interviews in EVMS third year medical students

Investigator: Claire Weaver
Co-Investigator(s): Taylor Dobyns, MD Student
Department(s): School of Medicine

Abstract

Introduction:
The 2018 National Resident Matching Program survey of United States residency program directors across all specialties found that the three most important factors in ranking applicants were interactions with faculty, interpersonal skills, and interactions with house staff during their interview (2). Despite some studies suggesting that interview scores were the most important factor for ranking of residency applicants, many medical students report that they had limited experience participating in interviews of any kind (1,2). The limited data that does exist about mock interviews for 4th year medical students suggests that students find mock interviews to be very helpful, however further studies are needed. Herein, this presentation will describe student attitude of usefulness toward the mock interview program at Eastern Virginia Medical School (EVMS).

Methods:
Third year medical students from EVMS were required to complete a mock interview as a part of their career exploration rotation during the 2021-2022 academic year. They then completed required eValue surveys at the end of their career exploration rotation using the Likert scale regarding the usefulness of the mock interview session. The Likert Scale ranged from 1 (poor) to 5 (excellent) with 3 being average. Raw data was extracted from the eValue survey results and the mean Likert score was calculated, as well as the proportion of respondents who found the mock interviews to have excellent usefulness or above average usefulness.

Results:
46 students completed the survey, and the responses are currently being analyzed. 92.5% of students found the mock interview session either above average or excellent in terms of usefulness. The average score on the Likert scale was 4.5.

Conclusion:
Medical student rankings from residency programs are heavily dependent on the residency interview and the residency interview may even play a role in whether students match into the specialty of their choice. It is therefore essential that medical students be well-prepared for interviews. Once data analysis is complete, this data can be used to determine what strategies administrators of medical schools may employ to help prepare medical students for residency interviews and possibly improve match rates.

Types of bias to consider for this data: Extreme responding bias, response fatigue

Sources:
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2. Donaldson K, Sakamuri S, Moore J, Everett EN. A Residency Interview Training Program to Improve Medical Student Confidence in the Residency Interview. 2020 Jul 2;16:10917. doi: 10.15766/mep_2374-8265.10917. PMID: 32704533

Abstract Title: Corticotroph hyperplasia caused by NR3C1 germline variants in patients with ACTH-dependent hypercortisolism

Investigator: Camille Williams
Co-Investigator(s): John Christopher Magnotto, Brigham and Women's Hospital\Division of Endocrinology, Diabetes, and Hypertension
Department(s): Brigham and Women's Hospital-Division of Endocrinology, Diabetes, and Hypertension

Abstract

INTRODUCTION:
Pituitary adenomas are benign tumors that develop in hormone producing cells of the pituitary gland. Tumors that secrete bioactive ACTH cause Cushing's Disease, a rare endocrinopathy characterized by excessive cortisol. Primary management of Cushing's Disease is transsphenoidal surgical resection of the adenoma. However, a clinical dilemma presents when patients with workup suggestive of pituitary ACTH secretion and clinical features of Cushing's Disease undergo surgery, but an adenoma is not identified. A subset of patients with pituitary-dependent hypercortisolism and hyperplasia of corticotroph cells, is identified. Surgical intervention does not treat hypercortisolism and symptoms persist in patients with corticotroph hyperplasia. With the goal to identify a genetic cause of ACTH-dependent hypercortisolism in patients with corticotroph hyperplasia, we performed whole-exome sequence analysis.

METHODS:
Whole-exome sequencing was performed on patient DNA extracted from pituitary tissue and leukocytes of blood from 14 patients with ACTH hyperplasia. Variants in *NR3C1* were confirmed via Sanger sequencing. *In vitro*, luciferase reporter assays were performed to determine transcriptional activity of the glucocorticoid response element and immunocytochemistry was performed to assess GR translocation following dexamethasone exposure.

RESULTS:
We identified four germline mutations in *NR3C1* variants in 4 of the 14 patients with ACTH hyperplasia. 2 novel missense mutations, I762T and C477W, were found in the ligand-binding domain and DNA-binding domain, respectively. 2 previously identified rare missense variants, A229T and F65V, were found in the N-terminal domain. In luciferase reporter assay, a significant decrease in transcriptional activity of glucocorticoid response elements was observed in all mutants, F65V, A229T, I762T, and C477W, compared to wildtype when treated with dexamethasone. Immunocytochemistry data revealed decreased translocation of all mutants, F65V, A229T, C477W, and I762T, when exposed to dexamethasone. Notably, less translocation was observed for I762T and C477W compared to A229T and F65V with dexamethasone treatment.

CONCLUSION:
In vitro studies demonstrate that mutations in *NR3C1* identified in patients with corticotroph hyperplasia clearly inhibit the transcription of glucocorticoid response elements, and furthermore, inhibit the translocation of the glucocorticoid receptor into the nucleus, when exposed to dexamethasone. These in vitro data reveal that loss-of-function mutations in *Nuclear receptor subfamily 3 group C member 1 (NR3C1),* which encodes a glucocorticoid receptor, impairs cortisol negative feedback through impaired glucocorticoid receptor function, resulting in elevated ACTH secretion and pituitary hyperplasia of corticotroph cells. Our findings elucidate the molecular mechanisms responsible for a portion of patients with hyperplasia and expands the understanding of this disorder with the hopes of preventing ineffective transsphenoidal surgery. This may provide insight into the use of screening as a diagnostic tool for detection of ACTH hyperplasia which can potentially circumvent unnecessary interventions.

Abstract Title: Digital PCR as a tool to measure absolute abundance of RNA in single oocytes

Investigator: Jamie Wilson
Co-Investigator(s): Nehemiah S. Alvarez, Department of Physiological Sciences, EVMS, Norfolk VA; Pavla Brachova, Department of Physiological Sciences, EVMS
Department(s): Physiology

Abstract

Introduction:
Failure of the ovary is one of the earliest signs of natural female aging, called reproductive aging. In a woman's mid-30's, fertility begins to decline and precipitously falls until menopause occurs in the early 50's. Reproductive aging is best characterized by a progressive loss in the number of follicles, and coincides with an increase in poor quality oocytes. Oocyte quality is dependent on RNA that is stored during times of active transcription. During meiotic maturation, transcription ceases, and the oocyte utilizes stored RNA to maintain cellular processes until the early embryonic genome is activated. Because oocytes are transcriptionally quiescent, it is important to understand how RNA dynamics are altered during oocyte maturation in young and aged mice. Our goal was to determine if digital PCR (dPCR) was a viable method to determine absolute abundance of transcripts in single oocytes and eggs. dPCR is a method of measuring RNA abundance, orthogonal to RNA-sequencing or quantitative PCR methods. It is a useful tool to calculate absolute abundance of an RNA molecule in a given sample.

Methods:
Whole ovaries, individual germinal vesicle (GV) oocytes, or metaphase II (MII)-arrested eggs were collected from young (6 week) and reproductively aged (14 month) female C57Bl/6 mice stimulated with gonadotropins at two timepoints: 46h after PMSG and after 46h PMSG+16h hCG. Total RNA was extracted from whole ovaries or oocytes.

Complementary DNA (cDNA) was generated from whole ovaries, single GV oocytes, and single MII eggs in a reverse transcription (RT) reaction. Digital PCR (dPCR) was performed using a QuantStudio™ Absolute Q Digital PCR system. Gene target probes for RNA-specific adenosine deaminase 1 (*Adar*) were utilized in preparation of assays. Fluorescent signals were imaged and analyzed using QuantStudio™ Absolute Q software.

Results:
To test the detection limit of the Absolute Q digital PCR platform, we performed a serial dilution of total RNA from mouse ovaries to measure the RNA modification enzyme, *Adar*. We tested ovaries from three different mice, with dilutions of 22.5 ng, 2.25 ng, 0.225 ng and 0.0225 ng of total RNA. In each ovary sample we detected at least 1 *Adar* molecule in the dilutions containing 0.0225 ng of total RNA, which represent the hypothesized amount of RNA in a single GV oocyte. Next, we measured the amount of *Adar* RNA in single oocytes. We detected similar abundance of *Adar* in reproductively young and aged GV oocytes (young: 1114, median, n=7; aged: 1306 molecules, median, n=4), and similar abundance of *Adar* in reproductively young and aged MII eggs (young: 68 molecules, median, n=8; aged: 73.5 molecules, median, n=4).

Conclusion:
Our results demonstrate the Absolute Q dPCR platform can accurately measure absolute RNA abundance in single oocytes and eggs. Future studies will utilize multiplex reactions allowing for the measurement of 40 targets simultaneously. This approach will greatly enhance our ability to study the RNA transcriptome of single oocytes at single molecule resolution, and understand molecular changes occurring during reproductive aging.

Abstract Title: Improving Men's Health: A CQI project to increase engagement in community & clinic-based health behavior change programs

Investigator: Madeleine Wright
Co-Investigator(s): Harshit Amin, MS2, EVMS MD Program, Amy Paulson, MPH, EVMS Community Health and Research/Dept. of Pediatrics, Gamanuel Jean, MPH, EVMS MPH Program, Margaret Baumgarten, MD, EVMS Family Medicine, Carlos Hill, MPH, Meharry Medical College
Department(s): EVMS Community Health and Research/Dept. of Pediatrics

Abstract

Intro:
Men are a distinct patient population. Though they are at higher risk for morbidity and mortality from chronic illness, and more likely to engage in adverse health behaviors, they are less likely to engage with the healthcare system. Recruiting and retaining men to behavioral health programs are the main barriers to male participation in such programs. This quality improvement project sought to investigate facilitators and barriers to male engagement in health programs, and to hear directly from men about their preferences for programs.

Methods:
1738 patient records were pulled from the practices of Portsmouth Family Medicine (PFM) and Ghent Family Medicine (GFM) between December 1, 2021 and June 1, 2022 for male patients over the age of 18 with one or more of the following chronic conditions: Overweight/Obesity, Pre-Diabetes/Diabetes, or Pre-Hypertension/Hypertension. Patient data was organized into RedCap. Two interviewers conducted 117 interviews, first in-person in the PFM and GFM waiting rooms, and then via phone once phone calls proved more fruitful. Analysis of survey responses was conducted in Qualtrics and Excel.

Results:
At this time, data analysis has yielded a few trends. Participants stated 'no preference' for specific gender, race, or age for a personal health coach, and 'no preference' for specific gender or ethnicity for program material photographs. As these were oral interviews, results may show participant response bias from self-consciousness. Participants preferred to hear about programming by email, postal mail, or from their PCP. Despite many participants stating they had no barriers to enrollment, having more chronic conditions or a strong motivation to change did not increase interest in enrollment. Men cited gender roles, fear of healthcare, and stubbornness as possible reasons for poor male participation in health programming.

Conclusion:
Based on these conversations, future programs should strive to incorporate interactive features that appeal to male interests, such as outdoor activities or healthy cooking classes. Further investigation should be conducted to explore male preferences for program visual materials and health coach demographic preferences through focus groups or extended participant interviews, and results should be shared with local practices to implement programming changes.

Abstract Title: A Needs Assessment Exploring the Quality of Care for Patients with Sickle Cell Disease

Investigator: Mahlete Yared
Co-Investigator(s): Patti Kiger, Pediatrics/EVMS; Jason Dukes, Internal Medicine/EVMS; Chris Fungwe, MD2025/EVMS; Myles Perry
Department(s): Diversity and Inclusion

Abstract

Introduction:
Sickle cell disease (SCD) is a chronic illness that affects approximately 100,000 people in the United States. The average life expectancy is 47 years. Literature shows that SCD patients have the highest recurrent hospitalization rates of all patients with medical conditions and have an average annual out of pocket medical cost of $45,000 for insured patients and $1.6 million for uninsured. In the Hamptons Roads area of southeastern Virginia, no comprehensive adult SCD program or medical advocate exists for patients. Objectives: This study aimed to understand the experiences of SCD patients, families of patients, and providers with SCD care in the Hampton roads area to determine a need for improved navigation and management of SCD care.

Methods:
Qualitative exploratory research was conducted to determine patient and provider needs in SCD care. Patients and providers were selected using purposive sampling for standardized key informant Zoom interviews. Two separate questioning routes were formulated to address the comprehensive healthcare experience of SCD patients and their families and providers of SCD care respectively. The patient questioning route addressed three categories: patient experience, resources, and recommendations. The provider questioning route addressed four categories: SCD training, SCD experience, patient education, and resources. Eleven interviews (four patient and seven provider) were conducted, transcribed, and analyzed.

Results:
Through analysis of the provider interviews, the following themes were identified: 1) Providers attain most of their skill in managing SCD through patient experience, as there is no access to SCD specific training for providers. 2) The comprehensive sickle cell program at CHKD is an asset to pediatric patients, but the transition to and navigation of adult care needs improvement. 3) A mistrust exists between patients and adult sickle cell providers due to perceived lack of compassion and understanding of SCD patient experiences and unfamiliarity with SCD.

Conclusion:
Based on the identified themes, we recommend: 1) Implementing CME (continuing medical education) training on SCD to better educate nonhematological providers of SCD; and 2) Implement a comprehensive adult SCD program in the EVMS-Sentara system. The results of this needs assessment provide further insight into the healthcare experiences of SCD patients, families of patients, and providers in the Hampton roads area that will lend itself to future research on the subject matter.

Abstract Title: Evaluating the Impact of a Medical School Student-Run Research Society on Scholarly Activity

Investigator: Hemasree Yeluru
Co-Investigator(s): Jason Bard, MD 2024; Ryan Harris, MD 2024
Department(s): Office of Research, Associate Dean of Research Administration

Abstract

Introduction:
In January 2022, the United States Medical Licensing Exam Step 1 was slated to use a Pass/Fail scoring system. Due to the shift from numerical scoring, medical students may have been motivated to pursue more research opportunities to stand out on residency applications. To support students during this transition period, the EVMS Research Society (ERS) was created in fall 2020 and offered programs such as information sessions, workshops, journal clubs and a one-on-one mentorship program. One year after the conception of ERS, the current study was designed to evaluate the impact of the organization and identify potential areas of improvement. A survey was distributed to medical students to assess their research experience during their preclinical years, with the goal to examine research experience differences between students with and without the support of the ERS, comparing by ERS membership and graduation year.

Methods:
The study team created a 27-item questionnaire assessing Research Involvement (RI), Sense of Support (SS), and Confidence and Comfort (CC) in conducting research. The three-item SS and three-item CC scales were based on the Dental Student Research Inventory with answer options ranging from (1) Strongly Disagree to (5) Strongly Agree. The anonymous online survey was administered via REDCap to ERS and non-ERS members across the MD Classes of 2022, 2023 and 2024. Participants were instructed to answer the questions based on research experiences during their M1 and M2 years. An optional free response section was also included on the survey for comments or advice about the club. Bivariate analyses were conducted by biostatisticians from EVMS-Sentara Healthcare Analytics and Delivery Science Institute using the SAS 9.4 software.

Results:
116 medical students completed the survey: 63 in the Class of 2024 (54.3%), 32 in the Class of 2023 (27.6%), and 21 in the Class of 2022 (18.1%). 45.7% of respondents (n = 53) were ERS members, of which, the majority were from the Class of 2024 (92.5%; n = 49). Findings revealed that among students who were involved in research, class and ERS membership were associated with an increased number of research projects. Specifically, students from the Class of 2024 reported significantly more projects compared to the Class of 2022 (p=0.041; M = 4.38, M = 2.21), and ERS members reported a greater number of projects compared to non-members (p=0.002; M = 4.49, M =2.57). Both the SS and CC scales were found to be reliable (α = .84 and α = .86, respectively) and mean levels of each construct did not differ by graduation year or ERS membership status. Finally, common themes among qualitative comments included appreciation that the ERS matched students with research projects and hosted informative panels and workshops. Some comments also highlighted the need for EVMS to better facilitate the production of abstracts and publications and a belief that more scholarly production occurs at other institutions.

Conclusions:
This study revealed that students who are involved in research, particularly those who are members of the ERS, are engaging in more research projects since the conception of ERS. This may be a result of the resources provided by the organization, such as matching students with research mentors. Importantly though, the amount of scholarly work such as published abstracts or papers has not increased, and is not significantly associated with either graduation year or membership status. This suggests that despite an increase in research project experience, students are not publishing their work, which may be most important when applying for residency. Moreover, feeling supported and confident with research was not higher among ERS members compared to non-members, suggesting room for improvement for the ERS. A potential source of bias in this study is that students could have pursued more research opportunities solely based on the switch to a Pass/Fail Step 1, regardless of the implementation of ERS. As ERS grows, and a greater understanding of the evolving role research plays in residency applications is achieved, we hope to see EVMS expand its opportunities for students to engage in and produce scholarly work, with an improved sense of confidence in their research abilities.

Abstract Title: The Effect of the Transcranial Direct Current Stimulation (tDCS) device on Visuomotor Reaction Time and Procedural Learning

Investigator: Miguel Yerena
Co-Investigator(s): Gnel Pivazyan, Georgetown University Department of Neurosurgery
Department(s): Department of Neurology

Abstract

Introduction:
The effects of transcranial Direct-Current Stimulation (tDCS) have been demonstrated to increase or decrease cortical excitement and the ability to form action potentials in cortical neurons. This form of Non-invasive brain stimulation has been extensively researched and hypothesized to enhance specific areas of procedural learning pathways in healthy individuals. Our goal is to determine whether the administration of tDCS during training for a motor task can enhance movement-based versus the spatially-based representation of a motor skill.

Methods:
Using the serial reaction time task (SRTT) which involves learning a pattern of sequential movements, procedural memory will be assessed with and without anodal tDCS stimulation to the Left Primary Motor cortex (M1). Participants will be assessed on reaction time changes between the initial training session and a second session after a 24-hour delay using the SRTT.

Results:
We expect to see selective enhancement of movement-based skills with anodal stimulation of M1 and a subsequent decrease in reaction times during the second session when compared to sham tDCS.

Abstract Title: A Case of Acute Atraumatic Subdural Hemorrhage in a Pregnant Patient with Preeclampsia with Severe Features

Investigator: Marie Yrastorza-Daghman
Co-Investigator(s): Esai Hernandez, MD Student
Department(s): Internal Medicine

Abstract

Introduction:
Intracranial hemorrhage in pregnancy is a rare complication of preeclampsia with severe features occurring in only 0.01- 0.05% of pregnancies. Although uncommon, intracranial hemorrhage can significantly impact maternal mortality and health outcomes during pregnancy and postpartum. Main causes include rupture of aneurysms, arteriovenous malformations, and pregnancy induced hypertension such as preeclampsia. Specifically, the subdural hematoma is a form of intracranial hemorrhage that is rarely seen during pregnancy. Clinical features usually arise postpartum and include: severe headache, dizziness, stupor, and coma. Diagnosis is aided with medical imaging with a head CT being a common method of detecting subdural hematomas. The clinical features, patient presentation, and treatment of intracranial hemorrhage will be discussed in this case report following an EVMS patient suffering from a postpartum subdural hematoma in the setting of preeclampsia with severe features.

Case Information:
Our patient is a 38 yo female at 35w1d gestation who was admitted to SNGH for delivery of monochorionic diamniotic twins. Pregnancy was complicated by advanced maternal age and fetal growth restriction. Physical exam at admission was unremarkable, however blood pressure was elevated to 142/81 and labs were significant for AST/ALT of 101/194. The patient was diagnosed with preeclampsia with severe features and put on magnesium prophylaxis. Low-transverse c-section was performed for malpresentation of twin A. A day after delivery, the patient had a blood pressure of 160/95 and reported a headache to staff. Shortly thereafter she became unresponsive to sternal rub. A stroke alert was called and the patient was intubated Head CT showed a large subdural hematoma with a >1.2 cm midline shift. A decompressive hemicraniectomy was performed. This was complicated by cardiac arrest in the OR. Repeat Head CT demonstrated re-accumulation of hemorrhage. A second hemicraniectomy was performed on postpartum day 2, during which the patient required multiple transfusions due to hemorrhagic shock. After the operation, the patient lost function of her left lower and upper extremities, had a fixed left pupil and was nonverbal. Tracheostomy tube and PEG were placed and the post-op course was complicated by fever. The patient was transferred to the HER unit for long term recovery.

Discussion:
Subdural hemorrhages are most often caused by trauma. In younger patients, hemorrhages are most often caused by motor vehicle accidents, while falls account for the majority of hemorrhages in older patients. Less frequently, subdural hemorrhages can be atraumatic; with AV malformations, aneurysm ruptures and cocaine use accounting for the majority of cases. The literature includes only a few previous case reports of spontaneous intracranial hemorrhage in pregnant patients with preeclampsia. In our patient's case, we theorize that pregnancy-induced hypertension caused her subdural hemorrhage. Potential causes of subdural hematoma include aneurysm, AV malformations and seizures. To evaluate these possible causes it is routine to do an EEG and image the brain using CT. Head CT is an essential tool in detecting blood within the cranium that cannot be seen on a physical exam. However, there was no sign of aneurysm or AV malformations on the patient's Head CT, and EEG did not demonstrate seizure activity.

In addition to deducing the etiology of the bleed, it is essential to manage the patient's pre-existing preeclamptic symptoms as those can contribute to the prevention or development of hemorrhage. Preeclampsia treatment with blood pressure optimization and seizure prophylaxis is of great importance in preventing adverse outcomes in pregnant patients. In the case of any patient with acute subdural hemorrhage, craniotomies and decompressive craniectomies are the surgical treatments of choice; with studies showing little difference in mortality rates between both treatments.

Conclusion:
As seen in this case report, a subdural hematoma postpartum puts patients' health at great risk.

Although rare, the development of subdural hematomas during pregnancy can drastically alter patient outcomes and can result in death. It is of the utmost importance that physicians be mindful of the signs and symptoms of intracranial hemorrhages in pregnant patients diagnosed with preeclampsia. Additionally, when signs and symptoms of intracranial hemorrhage are recognized it is urgent that a proper workup be initiated immediately.

Abstract Title: A Step-Wise Increase for Short-Term Postoperative Complications is Associated with Increasing Body-Mass-Index in Adolescent Reduction Mammoplasty - an ACS-NSQIP Study of 1,215 Patients

Investigator: Victor Yu
Co-Investigator(s): Ian Mandybur, EVMS; Kendra Walker, EVMS; Adam Evans MD, Division of Plastic Surgery, EVMS
Department(s): Plastic and Oral Maxillofacial Surgery

Abstract

Introduction:
Macromastia is often a physically challenging and psychologically distressing condition for many adolescent patients, causing back, shoulder, and neck pain, in addition to unwanted attention, introversion, and development of eating disorders. Reduction mammoplasty has been shown to improve these physical and psychosocial problems and is often the best treatment in certain groups of patients, including adults. However, while risk factors for postoperative complications following adult reduction mammoplasty are well known, the risk factors for adolescent complications remain unclear. The purpose of this study was to investigate predictors of postoperative complications following adolescent reduction mammoplasty using a national database from 2012-2019. We hypothesize that there are both patient and case-based risk factors that can contribute to complications.

Methods:
The 2012-2019 American College of Surgeons' National Surgical Quality Improvement Program Pediatric (ACS NSQIP-P) databases were queried to identify primary reduction mammoplasty encounters using Current Procedural Terminology (CPT) code 19318. Based on the World Health Organization Body Mass Index (BMI) classification, patients were stratified into BMI <30, 30-34.9, 35-39.9, and >40. Other patient and case characteristics, and comorbidities were assessed for association for short-term (30-day) wound disruption or surgical site complications. Single variable analysis and a multivariable regression analysis were performed to identify independent predictors for any complications.

Results:
There were 1215 patients with an average age of 16.6 years who met inclusion criteria. Overall, the average BMI was 30.7 kg/m2, and 593 (48.8%) were nonobese while 622 (51.2%) were obese. The overall mean operative time was 183 minutes, and most patients (77.3%) were seen in an outpatient setting; the incidence of complications was 5.27%. The most frequent complications were superficial wound disruption/dehiscence and superficial surgical site infections. Following the multivariable analysis, independent predictors of complications included a BMI 35-39.9 (odds ratio [OR], 2.69; P=0.007), BMI >40 (OR, 4.51; P<0.001) and an American Society of Anesthesiologists (ASA) Classification >3 (OR, 2.57; P<0.012). Other risk factors which did not reach statistical significance yet are otherwise notable include a BMI 30-34.9 (OR, 1.46), and a history of asthma (OR, 1.16).

Conclusions:
Our results demonstrate that an increased ASA physical status greater than 3 and Class II/III obesity were independent risk factors for short-term postoperative complications in adolescent reduction mammoplasty. The detrimental effect that obesity has in adolescent reduction mammoplasty mirrors its role as a risk factor in adult reduction mammoplasty as well. Being aware of these risk factors can assist in identifying and stratifying higher risk patients for appropriate counseling prior to surgery and closer postoperative monitoring. However, reduction mammoplasty should remain a viable surgery for obese patients as it can significantly improve their quality of life.

Abstract Title: Crowdfunding for Plastic Surgery Procedure and Recovery Costs in the United States

Investigator: Victor Yu
Co-Investigator(s): Madeline Coleman, EVMS; Sai Kottapalli, EVMS Jason Pham, EVMS
Department(s): Plastic and Oral Maxillofacial Surgery, CHKD

Abstract

Introduction:
Crowdfunding in medicine has been shown to create significant benefit for patients and families. Platforms such as Gofundme allows patients and their supporters to reach a virtually limitless network of potential donors who can choose to donate to reduce costs associated with their care. The purpose of this study is to describe baseline characteristics of plastic and reconstructive surgery (PRS) patients who utilize Gofundme for medical cost support. We aim to determine which patient populations use crowdfunding services more often than others, the financial needs and goals of patients, and characteristics that make certain fundraisers more successful.

Methods:
Campaigns posted to GoFundMe, identified by the search term "plastic surgery" were identified. Campaigns from America and clearly identified as raising funds related to plastic and reconstructive surgery, including funds being used directly for a procedure or indirectly for needs postoperatively, were included. Campaigns meeting inclusion were coded with a shared online guide created by the authors. Information gathered included the current monetary contributions, the total goal amount requested, the number of donors, the demographic characteristics of the recipient, the type and of surgery, and various descriptive characteristics about the fundraiser itself. Disagreements and questions surrounding coding were regularly discussed among the authors to ensure uniformity.

Results:
65 campaigns met inclusion criteria. The majority of patients described in fundraisers were white (68.8%), male (56.3%), and adults (75.0%). For all campaigns, the average amount raised in USD was $10,969.66 with an average goal amount of $24,185.89. There were an average of 135 donors per campaign donating an average of $87.27. Six campaigns had successfully met their goal amount. Campaigns had, on average, 323 words in the main body of text. The majority of adult procedures were identified as reconstructive (n=22); the majority of pediatric procedures were craniofacial (n=5). There were 4 gender affirming procedures. The vast majority of fundraisers described how funds would be used to directly relieve financial burden to cover direct expenses related to the recipient's operation.

Conclusions:
Medical crowdfunding in the space of PRS is growing in response the large costs associated with these procedures. These results reaveal clear gaps in healthcare coverage that appear to be critical enough for patients and their supporters to warrant compromising their personal and medical privacy to relieve the tremendous burden of direct costs. Inclusion of more campaigns will continue to delineate discrepancies and provide more detail into this unique research area.

Abstract Title: The Impact of Hospital Volume on Thyroidectomy Outcomes in Pediatric Thyroid Cancer - A 663 Patient Complication Analysis of the Kids' Inpatient Database

Investigator: Victor Yu
Co-Investigator(s): Daniel C Sasson, Division of Plastic and Reconstructive Surgery, Northwestern University Feinberg School of Medicine; Daniel Scholfield, MD, Department of Surgery, Head & Neck Service, Memorial Sloan Kettering Cancer Center; Robbie Woods MD, Department of Surgery, Head & Neck Service, Memorial Sloan Kettering Cancer Center; Richard Wong MD, Department of Surgery, Head & Neck Service, Memorial Sloan Kettering Cancer Center; Jatin Shah, MD, Department of Surgery, Head & Neck Service, Memorial Sloan Kettering Cancer Center; Ian Ganly, MD PhD, Department of Surgery, Head & Neck Service, Memorial Sloan Kettering Cancer Center
Department(s): Department of Surgery, Head & Neck Service, Memorial Sloan Kettering Cancer Center

Abstract

Introduction:
Pediatric thyroidectomy (PT) is an uncommon procedure with complications capable of generating significant morbidity. This study aims to use a national pediatric database to identify factors associated with short-term (30-day) post-thyroidectomy complications in children with thyroid cancer.

Methods:
The 2016 and 2012 Kids' Inpatient Databases (KID) were used in this study. All children with thyroid cancer undergoing thyroidectomy were included. Complications were categorized into endocrine, nervous, pulmonary, and other. Hospital volume was also stratified into high-volume (performing the top 10% of total cases, HVC) or non-high-volume centers (NHVC). HVC and NHVC were compared by univariable tests. Factors associated with complications were determined using univariable and multivariable logistic regression analyses.

Results:
There were 663 patients with an average age of 15.93 years who met inclusion criteria. Most patients were seen in a NHVC (90.0%) and 37.3% of thyroidectomies were performed with a concurrent neck dissection. The overall incidence of any complication was 32.1%. Endocrine complications, including hypocalcemia and hypoparathyroidism, were most frequent (32.7%). Independent predictors of any or only endocrine complications were age (odds ratio [OR] = 0.927, p = 0.002, any); (OR = 0.926, p = 0.003, endocrine). Neck dissection (OR = 1.679, p = 0.004, any); (OR = 1.683, p = 0.005, endocrine). There was no statistically significant change in odds with hospital volume.

Conclusions:
The non-significant effect of hospital volume on surgical outcomes warrants further investigation to determine the difference of single-surgeon volume versus hospital volume in pediatric thyroid cancer surgery.

Abstract Title: Asymptomatic Aggressive Angiomyxoma in a middle-aged healthy male: a case report and brief review of literature

Investigator: Tarek Zagade
Co-Investigator(s): Kurt McCammon, MD, FACS, FPMRS/Department of Urology, Andrew Wang, MD/Department of Urology
Department(s): Department of Urology

Abstract

Introduction:
Aggressive angiomyxomas are benign, slow-growing tumors composed of myxomatous and collagenous stroma. These tumors are known for their high recurrence rates with reports of around 50% and tendency for local invasion. Treatment is surgical excision with adjuvant hormonal therapy as an option. They are rare with reports of under 400 cases in the current literature. They primarily present as a perineal, pelvic, or vulvar mass in reproductive-age women. Clinical course varies from asymptomatic to compression of pelvic structures causing urinary symptoms, pain, pressure, and dyspareunia. Metastasis and death is rare. Only 2 cases are reported in the literature with metastases to the lungs. It is rare for angiomyxomas to present in in males, as few cases have been reported. Here we report a rare case of a perineal aggressive angiomyxoma in a healthy middle-aged male.

Case Information:
A healthy 48-year-old Caucasian male was incidentally found to have a 6.7 x 5.9 x 2.4 cm ovoid lesion in the right perineum abutting the bulbar urethra during work-up for nephrolithiasis. Then, the patient was asymptomatic and recommended to undergo an MRI to characterize the lesion.

He was lost to follow-up for 10 months when he noted perineal discomfort. On perineal examination there was a visible, non-tender without fluctuance, erythema or inguinal lymphadenopathy. The patient had no urinary symptoms. Pelvic MR revealed a circumscribed mass in the right perineum measuring 7.3 x 3 cm axially and 8 cm craniocaudally. There was mass effect on the bulbar urethra but no gross invasion. Vessels were seen within the lesion. No regional lymph node involvement was noted.

Given risk of malignancy and symptoms, patient elected to undergo surgical excision. Intraoperatively, the mass was mobile. Cystoscopy and digital rectal exam were negative for invasion of urethral lumen and rectal wall. The mass was found to abut anteriorly the apex of the right corpus cavernosum, laterally the right ischial pubic ramus, medially the corporal spongiosum, posterior the peri-rectal muscle fibers, and superior the levator muscle. Final pathology revealed an 8 cm hypocellular lesion with myxoid stroma and abundant vasculature with surrounding muscular tissue. By immunohistochemistry, stromal cells were positive for desmin and CD34 and negative for S100 and EMA. Clinical follow up thus far is negative.

Discussion/Clinical Findings:
Angiomyxoma is a rare soft tissue tumor of myofibroblastic origin. In the literature, there are about 350 reported cases, with the vast majority being described in women. Tumor locations are mostly limited to the pelvis, perineum, and scrotum. Extra-pelvic sites have been described, such as the kidney, liver, or orbit. There is a female predominance with a ratio of 4-:1. Angiomyxoma is usually benign, and metastases are rare. These tumors are typically well-defined and displace local structures rather than invade them. Further, they are often misdiagnosed. Differential diagnosis for perineal mass in men includes perineal cyst, lipoma, abscess, urothelial carcinoma, leiomyoma, leiomyosarcoma, and liposarcoma.

Angiomyxoma is a pathologic diagnosis. They are characterized on histopathology as loose stromal connective tissue with spindle cells on a background of collagen and myxoid with vascularization. Immunohistochemical profiles of the tumor is helpful in differentiating angiomyxoma from other differential diagnoses such as myxoliposarcoma and histiocytoma as angiomyxomas characteristically stain positive for CD34, desmin, and vimentin. The tumor in our patient stained positive for CD34 and desmin, and negative for S100. Nevertheless, CT and MR with contrast are important diagnostic tools.

Treatment involves surgical excision with negative margins. Due to its slow-growing nature, angiomyxoma does not respond to chemotherapy. Radiation therapy has been reported in the palliative setting. Adjuvant hormonal therapy is an option when tumors stain positive for ER or PR receptors. Interestingly, negative margin status is not a negative predictive factor in recurrence free survival. Long-term data on follow-up is limited. Thus, surveillance is prudent in these patients.

Conclusion:
This report highlights a rare case of angiomyxoma in a healthy middle-aged male with a two-year asymptomatic period. Its diagnosis requires a high index of suspicion. Complete cure relies on radical excision. Long-term follow-up is warranted

Abstract Title: Reliability, validity, and sensitivity of finger tapping speed, errors, and associated overflow movements in youth clinically recovered from concussion

Investigator: Christopher Zazueta
Co-Investigator(s): Stacy Suskauer, MD, Kennedy Krieger Institute, Johns Hopkins University School of Medicine; Hsuan-Wei Chen, BS, Kennedy Krieger Institute, Johns Hopkins University School of Medicine
Department(s): Physical Medicine and Rehabilitation at Johns Hopkins University School of Medicine

Abstract

Introduction:
Mild traumatic brain injury (mTBI) has been shown to have lasting impacts on subtle motor function among children and adolescents. The objectives of this study were to evaluate inter-rater reliability, validity, and sensitivity of finger tapping metrics between youth medically cleared post-mTBI (MC post-mTBI) and age and sex-matched controls.

Methods:
Video and electrogoniometer data from 20 youth MC post-mTBI and 20 controls between the ages 10-17 were scored. The task consisted of eight blocks of 45 seconds of sequential finger to thumb opposition while resting the non-tapping hand. Tapping speed and mirror overflow were calculated. Tapping errors were scored based on video review with a scoring rubric reached by consensus of two independent scorers. Intra-class correlation (ICC) was used to determine inter-rater reliability for number of tapping errors. Validity was examined using Spearman's correlations between finger tapping variables and Physical and Neurological Examination for Subtle Signs (PANESS) values from the same visit. Sensitivity to mTBI status was examined using Mann-Whitney U tests.

Results:
High inter-rater reliability was achieved (ICC=.922). Tapping speed was weakly correlated with PANESS Total Timed score (r=.343, p=.03). Tapping errors were moderately correlated with PANESS Total Dysrhythmia (r=.406, p=.009). Mirror overflow was weakly correlated with PANESS Total Timed Overflow (r= .345, p=.029). Mirror overflow was higher among controls compared to youth MC post-mTBI (p=.020).

Conclusion:
A reliable process for scoring tapping errors was established. Validity of the finger tapping task was established against the PANESS, with weak correlations likely due to PANESS including a broader range of speeded tasks. Youth MC post-mTBI did not perform worse than controls; higher mirror overflow in controls may be due to their slightly younger average age and small sample sizes. Future studies will elucidate whether brain activation patterns during finger tapping task completion differ between groups in the face of similar task performance.

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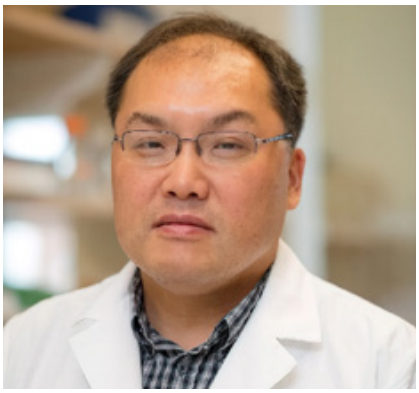

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Thank You!

Dr. William Wasilenko recently retired as EVMS Vice Dean for Research. We would like to express special appreciation and gratitude for his many years of dedication and support of EVMS Research Day.

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