ABSTRACTS

Medical Student
Virtual Research Conference
September 16-17, 2020

University of Iowa
Roy J. & Lucille A. Carver College of Medicine

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Medical Student Research Council

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Diversity in Academic Dermatology: Taking a closer look at the distribution of underrepresented minorities in academic dermatology

Roshan Abid, BA[1], Zakariyah Sharif-Sidi, BS[2], Edgar Martinez BS[3], Rithu Srikantha, MD[4], Amit G. Pandya, MD[5], Amy McMichael, MD[6], Nkanyezi K. Ferguson, MD[1]

[1]University of Iowa Hospitals and Clinics, Iowa City, IA, [2]Medical College of Wisconsin, Milwaukee, WI, [3]University of Texas Southwestern Medical Center, Dallas, TX, [4]Albert Einstein College of Medicine, Bronx, NY, [5]Palo Alto Medical Foundation, Mountain View, CA, [6]Wake Forest University, Winston-Salem, NC

Abstract: The United States population is becoming increasingly diverse, with 39.6% of the population identifying as a race other than non-Hispanic white in 2018. The U.S. Census Bureau estimates that this number will rise to over half the country's population by 2045. However, these rising population trends are not observed in many medical specialties– particularly at academic training centers. Among all U.S medical school full-time faculty in 2019, only 3.8% identified as Black and 5.8% identified as Hispanic. For academic dermatology, the numbers are even more staggering, with 2.7% identifying as Black and 4.9% identifying as Hispanic. Additional demographic data for fellowship-trained dermatologists at academic institutions is virtually nonexistent, making it difficult to identify barriers within the field. We know from previous studies examining patient-physician relations that in race-concordant visits, a more diverse physician workforce results in increasingly satisfied patients– an important link in achieving higher rates of continuity of care. To date, most studies exploring diversity in academic dermatology have focused on sex, race, ethnicity, and academic rank at the national level.

The purpose of this study was to further characterize underrepresented minorities (URMs) in academic dermatology. We designed a cross-sectional study to analyze the representation of URM faculty in academic dermatology during the 2019 – 2020 academic year. Race, ethnicity, gender, and fellowship training of URM dermatology faculty were collected using publicly available information on program websites and professional websites, such as LinkedIn. For the purposes of this study, faculty images, names, and personal biographies were used at the discretion of data collectors to determine faculty race and ethnicity. The list of faculty with URM race or ethnicity designations were then reviewed by a panel of three senior academic dermatologists, who cross-referenced the data with local faculty members in each region. For geographic comparison, United States Census regional population projections for 2019 were also collected by race and ethnicity for comparison

Publicly available data from 112 academic dermatology program websites demonstrated a total of 168 URM academic dermatologists. Geographic breakdown showed that all regions exhibited larger disparities in both Black and Latino representation among academic dermatologists when compared with Black and Latino representation of the respective regional populations. Moreover, roughly one fourth of Black academic dermatologists and Hispanic academic dermatologists achieved relevant fellowship training.

This study has allowed for further characterization of URM dermatologists in academic settings beyond limited self-reported data available through AAMC. Limitations of this study include reliance of program websites to be up-to-date and difficulty in accurately determining faculty race and ethnicity based on name and photograph. Future studies are needed to identify barriers to entry for URM dermatologists into academics and effective strategies to increase representation. The results of this study will hopefully provide a better understanding of the current state of diversity in academic dermatology, as barriers to entry and other factors affecting diversity are further explored.

AUTOMATIC VOLUMETRIC ANALYSYS OF THE DISTAL TIBIOFIBULAR SYNDESMOTIC INCISURA. A CASE-CONTROL STUDY OF SUBTLE CHRONIC SYNDESMOTIC INSTABILITY.

Authors

Samuel Ahrenholz (University of Iowa, Department of Orthopaedics and Rehabilitation)
Cesar de Cesar Netto, MD, PhD (University of Iowa, Department of Orthopaedics and Rehabilitation)

Introduction

Chronic subtle distal tibiofibular syndesmotic instability (DTFSI) is relatively common, and consequences of undiagnosed injuries can be devastating. Diagnosing acute and chronic injuries is challenging, and the most commonly used diagnostic tools are physical exam, weightbearing conventional radiographs, non-weightbearing bilateral CT scans, and MRI. Arthroscopic assessment, an invasive method, is currently considered the gold standard. Weightbearing CT has just emerged as an excellent dynamic non-invasive diagnostic test. Recent literature highlighted the accuracy of syndesmotic incisura area measurements in diagnosing subtle DTFSI.

Purpose of the Study

The aim of our study was to develop and validate the use of a novel automatic 3D volumetric assessment of the tibiofibular incisura, and to compare the measurements between patients with surgically confirmed DTFSI and controls.

Methods

In this IRB-approved case-control study, patients with suspected unilateral chronic subtle DTFSI underwent bilateral standing weightbearing CT (WBCT) examination before surgical treatment. DTFSI was confirmed by arthroscopic assessment. We also included control patients that underwent WBCT tests for forefoot related problems and no history of syndesmotic injuries. The syndesmotic incisura volume (mm^3) was measured starting at the level of the ankle joint to two proximal points, 10 and 15mm proximally to the joint. A 3D automatic measurement algorithm composed of automated segmentation of the distal tibia and fibula and recognition of the incisura volume based on Hounsfield units (HU) assessment was performed. Measurements were compared between DTFSI patients and controls. A partition prediction model, ROC curves and area under the curve (AUC) were performed to assess the diagnostic accuracy of the automatic volumetric analysis to detect DTFSI. P-values of less than 0.05 were considered statistically significant.

Results

In this preliminary report, four patients with DTFSI and seven controls were included. Mean value and 95% CI for 3D Syndesmotic Incisura volumetric measurements at 10 and 15mm points were: 1457 mm^3 (1233 to 1680)/2241 mm^3 (1951 to 2531) for controls, and 1679 mm^3 (910 to 2447)/2425 mm^3 (1408 to 3443) for patients with DTFSI (p-values of respectively 0.35 and 0.55). When comparing injured and uninjured DTFSI ankles, volume measurements at 10 and 15mm points were increased on injured ankles, with a Hodges-Lehmann difference of respectively 287 mm^3 (p=0.19), and 186 mm^3 (p=0.31). The partition model demonstrated that the volume of the first 10mm was the best predictor of DTFSI, with only a 3% chance of DTFSI when the incisura volume was below 1291 mm^3 (AUC=0.71).
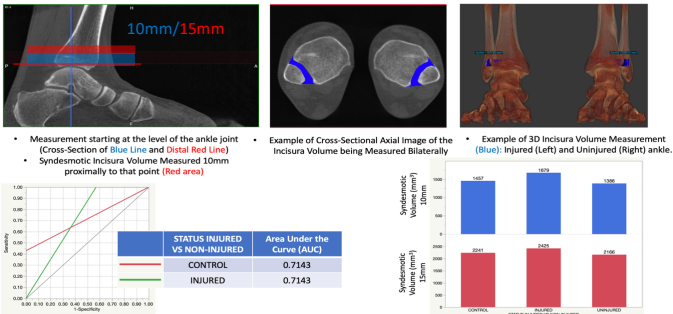

Figure 1. Example of measure methods and graphical plot representation of the results

Conclusion

Our study aimed to describe and validate the use of a novel automatic 3D volumetric measurement of the distal tibiofibular incisura in patients with chronic subtle ankle syndesmotic instability and controls. Our preliminary results demonstrated increased volumes on injured ankles when compared to contralateral uninjured ankles and controls. Measurements performed within the first 10mm length of the syndesmosis were found to better predict the presence of syndesmotic instability, with a volume of 1291 mm3 representing an important diagnostic threshold. Automatic 3D WBCT volumetric measurements may represent a useful non-invasive diagnostic tool for subtle and chronic syndesmotic instability.

Delayed Anterior Segment Complications After Treatment of Retinopathy of Prematurity with Laser Photocoagulation

Aparna S. Ajjarapu, BA; Alina Dumitrescu, MD

Introduction:
Retinopathy of Prematurity (ROP) is a disease that affects the retinal vasculature of premature infants and is a leading cause of childhood blindness worldwide. Laser photocoagulation is recognized as the standard treatment for ROP but it has been reported to be associated with ocular complications such as complications of the anterior segment. The majority of studies have reported on anterior segment complications in the short-term after laser treatment for ROP but few studies have reported on anterior segment complications in the long-term. Furthermore, delayed onset anterior segment pathology, such as band keratopathy, changes of the iris and anterior chamber, and cataract formation in the absence of inflammation or other risk factors, have been observed at the Pediatric Ophthalmology and Adult Strabismus Clinic at the University of Iowa Hospitals and Clinics.

Purpose:
To report on the clinical characteristics and long-term visual outcomes in a cohort of premature infants who had long-term follow up and developed anterior segment complications after laser therapy for threshold ROP.

Method:
A retrospective review of the medical records of premature infants with a diagnosis of ROP undergoing laser therapy from February 23, 1988 to May 7, 2020 was conducted. All patients that developed delayed anterior segment changes in the absence of prior intraocular surgery (other than laser photocoagulation) and intraocular inflammation (documented and with complete workup) were included.

Results:
181 charts of patients with ROP treated with laser over the study period were reviewed. A total of 12 eyes of 7 patients were identified that met the inclusion criteria. This represents 3.3% of our cohort. The mean gestational age of patients who developed anterior segment complications was 24.6 weeks. The mean birthweight was 687.6 g. All eyes of patients that had ROP underwent laser photocoagulation for threshold disease. Clinical symptoms of anterior segment complications included band keratopathy, iris and anterior chamber changes, cataract formation, and glaucoma. The average age when anterior segment complications were first noted was 8.6 years with patients being as young as 1 year and as old as 25 years. The average follow-up period of patients was 18.9 years. It was observed that vision was affected in all patients. 71% of eyes underwent additional procedures because of anterior segment complications (i.e. EDTA chelation, cataract surgery, glaucoma procedures) and out of these patients, 25% did not improve their visual acuity after the procedure. 57% of patients underwent strabismus surgery an average of 3.2 years after laser surgery with 2 patients having strabismus surgery before the first signs of anterior segment complications were noted and 2 patients having it afterwards. All patients developed progressive myopia that was treated with glasses or contact lenses. It has been postulated that laser treatment may lead to anterior segment ischemia due to thermal injury of the long posterior ciliary arteries leading to impairment of blood flow to the anterior segment. In addition, prolonged scleral depression along the horizontal meridians during treatment of ROP may also impair blood flow to the anterior segment.

Conclusion:
In this retrospective study, we describe for the first-time late onset anterior segment complications after treatment of ROP with laser photocoagulation. This is a serious but rare, delayed post-operative complication of laser treatment of ROP that results in significant and sometimes permanent vision loss. Furthermore, delayed anterior segment complications may require additional procedures for treatment. As such, long-term follow-up for these complications may be needed and patients, parents, and treating physicians should be aware and discuss them in the informed consent for laser treatment for ROP.

Using Thermal Imaging to Track Cellulitis

Amendola J, Segre AM, Miller AC, Polgreen LA, Comellas A, Polgreen PM

Background

Cellulitis is a common soft tissue infection, a major cause of morbidity and mortality, and a common reason for hospitalization. There is no definitive point-of-care test to confirm the diagnosis of cellulitis, thus the diagnosis is based almost exclusively on clinical history and physical exam.

Purpose

To improve the diagnosis of cellulitis, we used a thermal camera to determine how skin temperature of the affected area changes during a hospital stay in patients admitted to the hospital with cellulitis. Specifically, the purpose of this study was to show that (1) the use of an inexpensive thermal imaging camera, FLIR (Forward Looking Infrared), can be used as an objective measure of skin temperature in patients with soft tissue infections and that (2) the temperature and area of skin captured by the FLIR camera correlates with the clinical course of soft tissue infections in hospitalized patients.

Methods

We recruited patients admitted with a diagnosis of cellulitis. Daily thermal images of the affected limb were taken using FLIR over the course of the hospitalization. Clinical data including highest daily body temperature, ESR, CRP, WBC count on admission, and antibiotics administered were collected. Thermal images were processed to extract estimates of *scale* (extent of area with elevated temperature) and *severity* (temperature intensity of the infected region) which were then correlated with the patient's daily body temperature.

We estimated a longitudinal linear mixed effects model with a random intercept for each patient's affected body area. All observations on a given day were included, and we used an integer time indicator indexed to the initial day (i.e., t=1 for the first day the patient was observed, t=2 the second, etc.). We then analyzed the effect of this time trend on both scale and severity.

Results

We collected 2,295 thermal images from 43 patients, and each patient had between 2 and 8 days of photos included. For each day that the patient was observed, the scale decreased by -0.6023 (95% CI [-0.7072, -0.4970]) points on average, and the severity decreased by -9.49 (95% CI [-16.95, -1.95]) points on average.

Discussion

We found that both scale and severity obtained from the thermal images of body areas affected by cellulitis decreased during the hospital stay. Thus, using thermal imaging could be used to potentially help with the diagnosis of cellulitis and also track the clinical progress of patients diagnosed with cellulitis.

The Effect of Intrapartum Complications on Breastfeeding Success

Emily Anderson, M2
Stephanie Radke, MD – Clinical Assistant Professor, Department of Obstetrics & Gynecology
Shelby Green, MD – Resident Physician, Department of Obstetrics & Gynecology
Donna Santillian, PhD – Associate Professor, Department of Obstetrics & Gynecology
Kelli Ryckman, PhD – Associate Professor, Department of Epidemiology, College of Public Health

Background: Breastfeeding is the normative feeding modality for human infants and confers numerous health benefits for both mother and baby, as well as societal and ecological benefits. Women who achieve optimal breastfeeding duration are shown to have lower rates of cardiovascular disease and certain cancers. Infants too are seen to have a decreased risk in childhood illnesses that follows throughout their adult life. However protective breastfeeding may be to mothers and infants, many women face physiological challenges during their breastfeeding journey. It is known that women with postpartum anemia and women who were preeclamptic had lower rates of achieving their breastfeeding goals. Recognizing these challenges and addressing them early on can help more women achieve their breastfeeding goals. Unfortunately, there is very little literature that looks at intrapartum complications and their effects of successful breastfeeding.

Purpose of Study: We sought to quantify the impact of experience of severe maternal morbidity (SMM) on breastfeeding outcomes. Secondarily, we aimed to examine the effect each of these conditions individually, interactions, and any protective factors on breastfeeding outcomes. It was hypothesized that women who experience intrapartum complications will be less successful at exclusively breastfeeding than women without such complications.

Methods: A retrospective cohort analysis was performed on mother-baby couplets who delivered at the University of Iowa Hospitals and Clinics (UIHC) and also received well-child care through the UIHC outpatient clinics. Inclusion criteria were couplets consisting of full-term, singleton deliveries to first-time mothers where the baby was admitted to the Normal Newborn Nursery. Infant feeding methods were assessed at multiple time points: hospital discharge and at the 2-week and 2-month well-child visits. Data was abstracted from the medical record and certain variables were validated by direct chart review into a REDCaps database. Statistical analyses with multinomial regression was performed to examine for associations.

Results: A total of 1,861 mothers were examined. At time of discharge, women with an intrapartum complication who were supplementing and exclusively formula feeding had an RR of 2.4 (95% CI 0.95-6.19) and 3.2 (95% CI 1.03-10.16), respectively. However, at the time of 2-3-week visit, intrapartum complications are no longer statistically significant in association with solely formula feeding (RR: 1.9; 95% CI 0.56-6.26). At the 2-3-month visit, intrapartum complications are not associated with supplementing (RR: 2.0; 95% CI 0.56-7.10) but are with formula feeding (RR: 3.0; 95% CI 1.10-8.45), a trend similar to that at discharge.

Conclusion: Although more data needs to be collected and confounding modeling needs to be completed, we can start to see the impact intrapartum complications can have on breastfeeding success. However anecdotal, there is little literature to suggest this trend. This study is the first to start to examine the effect these intrapartum complications have on breastfeeding outcomes. Findings such as these will allow clinicians to better identify women at risk for failing to achieve their goals of breastfeeding and assist for better outcomes.

Ketamine Metabolomics in a Human Neuronal Cell Line

Brandon Bacalzo, B.S., Amanda C. Decker, Ph.D., Zoe M. Randall, B.S., Mark J. Niciu, M.D. Ph.D.

Background

Major depressive disorder (MDD) is a common mental health disorder defined by symptoms of depressed mood and loss of interest in normal activities of living. Treatment-resistant depression (TRD) is a subset of MDD, defined as two or more unsuccessful treatment attempts. This condition is personally debilitating and incurs a high healthcare cost due to frequent placement of TRD patients in high acuity facilities, such as inpatient units. In recent years, it has been found that intravenous administration of a subanesthetic dose of the N-methyl-D-aspartate receptor antagonist and glutamate modulator ketamine is effective in treating TRD, usually within hours-to-days in responders. However, the mechanisms by which ketamine achieves its antidepressant effects are not well known, especially in patients and human model systems. We propose that increased energy demands and expenditure are critical for the rapid synaptic plasticity underlying the antidepressant efficacy of racemic ketamine and its bioactive metabolites. In this study, we utilize differentiated human neurons with functional NMDARs to probe neuronal bioenergetics in response to racemic ketamine and its bioactive metabolites.

Methods

A human neuroblastoma cell line (SK-N-SH) (ATCC®, HTB-11™) and maintained until use in the experimental paradigm. After differentiation, these cells were treated with racemic ketamine and several bioactive metabolites, i.e., (S)-norketamine, (R)-norketamine, and (2R,6R)-hydroxynorketamine, at varying doses and durations of exposure. Mitochondrial stress tests were performed in live cells using a SeahorseXFe24 analyzer (Agilent Technologies, Santa Clara, CA,, U.S.A., which, through the addition of various mitochondrial inhibitors and uncouplers measures mitochondrial and non-mitochondrial respiratory dynamics across eight parameters,i.e. non-mitochondrial oxygen consumption, basal respiration, maximal respiration, proton leak, ATP production, spare respiratory capacity, and coupling efficiency. Single factor ANOVA and Tukey HSD analysis were used to compare group means with statistical significance set at $p < 0.05$.

Results

The administration of racemic ketamine (dose range: 2.5-50 µM , duration: 1-17 hours) did not appear to influence oxygen consumption relative to a vehicle control. Similarly, 10 µM (2R,6R)-HNK did not influence oxygen consumption with overnight exposure. Overnight low dose incubation of (R)-norketamine similarly did not influence oxygen consumption relative to control. However, in a single assay, an overnight incubation of 5 µM (S)-norketamine decreased ATP production, proton leak, spare respiratory capacity, basal respiration, and maximal respiration relative to control and (R)-norketamine. Interestingly, the difference in means across control groups for these experiments (across seven of eight parameters measured) is statistically significant (p-values < 0.01)

Discussion

The lack of apparent change in neuronal oxygen consumption in differentiated SK-N-SH cells exposed to racemic ketamine and (2R,6R)-HNK was unexpected. Yet, experiment controls show the same or greater variance than experimental conditions, calling into question the validity of the assay. Additionally, we look forward to utilizing a potentially more robust preclinical model in the future, human cortical spheroids (hCS). hCSs are stem cell-derived three-dimensional cultures that contain differentiated, functional GABAergic and glutamatergic neurons as well as astrocytes with tripartite synaptic architecture, thereby more closely modeling the complex synaptic architecture and plasticity of the human brain than SK-N-SH cells.

Patent Ductus Arteriosus Predicts Response to Late Surfactant Administration in Premature Infants

Student: Madeline Beauchene. Mentor: Patrick J McNamara
Other Collaborators: Adrianne Bischoff, Alison Cunningham, John Dagle, Megan Fellows, Regan Giesinger, Jonathan Klein, Danielle Rios

Background: Although beneficial in the acute treatment of Neonatal Respiratory Distress Syndrome (RDS), surfactant use beyond 48 hours of life remains controversial. Administration of surfactant beyond day 6 of life leads to a significant improvement in respiratory severity score in 70% of babies with post surfactant slump which occurs in 20% of premature infants with RDS (Katz et al), however this effect was not found in the TOLOSURF trial (Ballard et al) due to the treatment of all intubated infants regardless of the severity of their respiratory failure. Surfactant administration immediately after birth has been shown to reduce pulmonary vascular resistance due to improved lung compliance and subsequent increased pulmonary blood flow and ductus arteriosus (DA) size. It is biologically plausible that, by a similar mechanism, late surfactant may augment shunt volume in patients with an open DA. Clinically this may negate improvement in respiratory status from surfactant therapy or may precipitate decompensation or the presence of pulmonary edema may be one of the causes of the slump.

Aim: The primary aim of our study was to determine the clinical and echocardiography phenotype of those patients who positively respond to late surfactant compared to those who either have "no" or "negative" response. We hypothesized that the presence of a PDA is associated with lower likelihood of positive response to late surfactant.

Methods: A retrospective cohort study of infants $\leq 26^{+6}$ weeks gestation, admitted to UIHC NICU between September 2018 and July 2020, was performed. Patients were included if ≥ 1 dose of surfactant was administered at ≥ 7 postnatal days and echocardiography evidence of PDA status was available. Neonates with structural heart disease and those who died within 48h of receiving the qualifying dose of surfactant were excluded. The response to each dose of surfactant was categorized based on change in respiratory severity score (RSS) over 48h as positive [$\geq 15\%$ improvement], negative [$\geq 15\%$ deterioration] or non-response. Patients were classified as either PDA [≥ 1mm] or no PDA [<1mm] at the time of surfactant administration and intergroup comparison in demographic and outcome characteristics was performed using univariate analysis. Logistic regression was performed to evaluate the role of PDA in predicting positive and negative response after adjusting for covariates found to be significant on univariate analysis. A ROC curve for PDA score to predict negative response was generated.

Results: Ninety-one patients screened, thirty-five patients received 71 doses of surfactant on or after postnatal day 7. The median gestational age and birthweight were 23.3 [22.7, 25] and 595g [508, 696] respectively and 20 (57%) were male. The majority were both inborn (n=33, 94%) and received postnatal hydrocortisone (n=34, 97%). The surfactant administered was either Infrasurf (n=40, 56%) or Curosurf (n=31, 44%). Of the 71 doses, 27 (38%), 16 (23%) and 28 (39%) resulted in a positive, negative response and no response respectively (**Fig 1**). Among the doses resulting in positive responses most (n=25, 92%) were classified as no PDA (p=<0.001) whereas among the negative responses, the echocardiography phenotype was consistent with PDA physiology in a majority (n=11, 69%) of cases (p=<0.001). Among the babies who had a PDA 8% (n=1) were positive responders and 44% (n=7) were negative responders. Conversely, among those with no PDA status, 63% (n=12) were positive responders and 13% (n=1) were negative responders. Response was independent of surfactant type. On logistic regression, no PDA status was independently associated with positive response [OR 26 (2, 334), p=0.012] and PDA >1 mm was independently associated with a negative surfactant response [OR 12 (1.1, 126), p=0.042]. Higher PDA score was associated with a negative response to surfactant with an AUC of 0.78 [0.65, 0.91], p=0.001 and a PDA score of >5 has both a sensitivity and specificity of 0.75 to predict respiratory deterioration.

Conclusions: In neonates less than 27 week's gestation, the absence of a PDA is associated with a positive response to surfactant after postnatal day 7. Targeted Neonatal Echocardiography evaluation of PDA status may enhance diagnostic precision and refine patient selection for late surfactant treatment.
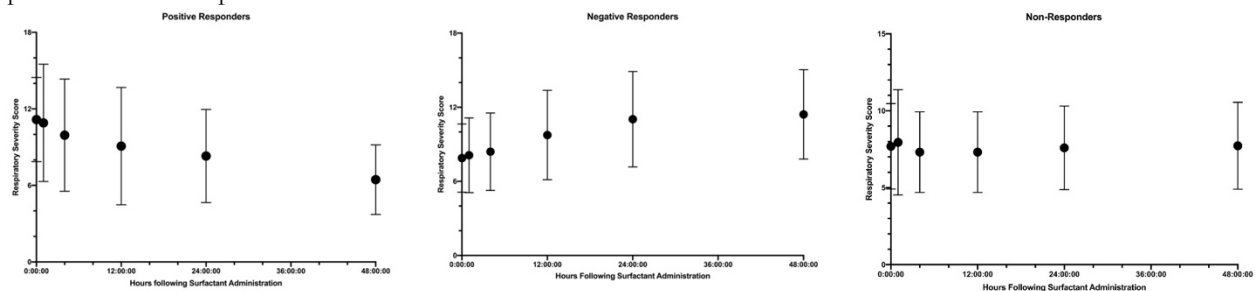

Fig 1. Change in Respiratory Severity Score after late (> day 7) administration of surfactant in positive, negative and non-responders

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Optimization of an ELISA to detect *Anaplasma* exposure in visceral leishmaniasis patients in Brazil

Greta Becker[1], Danielle Pessoa-Pereira[2], Breanna Scorza[2], Christine Petersen[2]

[1] University of Iowa Carver College of Medicine
[2] Department of Epidemiology, University of Iowa

Background

Visceral leishmaniasis (VL) is a vector borne, zoonotic, disease caused by the protozoan parasite, *Leishmania infantum*. The disease is transmitted via the bite of phlebotomine sandflies. In North and South America, VL is present in 12 countries, with over 3,000 cases reported each year in Brazil alone. The disease prevalence in humans in Brazil mirrors the seropositivity of dogs, as dog ownership predisposes humans to VL infection. In addition to *L. infantum* exposure, recent epidemiological studies in the endemic area of Natal, Brazil demonstrated abundant canine exposure to the tick-borne pathogen, *Anaplasma phagocytophilum*. Dogs exposed to *A. phagocytophilum* were significantly more likely to be seropositive for *L. infantum,* and exposure to tick-borne diseases increased the risk of progression to clinical canine leishmaniasis. Tick-borne illnesses are severely underreported in Brazil. However, trends in North America showcase an increasing number of yearly cases of human tick-borne illnesses over time. In 2019, Olivia Chase, now M3, traveled to Natal, Brazil and identified a 15% human *Anaplasma* exposure in VL negative endemic controls, but the interaction between *A. phagocytophilum* and *L. infantum* seropositivity was not clear due to high seroreactivity in *L. infantum* patient serum.

Purpose

The purpose of this study is to identify if there is a correlation between human exposure to *A. phagocytophilum* and *L. infantum* seropositivity. We hypothesize that once controlled for globulin levels, patients with visceral leishmaniasis will have higher seropositivity to *A. phagocytophilum* than endemic control individuals.

Methods

As an obligate intracellular bacterium, *A. phagocytophilum* must be grown in a human leukocyte cell line, HL-60. Exposure to *A. phagocytophilum* can be determined via an indirect enzyme-linked immunosorbent assay (ELISA) using soluble *A. phagocytophilum* total protein extracted from cell culture. Last summer, exposure in the VL cohort could not accurately be determined due to nonspecific binding likely caused by hypergammaglobulinemia, a known clinical manifestation of VL and the potential of non-specific binding to HL-60 cells. The ELISA will be repeated using uninfected HL-60 cells, as testing with uninfected cell antigen will help differentiate between background cross reactivity vs. true co-exposure with *A. phagocytophilum* in the VL positive cohort. Since travel to Brazil was not possible this summer, negative human serum and *A. phagocytophilum* positive canine serum were used to evaluate the background from the cell line vs. positive (canine) samples.

Results

Non-specific binding from uninfected HL-60 cell antigen was observed in both negative human and positive canine serum.

Conclusions

This project highlights some of the difficulties associated with diagnostic serological testing. Given that non-specific binding from host cell lysate is present in the *Anaplasma* ELISA, eventually we will return to Brazil to repeat the ELISA on VL positive human serum samples using uninfected HL-60 cells to help differentiate cell lysate causing cross reactivity from true co-exposure with *A. phagocytophilum*. Completing this project will better elucidate the role tick-borne coinfections play in the progression of VL and the role dogs play in vector transmission to ultimately improve VL intervention efforts in Brazil.

Title: Optimization of Adipocyte Spheroid Model for Testing of Polychlorinated Biphenyl Toxins
Authors: Riley Behan, Jesse Liszewski, Aloysius Klingelhutz, James Ankrum
Date: August 28, 2020

Despite being banned in the 1970's, Polychlorinated biphenyls (PCBs) persist in the built and natural environment and pose a significant health risk to the public. Human exposure to PCBs have been linked to cancer, obesity, and metabolic disease. However, with over 200 chemically distinct PCBs in the environment, research is needed to determine which are the most harmful to human health. Since PCBs are associated with obesity and known to accumulate in adipose tissue, we sought to develop a screening platform to determine which PCBs directly impact adipose function. In order to properly screen these toxins, a robust adipose model system is needed. Previous adipose models have been incredibly limited due to the lack of available cell lines, difficulty culturing, and inability to correlate 2-dimensional models to 3-dimensional human adipose tissue. However, novel techniques have been developed to create 3-dimensional adipose organoids without the need for an exogenous scaffold. Here we show how this technique can be applied to the creation of an adipose model system that can be used to determine the effects of PCBs on adipocytes. To achieve the highest level of test sensitivity, an optimal adipose model should have high levels of adiponectin secretion, a marker of differentiation, and low levels of IL-8 secretion, a marker of inflammation. By examining the effects of different seeding cell densities, differentiation medias, and PCB 126 exposure on the secretions of adipocyte spheroids, we determined an intermediate size of 5,000 cells per spheroid would provide a robust model system for toxin screening. Future work with the developed adipose model will include screening for the effects of different PCB congeners and metabolites on adipocyte function as well as integration of the model into a biomimetic chip to better understand the systemic effects of the toxin.

The Effect of a Triage Physician in the Emergency Department on Press Ganey Scores and Other Metrics Associated with Patient Satisfaction

Nathan Behrens, Uche E. Okoro, MBBS MPH DrPH, Michael Takacs, MD MS FAAEM

Background

Many Emergency Departments use a physician or midlevel provider in triage, but the effect on Press Ganey patient satisfaction scores is not well understood. The two prior studies that evaluated the effect of a triage physician on Press Ganey scores found different results, and no prior studies have included a triage system like the one used at the University of Iowa Emergency Department. We hypothesize the presence of a physician in triage will improve Press Ganey patient satisfaction scores compared to when there is no physician in triage, and length of stay will also be shortened.

Methods

This is a retrospective cohort study comparing composite Press Ganey satisfaction scores, scores on 11 individual Press Ganey questions, and patient's length of stay between days when a physician was present in triage alongside a midlevel provider and days there were two midlevel providers and no physician. Data was obtained from October 1, 2019 to February 2, 2020 for all patients who arrived at the Emergency Department between 3-11 pm and completed a Press Ganey survey. There were 123 patients that met inclusion criteria, 42 were seen when there was a physician and midlevel provider in triage and 81 were seen when there were two midlevel providers and no physician in triage.

Normally distributed continuous data was analyzed with a TTEST, non-parametric continuous data was analyzed with a Mann Whitney U Test and the Hodges-Lehmann approach, and categorical data was analyzed with a Fisher's Exact Test.

Results

There was no statistically significant change in composite Press Ganey scores (p=0.5992). An estimate of median difference between the presence and absence of a physician in triage together with the 95% CI for the composite Press Ganey Score was 0.6(-2.5 -4.9). Length of stay was not significantly affected by the presence of a triage physician (p=0.5664) with an estimated median difference between groups and 95%CI of -1.0(-68 – 36). Only one of the 11 individual questions analyzed had statistically significant improvement (p=0.04).

Conclusion

The presence of a triage physician had no effect on either composite Press Ganey score or patient's length of stay. Further work is needed to validate these results across multiple centers with similar triage models.

Title: Bringing Remote Healthcare to New Heights: Characterizing the Patient Population in the Pangi Valley of India to Guide Patient Care Strategies
Student Author: Lisa Bell, BS; Faculty Mentor: Hans House, MD

Background: The Himalayan Health Exchange (HHE) is a global health service organization with a mission to provide healthcare to patients in the underserved, mountainous regions of Himachal Pradesh, India by assembling mobile clinic sites in villages throughout the region. These clinic sites, staffed by medical students from around the world and U.S. board-certified attending physicians, are designed to respond to the primary care needs of this population. Minimal concrete information regarding common chief complaints or medication needs of the patient population served on HHE Pangi Valley medical expedition is available, which created the basis for this project.

Purpose: This is a data-driven quality improvement project aimed to better understand the Pangi Valley patient population and to assess how well HHE is responding to its patient-community's medical needs. Results of this project will be used to identify potential areas of growth with HHE and will serve as the basis for an open dialogue with HHE leadership about potential modifications to its care structure in future medical expeditions.

Methods: This project was deemed to not be Human Subjects Research by the IRB. During the June 2019 HHE Pangi Valley medical expedition, data from consecutive patients was collected. Information was categorized by age, gender, chief complaint, diagnosis, and management. To ensure de-identification, patient age was only recorded according to the WHO age categorizations: Infants (<1 year old), Child (1-10 years old), Adolescent (10-19 years old), and Adult (>19 years old). Data was then aggregated and analyzed to determine the most common chief complaints, diagnoses, and disease management strategies overall and in each individual age group.

Results: Of the 900 patients seen, data was available for 735. Patient demographics were as follows: 4 infants, 64 children, 164 adolescents, and 503 adults. 53% of patients were female and 47% of patients were male. Overall, there were 51 unique chief complaints - and the top 10 chief complaints were: 1. Musculoskeletal pain, 2. Eye pain, 3. Stomach pain, 4. Well check, 5. Headache, 6. Blurry vision, 7. Cough, 8. Skin rash, 9. Tooth pain, and 10. Ear discomfort. Of these top 10 chief complaints, the top 10 diagnoses were: 1. Dry Eye ($n = 126$), 2. GERD/Suspected PUD/suspected *H. Pylori* infection ($n = 87$), 3. Muscle strain ($n = 54$), 4. Osteoarthritis ($n = 54$), 5. Viral URTI ($n = 38$), 6. Constipation ($n = 31$), 7. Dental caries ($n = 29$), 8. Ceruminosis ($n = 18$), 9. Dehydration ($n = 12$), and 10. Helminthic infection ($n = 11$). The top 10 chief common chief complaints in children and adolescents differed from the top 10 overall, when analyzed by age group. In both children and adolescents "Well check" was the most common chief complaint. In addition, 80% of both children and adolescents presented with only 1 chief complaint, while only 59% of adults had 1 chief complaint and 29% of adults had 2 chief complaints. There were not enough infants in the patient population to evaluate trends in this age group.

Discussion/Conclusion: The results of this patient-population-analysis will be shared with HHE organizational leadership to help guide medication selection when developing the pharmaceutical inventory for upcoming trips. It will also be shared to assist learners who are planning on participating on future HHE Pangi expeditions to prepare, in advance, to provide care for these most common complaints and diagnoses. One challenge with this project was the lack of consistency with recording of patient information; this limited the available data for this project to include only 735 of the 900 patients examined. To further characterize the patient population(s) served by HHE, a more robust and uniform record-keeping system would likely be necessary. A future potential project could involve developing a user-friendly EMR that does not require internet access for these mobile HHE clinics.

In looking at the management strategies for the most common diagnoses, the most remarkable finding was that only 2 of the 87 GERD/Suspected PUD cases received triple therapy for suspected *H. Pylori* infection. There are many potential detrimental health implications of chronic *H. Pylori* infection. Thus,a follow-up project to prospectively determine acute *H. pylori* infection prevalence by stool antigen testing was planned but had to be put on hold due travel restrictions from the COVID-19 pandemic.

Initial Characterization of Porcine Pancreatic Ductal Organoids

Alaina Berg, BS; Yunxia O'Malley Ph.D.; Aliye Uc, M.D.

University of Iowa Carver College of Medicine, Stead Family Department of Pediatrics

Background

Cystic Fibrosis (CF) is an autosomal recessive disorder caused by mutations in the gene that encodes the cystic fibrosis transmembrane conductance regulator (CFTR). CFTR is expressed on the apical surfaces of epithelial cells and it is primarily involved in anion secretion. Defects in CFTR function lead to viscous and acidic secretions that can cause inflammation and end-organ damage. Pancreas is universally involved in CF. There are over 2,000 mutations described in the *CFTR* gene, causing anywhere from recurrent acute pancreatitis to exocrine pancreatic insufficiency in early life. The contribution of CFTR defects to exocrine pancreatic disease are poorly understood due to lack of animal models, unavailability of human tissues and challenges to grow pancreatic duct epithelial cells *in vitro*. Pancreas duct organoids have shown promise, but they have never been isolated from an animal model that develops CF pancreatic disease.

Purpose

Our goal is to identify the characteristics of newly isolated non-CF porcine pancreas duct epithelial organoids.

Methods

Pancreata were obtained from newborn pigs following euthanasia to isolate RNA and ductal epithelial cell organoids. Organoids were grown based on previously published methods.[1] RNA was extracted from whole pancreas tissues of non-CF pig ductal organoids at passages 0, 1 and 2 (P0, P1, P2). The following primer pairs were utilized: CFTR, E-Cadherin, Sox9 as ductal epithelial cell markers; amylase as acinar cell marker; glucagon, insulin, somatostatin as islet cell markers; and ATP12A (H+/K+ ATPase), NKCC1 (Na+/K+/2Cl- cotransporter), SLC26A3 (chloride anion exchanger) as markers for anion transporters. The primers were tested firs on the whole pancreas cDNA, and only the pairs that produced a strong, single band at the expected product size were utilized. Polymerase chain reaction and gel electrophoresis were completed for each product to compare the expression in whole tissue to organoid cultures.

Results

Epithelial duct cell markers (CFTR, E-Cadherin, and Sox9), amylase and NKCC1 were expressed in organoid cultures at all passages. Glucagon and ATP12A were not expressed in P0 and P2, but detected in P1 organoids. Insulin and somatostatin were both expressed in P0 and P1, but not in P2 organoids. SLC26A3 expression was not detected in any of the organoid cultures assayed.

Conclusion

Ductal epithelial organoids can successfully be isolated from newborn pig pancreas. Although impure at early passages, organoids demonstrate the typical characteristics of their ductal origin and express CFTR. Future work will involve characterization of further passages and isolation of CF ductal organoids.

Reference:

1. Broutier L, Andersson-Rolf A, Hindley CJ, et al. Culture and establishment of self-renewing human and mouse adult liver and pancreas 3D organoids and their genetic manipulation. *Nat Protoc*. 2016;11(9):1724-1743. doi:10.1038/nprot.2016.097

The anatomic basis of visuospatial cognition

Claire Berns-Leone, M2
Aaron Boes, MD, PhD

INTRO: Stroke is a leading cause of disability worldwide, and cognitive dysfunction is a common sequela among stroke patients that negatively impacts quality of life. The visuospatial domain of cognition is of particular interest due to its importance in functional outcomes after stroke. Developing a better understanding the anatomical correlates of visuospatial cognition is important as it could be used in developing a clinical tool to aid in post-stroke prognosis. Here, we leverage data from a large cohort of individuals with focal brain lesions to better understand the neuroanatomical basis of visuospatial cognition. The aims of the present study were 1) to explore the relationships between different neuropsychological tests of visuospatial cognition and 2) to understand which lesion sites are closely associated with visuospatial impairment after focal brain damage.

METHODS: Subjects for this study were obtained from the Iowa Lesion Registry, a database of 977 UIHC patients with focal brain lesions. Scores from seven neuropsychological tests of visuospatial cognition were included and the latent factor structure of the tests was investigated using exploratory factor analysis. Factor scores, representing performance in each latent visuospatial variable, were derived for each patient. We analyzed the relationship between visuospatial ability and lesion location using sparse canonical correlation analysis, a multivariate lesion-symptom mapping technique.

RESULTS: Two solutions of the exploratory factor analysis were evaluated: a one-factor solution with all tests loading onto a general visuospatial ability factor, and a two-factor solution corresponding to 1) visuo-constructional ability and 2) visuospatial perception and reasoning. Lesion-symptom mapping revealed an association between right posterior putamen lesions and impaired performance on all factors. Poor factor scores in general visuospatial ability and visuospatial perception and reasoning were also associated with right hemisphere white matter lesions. Impairment in visuo-constructional ability was also associated with lesions in left hemisphere frontal white matter.

DISCUSSION: Our results align with a large body of evidence demonstrating a right hemisphere lateralization of visuospatial ability, and our results extend these findings in highlighting the right putamen and white matter as sites most critical for visuospatial ability. This is crucial in aiding clinicians in providing accurate prognostic evaluation of stroke patients early in their clinical course. Early prediction of domain-specific cognitive deficits will allow for tailored cognitive rehabilitation and appropriate allocation of resources.

Cortical thickness and surface area in individuals with adult-onset myotonic dystrophy type 1
Presenter: Gabby Bierlein-De La Rosa
Primary Investigators: Peg Nopoulos, Ellen van der Plas
Other collaborators: Kathleen Langbehn

Myotonic Dystrophy Type 1 (DM1) is the form of muscular dystrophy that is the most likely to have an adult onset. DM1 is caused by an expanded CTG trinucleotide length in the 3′ untranslated region of the dystrophia myotonica protein kinase (DMPK) region and has many deleterious symptoms including cataracts, heart problems, respiratory failure, cognitive deficits, impaired social functioning, muscle weakness, and muscle atrophy. This disorder occurs once in about 8000 people worldwide (Langbehn et al., 2020) and has no cure and no specific treatment. There is much research to be done in the area of muscular dystrophy and therefore, foundational work is vital to understanding the role the central nervous system plays in DM1, and by extension, is vital to helping identify neuroimaging biomarkers and targets for therapy.

Based on previous studies that found differences in cortical features between DM1 participants and controls (Serra et al., 2020), the current study examines cortical thickness and surface area in individuals with adult-onset DM1 as compared to healthy controls. This was done with specific focus on three main questions: Are there differences in cortical thickness and cortical surface area in individuals with DM1 as compared to healthy adults? Within DM1, is there a relationship between CTG repeat length, cortical thickness, and surface area? And; Are there differences in age-related change in cortical thickness or surface area between DM1 and controls?

A prospective, longitudinal study design was used, where participants were examined on a maximum of three occasions that were 1 year apart. Both adults with DM1 and controls came into the UIowa hospital and received an MRI as well as several behavioral tests at every visit. After the MRI data was recorded, FreeSurfer was used to extract cortical indices. Cortical thickness and surface area were then evaluated using a region-of-interest approach.

To analyze the data, mixed linear models adjusting for random effects of family and participants were run. The dependent variables that were analyzed were cortical thickness and cortical surface area and the independent variables were group, age, and sex. A group*age interaction was also explored.

In the context of the above research questions, analysis uncovered several notable results. DM1 and control participants differed in cortical thickness in the parietal and occipital lobe, with DM1 participants having thinner cortices in these lobes than controls on average. No significant differences were found in the cortical surface areas of DM1 participants as compared to controls. There was also no significant effect of CTG repeat length on cortical features and, in general, age-related change was similar across groups (i.e., no significant age*group interaction).

The current study replicated findings of previous studies in DM1 on a larger scale. These differences found in cortical thickness may explain some of the cognitive deficits observed in DM1 individuals, particularly visual-spatial deficits, as indicated by significant differences found in the occipital and parietal lobes. Overall this study found that differences exist between cortical thickness and cortical surface area between adult individuals with DM1 and adult controls.

Sources:
Langbehn KE, van der Plas E, Moser DJ, Long JD, Gutmann L, Nopoulos PC. Cognitive function and its relationship with brainstructure in myotonic dystrophy type 1. *J Neuro Res*. 2020;00:1–10. https://doi. org/10.1002/jnr.24595

Serra L, Bianchi G, Bruschini M, Giulietti G, Domenico CD, Bonarota S, Petrucci A, Silvestri G, Perna A, Meola G, Caltagirone C and Bozzali M (2020) Abnormal Cortical Thickness Is Associated With Deficits in Social Cognition in Patients With Myotonic Dystrophy Type 1. *Front. Neurol.* 11:113. doi: 10.3389/fneur.2020.00113

Clinical Application of Coronary Computed Tomography Angiography in Patients with Suspected Coronary Artery Disease

Jared N. Blad, BS, Hayden L. Smith, PhD, Jonathan R. Hurdelbrink, PhD, Steven R. Craig, MD, Brent Wolford, MD, Elizabeth Wendl, MD, Saurabh Aggarwal, MD, Nelson Garcia-Telles, MD

Abstract:

Background: Stress testing is a common initial diagnostic approach for evaluating patients with suspected coronary artery disease (CAD). The PROMISE, SCOT-HEART, and EVINCI studies provided evidence supporting the use of coronary computed tomography angiography (CCTA) for the evaluation of patients with stable angina. In 2016, the National Institute for Health and Care Excellence began recommending CCTA as a first-line approach for patients presenting with stable angina in the United Kingdom. Currently, CCTA is not recommended as a first-line test by the American College of Cardiology/American Heart Association guidelines for the diagnosis and management of patients with stable angina.

Objective: To assess the clinical application of CCTA utilization in outpatients seen at a single tertiary care center located in the United States.

Design: Retrospective review of observational data.

Participants: Patients 18 years or older who underwent CCTA ordered by a physician or provider at the study institution during the period of January 2018 to February 2020.

Key Results: A medical record review revealed 170 patients that met the study inclusion criteria. It was found that 58.9% of patients underwent stress testing within 6-months prior to CCTA. Fifty-five percent of patients who had abnormal stress tests findings, demonstrated no CAD on CCTA. Of patients with normal stress tests, 24.4% demonstrated CAD on CCTA. Twenty-five patients underwent invasive coronary angiography (ICA) within 6-months following CCTA. The positive predictive value of CCTA was 91.3% (95% CI: 72.0%, 99.0%) and the negative predictive value was 100.0% (95% CI: 15.8%, 100.0%) when compared to ICA. In addition, CCTA demonstrated myocardial bridging in 10% of patients and revealed an anomalous coronary vessel in 8.8% of patients.

Conclusions: Utilizing CCTA as a first line diagnostic test in the workup of stable angina may improve diagnostic certainty while aiding in early identification of non-CAD causes of angina.

Behavioral deficits in the Protocadherin-10 (Pcdh10) mouse model relevant to autism

Kelsey L. Blocklinger, Sarah L. Ferri, and Ted Abel
Department of Neuroscience and Pharmacology, Iowa Neuroscience Institute, University of Iowa

Background: Autism spectrum disorder (ASD) is four times more common in males than in females, and includes reduced sociability and fear conditioning impairments. Human genetic studies have implicated protocadherin-10 (*Pcdh10*), a gene involved in dendritic spine development, in ASD. Our lab previously reported that male mice heterozygous for a deletion of *Pcdh10* (Pcdh10$^{+/-}$) had social approach and fear conditioning deficits, in addition to abnormalities in the basolateral amygdala (BLA). Here, we were interested in exploring the necessity of *Pcdh10* specifically in the BLA for social affiliative behavior. We utilized a conditional gene inactivation protocol that relies on the DNA recombinase Cre to restrict deletion of *Pcdh10* in the BLA in adulthood of *Pcdh10*-floxed mice. Due to the male bias of ASD, we hypothesized that male *Pcdh10*-floxed mice injected with a Cre virus would exhibit social approach and fear conditioning impairments compared to wild-type littermates. We expected female mice to not show significant behavioral deficits.

Methods: Young adult (56-72 d) male and female mice carrying 0, 1, or 2 copies of the *Pcdh10*-floxed allele received a stereotactic infusion of a fast-expressing helper-dependent adenovirus expressing Cre recombinase into the BLA. One week after infusion, mice were assessed for social approach behavior, in which mice were given 10 min to habituate to a 3-chambered arena (Phase 1) followed by 10 min to interact with a nonsocial cylinder containing a novel object or a social cylinder containing a novel social stimulus mouse (Phase 2). Mice were also assessed for contextual fear conditioning learning, in which freezing behavior is measured at a baseline state in a chamber followed by a moderate foot shock. Freezing is then measured again 24 hours later in the same chamber. After behavior testing, mice brains were extracted, and a cryostat was used to prepare coronal brain sections containing the BLA. Brain slices were viewed under a confocal microscope to characterize the location of eGFP-tagged viral infusion relative to the BLA ("BLA miss" vs. "BLA hit").

Results: We tested male and female *Pcdh10*-floxed mice and wild-type littermates (WT) that did not receive a Cre injection in the BLA ("no Cre"), received a Cre injection that missed the BLA ("BLA miss"), and received a Cre injection that hit the BLA ("BLA hit"). Mice underwent the Social Approach Test, with cylinder sniffing duration used as the primary measure of sociability. Post-hoc tests revealed that male *Pcdh10*-flox mice with BLA hit of the Cre virus had a significant decrease in social approach when compared to WT littermates, *Pcdh10*-flox no Cre, and *Pcdh10*-flox BLA miss male mice (p<0.01). Interestingly, female mice showed similar results. Post-hoc tests revealed that female *Pcdh10*-flox mice with BLA hit spent significantly less time sniffing the social cylinder (p<0.01). Mice were also assessed for contextual fear conditioning learning, with time spent freezing indicative of learned fear memory. Male *Pcdh10* $^{flox/flox}$ mice with Cre hit exhibited a non-significant increase in freezing time. However, post-hoc tests showed that female *Pcdh10* $^{flox/flox}$ mice exhibited a significant increase in freezing time (p<0.05).

Discussion: Abnormal amygdala structure and function in humans and rodents have been implicated in ASD. Social interaction strongly engages the basolateral amygdala, where *Pcdh10* is highly expressed. Although ASD is a neurodevelopmental disorder and these mice had *Pcdh10* throughout development, we show that deleting *Pcdh10* in the BLA in adulthood is sufficient to drive impairments in sociability and fear conditioning learning in both male and female mice. Future experiments will aim to quantify the extent of BLA lesion necessary to induce deficits. Studies of gene expression and brain region-dependent behavioral changes in ASD models are important future directions for understanding age- and sex-specificity of autism-relevant behaviors.

Perfect Match: Evaluating Cardiac Volumes for Optimizing Donor to Recipient Match for Pediatric Heart Transplant Recipients

Presenting Author: Eric Boeshart BSE, MA, M2

Co-Authors: Jennifer Maldonado BS; Ravi Ashwath MD; Bijoy Thattaliyath MD

Background: Heart transplantation in pediatric patients with end stage heart failure is the current standard of care. The survival of patients wait-listed for transplant is complicated by high mortality due to severe limitations of the donor pool and a lack of better understanding of the parameters that can best predict the optimum utilization and eventual success of an allograft. Our aim is to develop a method for providing better predictive data to the cardiac transplant team that can aid in improving listing criteria for pediatric heart transplantation with the best chance for donor organ to recipient match.

Methods: Data was collected from 300 patients who are under the age of 21, underwent CT scans and had no diagnoses related to the anatomical structure of the heart. The Total Cardiac Volume (TCV) was determined using standard clinical image analysis software. Multivariable linear analysis was performed with the addition of patient demographic data which was used to develop predictive models.

Results: The data showed that there was a positive correlation between the age of the patient, height, weight, and calculated body surface area (P values <0.0001). Body surface area (BSA) provided the strongest predictive value for TCV (R^2=0.8835, P<0.0001).

Conclusions: Trends within the data showed that variation between predictive and measured TCV varied more with age and could have implications on recipient-donor organ match for pediatric heart transplantations. Utilization of predictive models or measured TCVs from donor CT scans has the potential for greatly improving the safety and outcomes of heart transplants in the pediatric patient population.

Hospitals Reporting SEP-1 Compliance to Centers for Medicare & Medicaid Service Conduct More Sepsis Quality Improvement Practices

Ty B. Bolte, Morgan B. Swanson, Anna Kaldjian, Nicholas Mohr, MD MS, Jennifer McDanel PhD, Azeemuddin Ahmed MD MBA

Background

Sepsis is a common cause of death in hospitalized patients. The Centers for Medicare & Medicaid Service (CMS) Severe Sepsis and Septic Shock Bundle (SEP-1) is an evidence-based early management bundle focused on improving septic patients' outcomes. It is unknown which quality improvement (QI) practices are associated with SEP-1 compliance and if those practices reduce sepsis mortality. Identifying QI practices associated with improved bundle compliance and better outcomes will provide guidance on creating an effective sepsis campaign.

Specific Aims

The objectives of this study were to measure the association between specific elements of sepsis QI processes and two outcomes: (1) hospital-specific SEP-1 performance and (2) hospital-specific risk adjusted sepsis mortality.

Methods

This is a mixed methods study linking telephone survey data on QI practices from hospitals to SEP-1 performance data reported to CMS, and statewide inpatient and ED administrative claims data. The survey was designed to assess sepsis QI practices in eight categories. SEP-1 scores were examined as a continuous outcome and categorized as High Performing Hospitals (75th-99th percentile). The characteristics of hospitals were reported using descriptive and bivariate statistics. Univariable and multivariable logistic and linear regression models were used to estimate the association between sepsis QI practices and hospital SEP-1 performance.
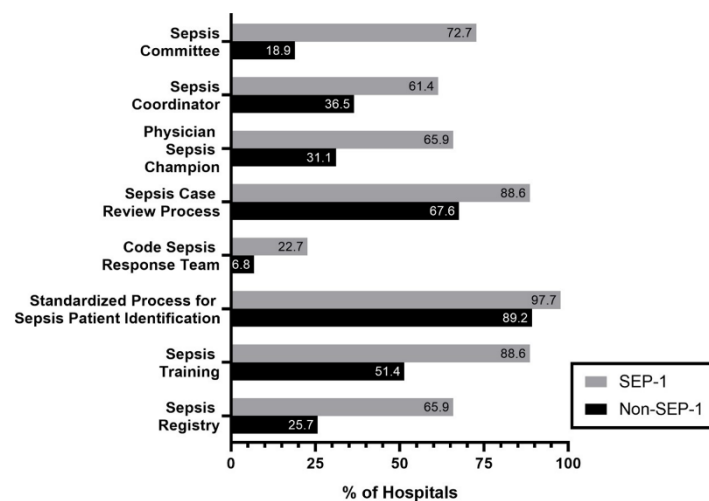

Figure 1: Sepsis QI practices by SEP-1 reporting status

Results

All 118 hospitals in Iowa participated in the survey (100% response rate). SEP-1 reporting hospitals were more likely to report results to providers (64% vs. 38%, p = 0.026) and use the case review process to develop sepsis care plans (87% vs. 64%, p = 0.013). The following were not found to be associated with top-preforming hospitals; presence of a sepsis committee (p = 0.437), sepsis coordinator (p = 0.858), physician sepsis champion (p = 0.362), sepsis case review process (p = 0.419), code sepsis response team (p = 0.679), or sepsis registry (p = 0.583).

Conclusion

Hospitals who report SEP-1 compliance to CMS conduct more sepsis QI practices. These practices are not associated with increased SEP-1 performance. It is possible these practices are being implemented to improve SEP-1 performance, and more time is needed for documented improvement.

Optimizing Renal Function and Quality of Life in the Cervical Cancer Patient with Hydronephrosis

Hannah Botkin, Kathryn Faidley, Emily Hill, MD, Bradley Erickson, MD
Department of Urology, UIHC

Background: Ureteral obstruction in the setting of cervical cancer is common. It can occur as a result of ureteral compression by the tumor itself, or from ureteral stricture caused by pelvic radiation through direct insults and/or retroperitoneal fibrosis. Obstruction leads to renal colic, renal impairment, and may preclude cervical cancer treatment and thus will generally require decompression in the form of retrograde ureteral stent (RUS) placement, or by percutaneous nephrostomy tube (PCN). Which of these two methods of drainage is superior has not been established, nor have the long-term outcomes of the renal units both during and after treatment of the cancer. As cervical cancer detection and treatments improve, patients are living longer. This makes it critically important to optimize renal function in these patients living with hydronephrosis, as well as minimize complications and optimize quality of life in these cervical cancer survivors.

Aims/Hypothesis: Our goal is to understand the natural treated and untreated history of hydronephrosis in the setting of cervical cancer. To accomplish this, our first aim is to determine the efficacy of RUS versus PCN for treatment of hydronephrosis. We hypothesize that compared to RUS, PCN will be superior in treating hydronephrosis, and will cause fewer complications for patients. Our second aim is to identify patient factors that predict hydronephrosis resolution without requiring reconstructive surgery. We hypothesize that advanced stage disease and worse ureteral obstruction at time of hydronephrosis presentation will be independent risk factors for non-resolution of hydronephrosis. Our final aim is to identify a subset of patients who may benefit from reconstructive surgery rather than long-term utilization of either RUS or PCN. We hypothesize that we will find a significant number of patients with no evidence of cancer after treatment, but with persistent RUS or PCN requirements that may be eligible for reconstructive surgery (thus eliminating RUS or PCN requirement).

Methods: We utilized hospital CPT codes to generate a list of patients who were treated for cervical cancer at the University of Iowa Hospitals and Clinics from Jan 1 2004- Dec 1 2019 who also had hydronephrosis. We obtained IRB approval, and performed a retrospective chart review utilizing both EPIC and Care Everywhere records. Data collected from the electronic medical record of each patient included demographics, cervical cancer stage and treatment, and the course, treatments, and complications of their hydronephrosis.

Results: Of the 1670 women treated for cervical cancer from Jan 1 2004- Dec 1 2019, 200 (11.98%) developed hydronephrosis. Of those 200 women, 63 (31.5%) presented with hydronephrosis at the time of their cervical cancer diagnosis with the remaining 137 (68.5%) developing hydronephrosis during or after cancer treatment. Of all 200 women with hydronephrosis, 160 (80%) had their hydronephrosis treated with either RUS (n=69; 43%), PCN (n=91; 57%), or both (n = 45; 28%). Complications from initial management were higher with RUS (68.1%; flank pain 55.3%, dysuria requiring medications 48.9%, stent failure 46.8%) versus PCN (45% p=0.001; flank pain 53.7%, recurrent UTI 53.7%). Further, a worsening of renal function following device placement - as measured by rising creatinine – was more frequent following RUS placement (n=16; 23%) than PCN placement (n=6; 6.6%) (p=0.0009). Conversion to PCN from RUS was required in 32 patients (46.4%), of which complications were experienced in 48.9%. Resolution of hydronephrosis occurred in only 27 women (16.9%) at a median time of 137 days (range 47-2173). Predictors of non-resolution included calyceal blunting (p=0.0048) and renal atrophy (p=0.049). Of all patients treated with stent or PCN who did not have resolution of their hydronephrosis, 32 (24%) had reconstructive surgery for definitive treatment of their hydronephrosis.

Discussion: Several conclusions can be drawn about this important patient population from our data. First, complications are common regardless of the method of drainage, though PCN appears to fail less often and likely leads to fewer bothersome lower urinary tract symptoms. Second, the method of initial drainage does not affect the likelihood of spontaneous resolution, though worse hydronephrosis portends a lower likelihood that it will resolve. Third, it appears that while many women may be eligible for reconstructive surgery, few are undergoing this surgery for reasons that were not made entirely clear by this study. However, because reconstruction is considered definitive treatment for hydronephrosis, may alleviate or eliminate the complications experienced by over half of women treated with RUS and PCN, and eliminates the need for frequent checks and changes of stents and PCNs (every 3 months), thereby improving and preserving quality of life for these cancer survivors, further study is warranted.

High and low ratios of neutrophils differentially regulate T-cell responses

Jayden Bowen[123], Sankar Baruah[1], Kathy Keck[1], Shubha Murthy[1], Julia Klesney-Tait[1]

Department of Internal Medicine[1], Interdisciplinary Graduate Program in Immunology[2], Medical Scientist Training Program[3]

Background: T-cells are the key players in antigen-specific immune responses and drive host defense and pathology in many diseases. Because of this, the activation and replication of T-cells is tightly regulated. Neutrophils are the most abundant leukocyte in the body and often outnumber other immune cells at sites of pathology by orders of magnitude. Neutrophils are also rapid responders, arriving before other leukocytes to surveil and respond to inflammatory insults. As such, they play an outsized role in shaping the immune microenvironment. Neutrophils have typically been found to inhibit T-cell responses; however, neutrophils can express many T-cell stimulatory proteins including MHCII, CD80/86, CD40, and OX40. **Aim:** Using an in vitro system of sub-optimal T-cell activation, we set forth to further characterize the role of T-cell:Neutrophil interactions in shaping T-cell activation and division. **Methods:** Murine T-cells were isolated from mouse spleens and cocultured for 72hrs with bone marrow derived neutrophils in the presence of activating antibodies (1ug/mL anti-CD28, wells precoated with 0.025ug/mL anti-CD3.) After 72hrs, T-cells were analyzed by flow cytometry for markers of activation and dilution of the intracellular dye CFSE, which reliably tracks division. Additionally, IL-2 in the supernatant was measured by ELISA. **Results:** In our system, T-cells displayed a biphasic response to neutrophils. Low numbers of neutrophils promoted T-cell activation (as measured by CD69 and CD25 expression) and division (as measured by CFSE dilution.) This effect was dependent on contact between T-cells and neutrophils as coculture in a transwell system (a 0.4um membrane separates T-cells from neutrophils) ablated T-cell division. In contrast, increasing numbers of neutrophils returned T-cell division to near zero. Additionally, neutrophils increased T-cell survival and IL-2 production. Using antibodies to IL-2 and IL-2Rβ, we unexpectedly found that low numbers of neutrophils promoted division in an IL-2 independent manner, while neutralizing IL-2 or blocking IL-2Rβ also rescued T-cell division from inhibitory numbers of neutrophils. T-cells upregulated the cell death receptor FAS when in the presence of large numbers of neutrophils and neutralizing IL-2 prevented the expression of FAS.

Discussion: Altogether these results suggest that neutrophils play an important role in tuning T-cell responses, and the ratio of neutrophils to T-cells determines whether T-cell responses are promoted or inhibited. Neutrophils promoting T-cell division in a contact-dependent and IL-2 independent fashion likely indicates that neutrophils provide a pro-activation and pro-division receptor ligand at low ratios. At high ratios, the IL-2 dependent expression of FAS by T-cells suggests that high ratios of neutrophils induce cell death by providing FAS-ligand. This finding is further supported by the well-described role of IL-2 in T-cell activation-induced cell death. Moving forward, we will identify the pro-activation signal(s) provided by neutrophils and directly investigate the role of the FAS axis in our system by utilizing FAS and FASL blocking and activating antibodies.

Anterior Inferior Iliac Spine Deformities: Incidence and Associations
Student: Nathan Cao, M3
Mentor: Kyle Duchman, MD – Department of Orthopedics and Rehabilitation
Co-Mentors: Robert Westermann, MD – Department of Orthopedics and Rehabilitation

Abstract:
Background/Purpose: Recent studies have suggested that subtle morphological differences of the femoral head and acetabulum may lead to hip and groin pain and possibly hip osteoarthritis (OA). Femoroacetabular impingement (FAI) syndrome is a condition that is characterized by abnormal contact between the acetabulum and femoral head, which arises from subtle morphological differences of one or both of these structures. FAI syndrome has been accepted as a frequent cause of hip pain and dysfunction in patients over a broad age range. In this study, we investigated the relationship between a specific variant of extra-articular FAI syndrome, namely anterior inferior iliac spine (AIIS) morphology, and how AIIS morphology relates to acetabular volume and version.

Methods: The study was conducted using cadaveric skeletons from the UI-Stanford Bone collection with full documentation of common demographic characteristics, including sex, age at death, race, and in most cases, occupation. AIIS morphology was categorized as Type I, II, or III as previously described. Acetabular volume was approximated by the equation for a half-ellipsoid as previously described. To measure acetabular version, the pelvises were reconstructed using rubber bands and 2.5cm thick foam to represent the pubic symphysis. The pelvises were then placed on a flat surface with the anterior superior iliac spines (ASIS) and pubic symphysis as the points of contact, allowing for the establishment of the anatomic frontal plane. Three separate axial measurements of version were taken using a goniometer; the cranial measurement taken 5mm distal to the acetabular roof, central measurement taken at the diameter of the acetabulum, and the caudal measurement 5mm proximal to the inferior edge of the acetabular rim. Global version was calculated as the mean of these three measurements. Descriptive statistics were performed, and demographic and morphological characteristics compared using Student's t-test and chi-square analyses for continuous and categorical variables, respectively. Findings were considered statistically significant with p-values <0.05.

Results: Of the 72 hips reviewed, 9 (12.5%) had Type 1 AIIS morphology, 44 (61.1%) Type 2, and 19 (26.4%) Type 3. Global acetabular version measurements taken from right hip bones were on average more anteverted than left hip bones ($13.9°\pm6.7°$ vs. $18.9°\pm11.0°$; p <0.001). Cranial acetabular version measurements taken from right hip bones were on average more anteverted than left hip bones ($8.0°\pm8.8°$ vs. $21.6°\pm13.8°$; p-value <0.001). Acetabular volume on the left hip bones was on average smaller than right hip bones (45.7 cm$^3\pm11.3$ cm^3 vs. 47.5 cm$^3\pm11.3$ cm^3; p = 0.016). When comparing acetabular volume and version between the three AIIS morphological subtypes, there were no significant differences noted.

Conclusion/Discussion: Only 9 of 72 specimens exhibited Type 1 morphology, which has previously been described as the most common AIIS subtype. These differences may be the result of variable activities that may influence AIIS morphology, as the majority of specimens were from persons classified as manual laborers, or increasing age. Although global version measurements are often used to predict or evaluate FAI, the cranial version measurement can also provide valuable insight. This is due to the fact that cam-type FAI typically occur in the anterosuperior aspect of the acetabulum, with cranial retroversion being thought of as a good predictor of developing cam-type FAI. Conversely, anteversion has been associated with hip dysplasia. Acetabular retroversion reflects overcoverage of the femoral head anteriorly and undercoverage posteriorly. This may have the effect of decreasing the right hip's susceptibility to cam-type FAI, while increasing the chances of hip dysplasia. The data would also suggest that left hips may be more susceptible to cam-type FAI, but less susceptible to hip dysplasia. However, previous literature has not found that FAI is more common on one side than the other. Acetabular volume was shown to be larger on right hips than left, pointing at a possible relationship between larger acetabuli and increases in acetabular anteversion. Although information on handedness was not documented in these specimens, acetabular versions measurements being more anteverted on right hips may also be the result of preferential use of the right leg over the left. Future studies may aim to repeat this study using a more diverse cohort of skeletal cadavers from individuals from the 21st century to see if data on prevalence and associations differ drastically from those found in this study. An ideal cohort would include more females, more individuals from ethnic populations, extensive documentation of occupation, and handedness of patients.

All-Terrain Vehicle Exposure and the Effect of Training Course Certification on Adolescent Safety Behaviors and Crash Experiences

Katharine Champoux
Mentor: Charles Jennissen, MD, Departments of Pediatrics and Emergency Medicine

Background: All-terrain vehicles (ATVs) have been a significant source of injuries and death in children and adolescents. In fact, more children less than 16 years of age in the United States have died from ATVs than from bicycle crashes. Adolescents frequently do not follow proper safety behaviors while riding ATVs such as carrying passengers (almost all vehicles are designed for an operator only), riding on public roads, and not wearing a helmet. Proper safety behaviors are taught to students in ATV training certification courses. However, there are no published data regarding how ATV training certification effects subsequent safe riding behaviors.

Purpose: Our objectives in this study was to determine the exposure of adolescents to ATVs including use frequency, use of the vehicle for recreation and work, participation in competitive ATV racing, and their crash and injury experiences. Moreover, we wanted to determine factors associated with having completed an ATV safety training course and if this had a positive impact on subsequent safe riding behaviors.

Method: A program called Safety Tips for ATV Riders (STARs) was presented to adolescents in schools by the Iowa Off-Road Vehicle Safety Task Force. One year later, a written survey was completed anonymously by participants to evaluate the program's long-term effect on safe riding behaviors. The survey included a number of questions addressing the youth's various ATV exposure experiences including injuries and crashes. Surveys were provided to the investigators for study and compiled using Qualtrics, a web-based survey tool. Frequency and chi square analyses were performed using SAS software, V.9.4 of the SAS System for Microsoft (SAS Institute, Cary, North Carolina, USA).

Results: A total of 4,906 students from 30 different school districts completed the study survey from Fall 2012-Fall 2019. Participants ranged from 10-18 years old, but three-quarters (75.5%) were 12-14 years of age. There were equivalent proportions of males and females. About one-fifth lived on a farm (18.5%) or in the country, but not on farm (22.3%), and almost three-fifths lived in town (59.2%). Just over two-fifths (42.0%) stated their families owned an ATV. Overall, 77% had ridden an ATV. Of those that had ridden an ATV in the past year, two-fifths (40.0%) reported riding at least weekly and over three-fifths (62.1%) rode at least monthly. Although the majority (51.3%) of youth used ATVs for recreation only, over two-fifths (42.7%) used them for both work and recreation and 6.0% used them for work only. Participation in organized competitive racing was by 8.5% of those that had ridden at ATV in the past year. In the previous 12 months, over one-fifth (21.8%) of riders reported having had a crash (rollover, collision or ejection), and 3.7% overall had an injury requiring medical attention. Of adolescents who had ridden an ATV in the past year, only 8.1% had completed an ATV safety training certification course. Those with higher proportions having had taken a course included younger riders, males, those whose families owned ATVs, and more frequent riders. However, the percentage that had taken a course was no higher than 14.3% for any of these demographic groups. Those completing a safety course had higher proportions that wore helmets (30.2% always or almost always vs. 20.5% of those who had not taken a course, p<0.0001) and lower proportions that reported riding with passengers (62.8 vs. 78.8%, p<0.0001), but had higher proportions that reported riding on roads and had been in a crash. Of those that had ridden an ATV in the previous year, 14.7% had ridden in a public off-highway vehicle (OHV) park. Although those 12-17 years are required to have a valid education certificate to ride in public Iowa OHV parks, only 16.9% of those reporting riding in parks had done so.

Conclusion: Adolescents in Iowa have high exposures to ATVs and crashes are common. Although most riders use ATVs for recreation (94%), nearly one-half of study participants also use them for work purposes. Formal safety training is infrequent with less than 10% completing this education. Those that received training did demonstrate greater helmet use and less riding with passengers than other riders. Multi-targeted approaches including education/training and enforced safety regulations are needed to increase safe riding behaviors in adolescents and decrease ATV-related deaths and injuries.

Differentiate Takotsubo Syndrome from Acute Coronary Syndrome: *Machine Learning from Bedside Echocardiography*

Student: Amanda Chang, M2
Mentor: Kan Liu, MD, PhD,
Collaborators: Fahim Zaman, PhD Candidate, Xiaodong Wu, PhD, Rakesh Ponnapureddy, MD, Shubha Deep Roy, MD

Purpose: To develop echocardiography machine learning (ML) algorithms to distinguish Takotsubo syndrome (TTS) from acute myocardial infarction (AMI).

Hypothesis: Machine learning classification of TTS from bedside echocardiography will be equally or more specific when compared to manual classification by front-line healthcare providers.

Background: Takotsubo syndrome (TTS) and acute myocardial infarction (AMI) may have similar clinical presentation and are difficult to distinguish with echocardiography despite having different pathophysiology, treatment guidelines, and prognosis (1, 2). To avoid missing AMI, current guidelines advocate using coronary angiography to guide first-line diagnosis and therapy (3). Misdiagnosing TTS as AMI will also lead to initiation of harmful pharmacological or device-based treatment, which worsens hemodynamic compromise (4). Machine learning (ML) has been proven as a valuable artificial intelligence technique to identify complex imaging markers, helping differential diagnosis in cardiovascular imaging research (5-7). We aim to develop a ML model based on bedside echocardiography images, to create equally or more specific classification between TTS and AMI (when compared to front-line healthcare providers).

Methods: Echocardiography imaging data was obtained from the University of Iowa Echocardiography Laboratory (TTS patients diagnosed since 2007), consisting of image scans of approximately 158 patients with TTS and well over 149 patients with AMI. A subset of the echocardiography images will be used to train a neural network to develop a predictive model based on extracted features from the images. A separate subset of the images will be used to test the algorithm. The results are compared to that of front-line healthcare providers (cardiologists, sonographers and residents).

Preliminary Results: So far we have developed a combined clinical and echo image database from 428 patients: 158 TTS patients, 149 AMI patients, and 121 healthy controls. Echocardiography images are reviewed by board-certified interventional and imaging cardiologists/cardiac sonographers/residents of internal medicine with pocus training). Meanwhile, a supervised ML algorithm has been developed with preliminary training with internal validation. (8,9)

Conclusion/Discussion: ML has the potential to improve the accuracy and efficiency of bedside diagnosis of TTS while avoiding harmful invasive procedures and mismanagement from misdiagnosis as AMI. Integrating echocardiography based temporal dimension information into ML algorithms will likely improve differential diagnostic power of real-time cardiovascular imaging tools.

Title: Urine copeptin as a novel predictor of preeclampsia during early pregnancy.

Ailynna Chen[1], Sabrina Scroggins[2], Kevin Chen[2], Donna Santillan[2], Mark Santillan[2]
[1]University of Iowa, Carver College of Medicine
[2]University of Iowa, Carver College of Medicine, Department of Obstetrics and Gynecology

Background: Preeclampsia (PE) and related hypertensive disorders of pregnancy are considered a leading cause of maternal death in the U.S and worldwide. The clinical symptoms for PE typically do not manifest later in pregnancy. Consequently, it is difficult to prevent, diagnose, or intervene in a timely manner. Previous research suggests that plasma arginine vasopressin (AVP) secretion as measured by copeptin is elevated in preeclamptic pregnancies as early as six weeks of gestation which have clinical value in predicting PE months before clinical signs and symptoms are evident. Further, AVP exhibits early renal and volume handling affects that can lead to PE. The aim of this study was to evaluate the predictive value of copeptin, a marker of AVP secretion, as an early predictor of preeclampsia.

Methods: This case-control study was conducted using maternal urine (< 21 weeks gestation) and clinical data obtained from the University of Iowa Maternal Fetal Tissue Bank (MFTB) (IRB# 200910784) and the national AHA PREDICTV cohort (IRB# 201503865). Copeptin and creatinine levels were measured using commercially available colorimetric assays. Urine osmolality was measured using a freezing point osmometer. Preeclampsia cases were determined based on the 2013 American College of Obstetrics and Gynecology (ACOG) criteria. Multivariable logistic regression was used to determine the association between urine copeptin levels at < 21 weeks gestation and the development of preeclampsia while adjusting for significant covariates. Natural log transformation was applied to all nonparametric continuous variables including urine copeptin, creatinine, and body mass index. The predictive value of urine copeptin levels for preeclampsia in pregnancy was evaluated using Receiver Operating Characteristic (ROC) curve analysis.

Results: Urine copeptin levels were measured in 49 preeclamptic cases and 162 non-preeclamptic controls. On average, the preeclampsia group had higher BMI, urine creatinine levels, and prevalence of hypertension, preexisting diabetes, and gestational diabetes compared to the controls (p<0.05). Median copeptin levels were significantly elevated at less than 21 weeks gestation among cases (0.293 ng/ml) compared to controls (0.198 ng/ml) (p=0.0019). The natural log of urine copeptin concentration remained positively associated with the development of preeclampsia after adjusting for significant covariates including urine osmolality and creatinine, BMI, chronic hypertension, preexisting diabetes, gestational diabetes, and body mass index (OR=2.686, 95% CI 1.291 – 5.590). The adjusted model including all covariates produced a ROC AUC value of 0.8264.

Conclusions:
We demonstrate that elevated urine copeptin concentration at less than 21 weeks gestation is associated with increased likelihood of preeclampsia development in pregnancy and could be a valuable early predictor of preeclampsia in pregnancy. Prospective studies in large, diverse patient populations are necessary to verify and refine this prediction model.

Genotype-Phenotype Correlation and Determinants of Visual Outcome in Patients with Albinism with Complete Genotype

Karen Chen M2; Alina Dumitrescu, MD

Introduction:

Oculocutaneous albinism (OCA) represents a heterogeneous group of disorders that affect melanin production. Albinism causes lifelong visual impairment, although the range of visual acuities range from legal blindness to only minimally decreased vision. Most affected individuals have a combination of clinical features that include nystagmus, hypopigmentation of the iris with iris transillumination defects (TIDs), foveal hypoplasia and optic nerve misrouting. Commonly, patients with albinism have only ocular and cutaneous pigment abnormalities. However, two systemic types of recognized albinism combine OCA with other pathogenic features like prolonged bleeding due to platelet dysfunction, pulmonary fibrosis, kidney failure and granulomatous colitis, Hermansky-Pudlak syndrome (HPS), and immunodeficiency, Chediak-Higashi syndrome (CHS). Genetic testing can be used to screen at least 19 different genes in patients who are suspected clinically to have albinism. These genes include seven genes (TYR/OCA1, OCA2/OCA2, TYRP1/OCA3, SLC45A2/OCA4, SLC24A5/OCA6, and LRMDA/OCA7, *GPR143/OA1*) associated with non-syndromic OCA, a locus mapped to chromosome 4q24[13] in OCA5, and 11 genes associated with syndromic OCA types HPS and CHS.

Purpose:

The purpose of this study was to analyze a cohort of patients with clinical diagnosis of OCA in addition to complete molecular diagnosis (genetic testing) to assess for correlation between phenotype and genotype and to try to identify determinants for visual outcome.

Method:

A retrospective review of the medical records of patients with clinical diagnosis of albinism, complete genotype and at least one complete eye exam that were seen at University of Iowa between 1980 and 2020 was completed. A clinical scoring system including the most common clinical features in albinism and considering various degrees of severity was developed.

Results:

350 charts were reviewed, 45 charts met the inclusion criteria for the study. As expected for our geographical location, this cohort was mainly Caucasian, with 82% non-Hispanic white patients, 9% Asian patients, 7% African American patients, and 2% multiracial patients. The most common mutations that were found were OCA1 and OCA2 which are autosomal recessively inherited, occurring in 40% and 35% of the patients respectively. Frequency rates for OCA3, HPS, and XLOA were each 7% and OCA4 and OCA6 were each found in 2% of patients. Clinical albinism scores were generally high in all genotypical subgroups. There was no statistically significant difference between groups as some did not have sufficient sample sizes. All patients, with all types of OCA, showed some degree of visual impairment. Half the patients had visual acuities between 20/40 and 20/100. Very few had visual acuity better than 20/40 or worse than 20/400. Most patient maintained or improved their visual acuity during follow up, and very few (11%) had a decrease in visual acuity. Patients with HPS seem to have less optic nerve abnormalities as well as a less complete genotype. Refractive errors were commonly present, with 71% of patients having hyperopia and astigmatism. Myopia appears more commonly in patients with OCA2.

Conclusion:

No definitive correlation between genotype and phenotype was found. Genetic testing is recommended in all patients who present clinically with albinism as clinical exams cannot identify syndromic forms, which may have severe systemic complications, from non-syndromic forms or rule out phenocopies. Additionally, early confirmation of OCA subtype through genetic testing may offer predictors for refractive errors, severity of visual acuity loss and degree of change of visual acuity over time.

The Genetics of Early-stage Melanoma in a Veteran Population

Kevin Cheung BS, Aaron Bossler MD PhD, Sarah Bell MS, Julie McKillip RN BSN, Brian Swick MD, Jennifer Powers MD

Background/Purpose:
Melanoma is currently the fifth most common cause of cancer in men and women in the United States, and in 2019, it accounted for an estimated 4,740 deaths in men and 2,490 in women. These findings are especially concerning for the military population as studies have shown that military personnel are at increased risk for melanoma compared to the general population. However, current understanding of military-associated risk factors is incomplete, and the genetics and pathophysiology of melanoma have not been well-studied in the veteran population. The purpose of this study is to characterize the genetic signature of early-stage melanomas from veterans who were successfully screened and timely diagnosed, which may shed light on pathogenesis of melanomas in this population and in turn influence clinical approach to prevention, screening, diagnosis, and treatment.

Methods:
Tissue samples of confirmed melanoma cases in a 7-year period between January 1, 2010 to January 1, 2017 were obtained from the Iowa City VAMC and analyzed by massively parallel or next generation sequencing (NGS). Exclusion criteria included concurrent internal malignant disease, stage at diagnosis 3 and 4, and unavailable or inadequate tissue sample. Statistical analysis was performed correlating genetic data with demographic and clinical information, which were obtained by chart review.

Results:
Samples from 135 patients admitted to the VA for treatment of melanoma met cohort criteria and were analyzed. The cohort comprised primarily older (average age 69), Caucasian (92%), males (97%). Military branch distribution was 63% in the army, 14% in the navy, 12% in the marines, and 11% in the air force. The most common mutations detected were BRAF (36%), TP53 (26%), NRAS (19%), CDKN2A (11%), KIT (8%), and BAP1 (7%). Those who had melanoma primary tumor in the trunk were at higher odds of BRAF mutation than those in the head/neck (OR = 3.33) or extremities (OR = 4.76) (p <0.01). Younger age was also at greater odds for having BRAF mutation (OR = 1.03, p = 0.01). Those who had melanoma primary tumor in the extremities were at higher odds of NRAS mutation than those in the trunk (OR = 2.04) or the head/neck (OR = 7.14) (p = 0.02). Nodular subtype compared to superficial spreading was also at higher odds of NRAS (OR = 1.53) as well as personal history of non-cutaneous cancer (OR = 3.05, p = 0.02). Patients with prior history of melanoma were at higher odds of having TP53 mutation (OR = 2.67, p = 0.04). Neither smoking status nor military branch were associated with BRAF, NRAS, or TP53 mutations.

Conclusions:
BRAF has been associated with intense intermittent sun exposure as opposed to chronic sun exposure, and has prevalence reported around 44-66% in the general population. Our cohort had a lower prevalence of BRAF compared to what has been reported in the general population, which supports the idea that veterans incur chronic sun exposure. This is in line with the fact that veterans are frequently stationed at equatorial locations as well as previous work that has reported poor sun protection education and practices in the military. Interestingly, NRAS mutation was found to be within a comparable range as the general population (19% vs. 20%). NRAS is associated with chronic sun damage and was expected to be higher. Its lower than expected prevalence in this cohort suggests that other exposures may be contributory or that melanoma in veterans proceeds through other pathways. It is worth noting that KIT mutations, which generally has 1-7% prevalence, was found to be 8% in our cohort. KIT mutations are interesting in that they are typically found on mucosal and acral areas, which points to non-UV exposures. Higher KIT mutations in veterans may therefore be suggestive of other risk factors like chemicals and radiation. Lastly, TP53 was found to be associated with previous history of melanoma. One study has found that functional p53 enzyme prolongs the remission period in melanoma, which provides evidence that p53 plays a protective role in preventing melanoma recurrence. This finding suggests that TP53 may be used to help identify veterans at particularly increased risk of recurrence. In conclusion, this study provides new information regarding both genetics of melanoma in a veteran population and early-stage tumors. Future studies may include comparative studies with matched controls, validation at other VA medical centers, larger studies to increase statistical power, and expansion of the gene mutation panel to identify other drivers of malignancy. Ultimately, these findings should influence how we educate, screen, and treat melanoma in veterans and active military personnel, and pave the way for continued research to identify exposures and risk factors unique to this population.

Testosterone Deficiency in Men Being Treated for Primary Pancreatic Cancer

Holly K. Conger[1], Austin G. Kazarian[1], Sarah L. Mott[2], Bradley T. Loeffler [2], Erin E. Talbert[2,3], Carlos H.F. Chan[2,4], Amy M. Pearlman[5]

[1]University Of Iowa, Carver College Of Medicine, Iowa City, IA, USA; [2]University Of Iowa, Holden Comprehensive Cancer Center, Iowa City, IA, USA; [3]University Of Iowa, Department Of Health And Human Physiology, Iowa City, IA, USA; [4]University Of Iowa, Department Of Surgery, Iowa City, IA, USA; [5]University Of Iowa, Department Of Urology, Iowa City, IA, USA;

Introduction: Few studies have investigated testosterone deficiency in non-prostate cancers. Previously, inflammation and opiod use has been associated with hypogonadism and shorter survival in advanced pancreatic cancer. Furthermore, a significant proportion of these patients note a lack of sexual interest or enjoyment in the small number of studies conducted on this topic. Despite many of these patients experiencing symptoms of testosterone deficiency such as fatigue, weakness, cognitive dysfunction, and decreased lean muscle mass, there exists sparce literature on testosterone testing patterns in practice and the prevalence of testosterone deficiency in this population.

Objective: To analyze testosterone testing patterns and assess testosterone levels in patients with primary tumors of the pancreas.

Methods: The electronic medical record at a National Cancer Institute-designated comprehensive cancer center delivering high-volume pancreatic cancer care since 2006 was queried to identify male patients with billing codes for masses of the pancreas (C.25X) who also had an available testosterone laboratory level. Testosterone levels, as well as demographics and clinicopathologic variables, were assessed. Available testosterone levels were analyzed for testosterone deficiency, which was defined per the American Urological Association guidelines as a total testosterone <300 ng/dL.

Results: 1,566 male patients with a pancreatic mass billing code were identified, of which 35 (2.2%) had both a primary pancreatic tumor and a testosterone level in their chart. Of this cohort, 16 (46%) patients had a low testosterone level while an additional 4 (11%) patients had a normal testosterone level, but were on testosterone replacement therapy at the time of the testosterone draw. When selecting for testosterone levels drawn within one year of cancer diagnosis, 12 (34%) patients were identified. Of these 12 patients, 4 (33%) had measured low testosterone, and an additional 3 (25%) patients were already on testosterone replacement therapy at time of lab draw. The most common reason prompting a provider to check a testosterone level in these 35 cancer patients were complaints of fatigue (14, 40%), followed by low libido and/or erectile dysfunction (8, 23%), or monitoring ongoing testosterone replacement therapy (4, 11%).

Conclusions: Very few patients with primary tumors of the pancreas have testosterone values assessed despite reporting concerns commonly associated with testosterone deficiency. Over half of those with testosterone levels obtained within one year of cancer diagnosis had low testosterone or were on testosterone replacement. In this population commonly experiencing constitutional symptoms which could be attributed to either malignancy or testosterone deficiency, testosterone appears to be significantly under assessed and under treated. Further studies are required to assess whether or not testosterone supplementation improves patient-reported outcome measures.

Title: Skin Transmission of Ebola Virus

Tyler P Crowe[1], Kelly N Messingham[1], Aloysius J Klinglehutz[2], Robert Davey[3], and Wendy J Maury[2]

Departments of [1]Dermatology and [2]Microbiology, University of Iowa, Iowa City, IA; [3]National Emerging Infectious Disease Laboratories, Boston University, Boston, MA

Background: The 2013-2016 West African Ebola outbreak highlighted the gaps in our understanding of, and effective treatments for, filoviruses. In this outbreak some 28,000 people were infected, with ~40% mortality. The only treatment available is palliative care, as there is no cure. Ebola (EBOV) has been found on the skin surface at late times of infection when viremia is high. Further evidence suggests that virions on the skin surface serve as a source of virus transmitted to others. For transmission, live virus must arrive at the skin surface, but how this happens, is not known. Because the skin is a complex multicellular organ containing a variety of cell types and structures, understanding which skin cell types provide a reservoir for viral replication is critical for understanding disease transmission.

Purpose of the study: The goal of this study is to determine if the skin acts a reservoir for filoviruses, and to identify the cell types involved and a time-course of infection.

Methods: EBOV infection was studied using a combination of *in vivo* and *in vitro* models using a BSL4 strain of EBOV (wild type) infection of rhesus macaques (non-human primate, NHP) and human skin and BSL2 VSV-GFP-EBOV infections of mice. Mouse and NHP were studied *in* vivo, using the BSL2 and BSL4 viruses, respectively. NHP and human skin was also studied *in vitro* by culturing in transwells with the BSL2 virus. In all cases, all skin was harvested, fixed, paraffin embedded, stained with fluorescent antibodies and images were collected using epifluorescence or confocal microscopy.

Results: *In vivo* infection of NHP and mice resulted of infection of dermal immune cell and fibroblasts for both BSL4 and BSL2 viruses. *In vitro* models confirmed these findings, and also showed infection of epidermal keratinocytes and follicular cells when the virus was applied to the epidermis. Notably, regions of skin where epidermal integrity was compromised displayed a higher degree of infection.

Conclusions: Cells from every layer of the skin were found to be infected with virus, including keratinocytes, fibroblasts, and CD45+ immune cells. Epidermal keratinocyte and follicle infection results indicate possibility of viral transmission via skin. These results should be considered to better decrease community spread during future outbreaks. Ongoing studies are refining the time-course and defining cells mediating viral transmission to the skin after ip infection of mice, as well as determining if skin abrasion increases the likelihood of transmission into a new host.

Exposure to persistent hemodynamically significant ductal shunt is associated with the development of Retinopathy of Prematurity.

Alison Cunningham M2, Regan E Giesinger MD, Patrick J McNamara MD, John M Dagle, Jonathan M Klein, Amy H Stanford, Danielle R Rios MD, Madeline Beauchene M2, Megan Fellows M4

Introduction: Persistent hemodynamically significant patent ductus arteriosus (hsPDA) shunt following preterm birth has been associated with necrotizing enterocolitis and bronchopulmonary dysplasia. Retinopathy of Prematurity (ROP) is a potentially blinding condition, which primarily impacts the most immature infants. High quantities of delivered oxygen in the early postnatal period is a known risk factor for later development of ROP. Persistent ductal shunt has been associated with the development of ROP in some studies. A link between these two disease entities is biologically plausible because pulmonary over-circulation promotes increased oxygen content and escalation of pre-ductal cardiac output which leads to a net increase in ocular tissue oxygen delivery. The aim of this study was to characterize the association between moderate-high volume PDA shunt and ROP. We hypothesized that extremely preterm neonates with prolonged exposure to moderate-high volume PDA shunts are at increased risk of the composite outcome of death or severe ROP.

Methods: A retrospective cohort study was conducted, including all neonates born $\leq 26_{+6}$ weeks gestation and admitted at <24h postnatal age to the NICU, at the University of Iowa Stead Family Children's Hospital between September 2018 and July 2020. Exclusion criteria included congenital cardiac abnormalities other than a PDA, atrial level communication, or small (<1mm) muscular ventricular septal defect. All patients underwent standardized targeted neonatal echocardiography assessment within the first 24h, day 5-7 and 8 weeks postnatal age at minimum. The Iowa PDA score was calculated based on objective criteria. Patients were considered exposed to hsPDA if the score was ≥ 6 at any time prior to 32 weeks postmenstrual age. The remainder of the cohort were classified as 'no hsPDA'. All reports from regular ROP screening, beginning at 31 weeks PMA, were reviewed. The primary outcome was death or severe ROP [$\geq$ stage 2 with plus disease or $\geq$ stage 3] and secondary outcomes included any ROP $\geq$ stage 1, treatment with Avastin or ROP surgery. Univariate analysis was performed to compare demographics, antenatal characteristics and known/possible risk factors for ROP [e.g. culture positive sepsis, early postnatal hyperglycemia, severity of respiratory distress syndrome] and outcomes between groups. Logistic regression was performed to adjust risk of ROP for factors with p<0.05 on univariate analysis. Magnitude of PDA exposure (mean PDA score * duration of PDA exposure) was calculated and a receiver operator characteristics (ROC) curve generated for the outcome of ROP $\geq$ stage 2.

Results: A total of 86 patients were screened, of whom 54 (63%) were classified as having hsPDA. hsPDA patients were younger [24.1±1.5 vs 25.2±1.4, p=0.001] and lighter [655±164 vs 758±175, p=0.007] at birth. Antenatal characteristics [intrauterine growth restriction, antenatal steroids, pre-eclampsia, chorioamnionitis, maternal diabetes] and postnatal disease severity [sepsis, surfactant administration] were similar. Compared to control patients, babies with hsPDA experienced more death or severe ROP (p<0.001), more ROP of any stage (p=0.002) and had a higher overall burden of ROP (p=0.02) with no difference in ROP intervention. Patients with hsPDA also had a higher burden of hyperglycemia in the first 2 weeks (p=0.015) and were more likely to receive hydrocortisone (p<0.001). On multivariate logistic regression, the risk of death or severe ROP was associated with hsPDA [OR 12.8 (2.5, 65), p=0.002] and hyperglycemia [OR 1.3 (1.03, 1.5), p=0.026] independent of gestation age, surfactant use, and hydrocortisone exposure. Importantly, magnitude of PDA shunt exposure remained independently associated with development of any ROP among survivors to 31 weeks PMA [OR 1.2 (1.03, 1.5), p=0.004] after adjustment for all factors. Among 22-23$_{+6}$ week patients, shunt exposure predicted stage 2 or greater ROP with an AUC of 0.79 (p=0.02). A score of 7, which has clinical equivalence to 7 days exposure to high-volume shunt, predicts stage 2 ROP with a sensitivity of 80% and a specificity of 78%.

Conclusions: Among infants born <27 weeks gestational age, the presence of hemodynamically significant PDA shunt is associated with a composite of death or severe ROP, as well as ROP of any stage. Shunt modulation represents a biologically plausible avenue for investigation in the prevention of preterm eye disease.

Evaluation of an Algorithm Utilizing the Pediatric Appendicitis Score in the Reduction of CT Scans in the Emergency Department

Jack Curran, BA | Stephany Walk, DNP, ARNP, CPNP | Julia Shelton, MD, MPH

Purpose: This study aims to evaluate the implementation of a Pediatric Appendicitis Score (PAS) algorithm in the emergency department (ED) setting and its effectiveness at reducing the number of CT scans conducted on pediatric patients with suspected appendicitis.

Hypothesis: The focus of this study is to determine if the introduction of a PAS-based algorithm has reduced the number of CT scans performed to evaluate suspected pediatric appendicitis. It is hypothesized that the algorithm has been an effective tool for the pediatric ED providers and that the overall numbers of CT scans (primary outcome) conducted since its introduction will be lower than those seen in the 18 months prior. It is also hypothesized that the number of RLQ abdominal ultrasound studies (secondary outcome) will have increased since the implementation of the algorithm.

Background: In pediatric patients, acute appendicitis is the most common cause of emergent abdominal surgery. Due to the frequency of appendicitis in the pediatric patient population, it is high on the differential for patients presenting to the ED with abdominal pain. Imaging is a key component in the diagnosis of appendicitis, and many institutions use CT scans for this purpose. Despite high sensitivity and specificity of CT scans, this imaging modality exposes the pediatric patient to high levels of ionizing radiation and often come at a great cost to the patient. Ultrasound has therefore become the preferred method of abdominal imaging in detecting acute appendicitis due to its convenience, low cost, and lack of radiation exposure. Recently, the Pediatric Appendicitis Score (PAS) has become increasingly utilized by ED providers. It includes components of the history/physical exam, ultrasound, and laboratory results to more accurately diagnose appendicitis. Using this as a diagnostic algorithm for appendicitis has been effective and is a promising way to reduce the number of CT scans done on pediatric patients in the ED setting

Methods: The PAS algorithm was developed and introduced to the UIHC ED in December of 2018. This project is a retrospective study reviewing pediatric patients who presented to the UIHC emergency department (including transfer patients) between June 1, 2017 and June 1, 2020 with chief complaint of abdominal pain. Inclusion criteria in this study were patients aged 0-17.99 years of age at the time they presented to the ED, and diagnosis in the patient chart of abdominal pain of any type. Exclusion criteria for this study was patients presenting with post-surgical abdominal pain. A total of 1,365 patients meeting the criteria were identified. The selected timeframe includes patients seen in the 18 months prior, as well as the 18 months following the initial implementation of the PAS algorithm to allow for comparison of the two cohorts. Data obtained from patient charts included basic demographic information, ED course, diagnosis, surgical consults, imaging done, PAS score, if patient was transferred from an outside hospital, and if an appendectomy was done. The primary outcome in this study is the number of CT scans conducted before vs. after the implementation of the algorithm. The secondary outcomes include number of ultrasounds performed, surgical consults, and appendectomy cases in the OR before and after the implementation of the algorithm.

Significance: Due to COVID-19 related delays with obtaining access to the UIHC patient database, data analysis for this project is still in progress. Once completed, the outcomes of this study will provide important information regarding the effectiveness of the PAS in the emergency setting, including number of CT scans and ultrasonography studies conducted. If it is determined that the algorithm is effective in reducing CT scans while maintaining diagnostic accuracy, we will then be able to work towards creating more educational resources to help increase its use including dissemination and implementation at nearby hospitals. Implementing this algorithm at regional hospitals could improve efforts to reduce unnecessary CT scans in this vulnerable population.

Demographics, risk factors, and obstetric complications at Tibebe Ghion Specialized Hospital, Bahir Dar, Ethiopia: A cross-sectional study

Student: **Jessica De Haan**
Mentor: Mary Rysavy

Background

The most recent data from Ethiopia shows a maternal mortality rate of 412 maternal deaths per 100,000. The concept of a maternal near-miss event, whereby a woman narrowly escapes death in a case of a severe obstetric complication, permits an examination below the tip of the maternal mortality iceberg to propose improvements that can prevent future deaths. Hypertensive disorders of pregnancy are a leading cause of maternal mortality and morbidity worldwide. In Ethiopia hypertension is estimated to complicate 6% of all pregnancies and contribute to 19% of maternal deaths.

Objectives

Investigate the patient population presenting for obstetric care at Tibebe Ghion Specialized Hospital (TGSH) in Bahir Dar, Ethiopia. Determine the prevalence and contributing factors for severe maternal outcomes (maternal near miss events), mortality, and particularly hypertensive disorders of pregnancy.

Methods

From Feb 26, to June 10, 2020, demographic and outcome data were collected on all delivering pregnant women at TGSH as part of a quality improvement initiative. Data were entered into a REDCap database using the REDCap mobile app. One of the on-site primary investigators reviewed the database for errors and reconciled concerning entries with original clinical charts. The WHO Maternal Near Miss (MNM) criteria modified for Sub-Saharan Africa was used to define maternal near miss events. Statistical analysis was performed by statisticians at both Bahir Dar University and the University of Iowa.

Results

Data was collected on 637 women at TGSH out of 658 total deliveries. The patient demographics showed a median age of 26 years old, estimated monthly income of 3000 birr ($84), and almost exclusively married. Thirty percent were unable to read and write, 29% had a primary level education, and 40% had a high school or college level education. About 75% of patients reported living in an urban area and 25% in a rural region. Living in a rural area showed an Odds Ratio of 3.71 for experiencing a MNM (p-value <0.001). The majority of patients were primigravida and nulliparous with full-term gestations. The majority of our patients had between 4-7 antenatal visits. Antepartum complications included hypertensive disorders of pregnancy (7.5%), anemia (5.3%), syphilis (3.1%), Hepatitis B (2.4%), gestational or pre-existing diabetes (1.5%), HIV (1.4%), and malaria (0.3%). There were 70 events that qualified as a maternal near miss event giving a MNM rate of 11%. Furthermore, having a hypertensive disorder of pregnancy showed an Odds Ratio of 10.41 for likelihood of experiencing a maternal near miss event (p-value <0.0001) and an increased risk of delivering a newborn with Apgar score <7 at minute 5 (OR 2.27, p-value 0.032). There were no recorded maternal deaths.

Conclusion

Our survey showed women presenting at TGSH reported to have slightly higher education status and income level, higher proportion from an urban area, and more antenatal care compared to women in prior studies from the region. TGSH had less than half of the MNM rate of the surrounding Amhara region. Hypertensive disorders of pregnancy were the largest contributor of risk for experiencing a severe obstetric outcome. This warrants further study into a quality improvement safety bundle implementation project that could reduce maternal near misses and prevent future maternal deaths. Encouraging at least 8 antenatal visits, as the WHO currently recommends, may yield the largest reduction of adverse outcomes due to early identification and treatment of hypertensive disorders of pregnancy.

Title: Qualitative Investigation of Facilitators and Barriers Associated with Adherence to Wahls and Swank Dietary Interventions

Authors: Cassidy Dean[1], Jacob Tinker[1], Mary Ehlinger[1], Tyler J Titcomb[1], Sandra E Daack-Hirsch[2], Terry L Wahls[1]

[1]University of Iowa Carver College of Medicine
[2]University of Iowa College of Nursing

Introduction: Preliminary studies evaluating dietary interventions among people with multiple sclerosis (pwMS) have observed favorable outcomes. However, due to the disabling symptoms of MS, pwMS have unique challenges in successfully implementing dietary changes. Per the WHO, less than 29% of patients are successful in implementing the recommended dietary changes, thus further information is needed to better understand how to facilitate adherence. A strong support system is thought to be key to successful adherence to dietary interventions; however, it is unknown whether dietary interventions increase feelings of burden among pwMS.

Objective: To inform future studies, this follow-up study was conducted to identify the facilitators and barriers associated with study diet adherence and to evaluate perceived burden and support among pwMS.

Methods: Participants who volunteered for long-term observation after completing a clinical trial evaluating two different popular diets among pwMS were contacted via Zoom or phone call and interviewed regarding their experiences with the study diets. Interviews were recorded and transcribed. A thematic codebook was created and interviews were coded and verified by two study investigators using MAXQDA software. Disagreements were discussed and resolved by a third study investigator. Themes among facilitators and barriers were identified. To assess burden and support, the participants were asked to complete the Self Perceived Burden Scale (SPBS) as well as the Multidimensional Scale of Perceived Social Support (MSPSS).

Results: All participants were female (n = 13, age = 51.5 ± 10.5 MS duration = 16.9 ± 9.8) with diagnosed Relapsing-Remitting MS (RRMS). The most common barriers to diet adherence were novelty, temptation, trouble eating required amounts, mindset and motivation, and lack of diet knowledge as the most significant theme. The most common facilitators to diet adherence included mindset and motivation, symptom improvement, positive support, dietitians and staff, and access to resources with positive motivation as the most significant theme. SPBS burden scores were 15.2 ± 1.6 on a 10-50 scale (10 = least burden; 50 = most burden). Total MSPSS support scores were 6.2 ± 0.9 on a 1-7 scale (1 = least support; 7 = most support). Hope for the future on a 1-10 scale (1 = no hope; 10 = extremely hopeful) had no significant change from 8.2 ± 2.2 to 9.0 ± 1.9 (P = 0.36).

Conclusion: The major themes regarding study diet adherence identified in this study are lack of diet knowledge and positive motivation. The study participants did not experience major feelings of burden while enrolled in this study, possibly due to the high level of perceived social support that was reported. Future dietary intervention studies could be improved by emphasizing frequent diet education and increasing the level of staff support throughout the study.

Title:
Comparison of virtual anatomy technologies for completing educational tasks using a decision matrix

Jordan Eisenmann M2,   Dr. Darren Hoffmann PhD

Introduction:
Current medical students are faced with an ever-growing amount of information to learn and retain during their training. One fundamental subject in medicine with a high density of knowledge is anatomy. While exploring potential solutions to support anatomy learning, students and educators will encounter dozens if not hundreds of programs and applications (apps) available at a reasonable price. While this may initially be seen as a boon, the quantity of options poses a new problem - finding the right app for their needs.

Hypothesis/ Aims:
We hypothesize that students and instructors will have distinct priorities in making decisions about purchasing educational anatomy technology. We further suspect that incorporating these priorities into the product review process (using a decision matrix approach) will allow for discrimination of closely-related products in the app marketplace to match a users needs.

Methods:
The decision matrix is an analytical tool used to assist entities in decision making. The tool first asks a person's subjective importance of a set of characteristics, and then asks the user to assess those characteristics in a set of products. In this study, we asked 10 CCOM students and 5 CCOM educators to evaluate the importance of 19 characteristics commonly found in anatomical learning apps on a 1-7 scale. The participants then completed three educational tasks each for three laptop-based apps: 3D Organon Anatomy (3DOrg), Human Anatomy Atlas 2019 (HAA19), and Complete Anatomy 2020 (CA20), which were identified in a prior study as superior over all other anatomy products in the app store. After completing these tasks, participants were asked to rate the quality (again on a 1-7 scale) of the same characteristics in each app. The "importance" rating is then multiplied by the "quality" rating for each of the 19 characteristics which are then summed for a total score for each app. The highest app total shows the preferred app for each individual participant. In addition to the decision matrix outputs, importance and quality data were directly compared by one way ANOVA and t-tests.

Results:
The decision matrix results showed that 6 students preferred CA20, 3 preferred HAA19, and 1 preferred 3DOrg. Of the educators, 2 preferred CA20, 2 preferred HAA19, and 1 preferred 3DOrg. The characteristics ranked as most important across students were: productivity/efficiency (6.500±0.5270), clear highlighting of structures (6.500±0.7071), and ability to switch between male and female models (6.300± 0.8233), all of which were significantly higher than several of the other characteristics, $p<0.05$. The characteristics educators ranked as most important were: level of detail (6.600±0.5477), intuitive controls (6.400±0.8944), and productivity/efficiency (6.400±0.8944), which were also significantly higher than many other characteristics, $p<0.05$. In free response prompts, both groups found CA20 to be highly detailed with many tools and options, but reported a substantial time investment to learn, and disliked the app's required yearly subscription. 3DOrg had the opposite issue as it had a very simple learning curve and was a one time purchase, but lacked detail and features. HAA19 fell between the two others in terms of detail and learning curve, and was also a one time purchase.

Conclusion/Discussion:
This study is a first step in the development of specific recommendations for virtual anatomy apps. These results will support students, educators and institutions who are choosing where to spend their money and invest their time on educational products. A clear limitation to the study was the small pool of participants only from one institution. Future study will aim to evaluate whether these trends are consistent at other institutions and across a broader population. These results can also be used to inform further studies where the decision matrix algorithm can be used to predict the most useful app for learners and test the reliability of the prediction model by evaluating satisfaction and learning outcomes.

Title: Pulmonary Embolism Imaging: Incidentals and Overtesting

Student: Jacob Elam, M3

Mentor: Prashant Nagpal, MD

Abstract:

Background: CT pulmonary angiography (CTPA) is one of the most ordered and frequently overutilized. There are multiple reasons for overutilization of the CTPA despite clinical guidelines in place to prevent that. One of the reasons for overutilization is added relevant diagnostic information that CTPA provides above and beyond ruling out pulmonary embolism (PE). Although such overutilization also adds to the medical expenditure due to incidental findings that may require follow-up.

Purpose: To study the incidental findings on CTPA exams in patients without PE and classify them as Type I, Type II or Type III depending on clinical significance.

Methods: We retrospectively analyzed 2083 CTPA exams which were negative for the diagnosis of PE between 2016 and 2018 at the University of Iowa Hospitals and Clinics. Incidental findings and patient demographics (Age, Sex, BMI, Site of referral) were noted. Incidental findings were further classified as: Type I, II and III. Type I findings included the incidental finding that may explain clinical symptoms, type II findings included the findings that required follow up, and type III included findings of limited clinical significance. The statistical significance between the type of inclidental findings and patient demographics was further studied using logistic regression model.

Results: Incidental findings are present in majority (56.46%; 1176/2083) of PE negative CTPA exams. 41.48% (864/2083) of PE negative CTPA exams showed a Type-I incidental; a finding that may explain clinical symptoms. However, 27.03% of CTPA exams showed Type-II incidentals (requiring follow-up). Two most common Type-I incidentals include Pneumonia (59.68%) and Fluid overload (23.16%). Two most common Type-II incidentals include progressive primary or metastatic disease (18.64%) and new or indeterminate lung nodule (18.49%). Males were found to be more likely to have Type 1 incidentals than females (OR = 1.07, 95% CI = [1.03, 1.18]). Increased age and lower BMI was shown to be significantly associated with increased odds of a Type 1 incidental (OR = 1.002, 95% CI = [1.001, 1.003] and OR = 0.993, 95% CI = [0.991, 0.995] respectively). ICU patient location had highest odds of having a Type-1 incidental and outpatient setting had lowest odds.

Conclusion: Significant proportion (41.48%) of CTPA exams, even when negative for PE show an 'incidental' finding that can explain patient symptoms of chest pain or shortness of breath. This may be one of an important driver for overuse of CTPA exams. However, with more than one fourth of cases have an incidental finding that needs follow-up contributing to downstream testing and increased health-care costs.

Identification of novel biomarkers in progression of Canine Leishmaniosis

Jonah M. Elliff, Eric Kontowicz, Breanna M. Scorza, Christine A. Petersen

Visceral leishmaniasis (VL) is a *Phloebotimine* sand fly transmitted neglected tropical disease caused by intracellular protozoan *Leishmania* parasites*.* Endemic in areas of the Middle East, Asia, East Africa, South America, and the Mediterranean region, VL is fatal if untreated causing approximately 20,000 deaths annually (WHO). Dogs are the primary reservoir host for *Leishmania infantum*. The disease caused by *L. infantum* in dogs, referred to as Canine Leishmaniosis (CanL), shares many clinicopathologic features with human VL. Infection leads to symptomatic disease in a minority of cases, and the early clinical manifestations are poorly understood in both canine and human disease. A better understanding of the clinicopathological patterns that precede disease progression will help project severity, guide treatment options, and pave the way for more effective prophylactic strategies. To better characterize clinicopathologic signs of early CanL and to identify biomarkers of progression, a cohort of dogs with asymptomatic *Leishmania infantum* infection was enrolled and followed over a course of 2 years. Blood was drawn every three months and a serum chemistry panel and complete blood count were performed. CanL clinical disease was measured via *Leishmania*-specific serology, qPCR to assess parasitemia, and physical examination. Using these parameters, we assessed and identified potential biomarkers of VL progression. These data will be incorporated into a predictive model to evaluate their roles as novel positive predictive values of leishmaniasis disease progression. These potential biomarkers include serum alkaline phosphatase, calcium, and the albumin/globulin ratio. Assessing these biomarkers will give both physicians and veterinarians better tools to assess the risk of progression of leishmaniasis and to inform and guide novel treatment strategies in dogs and humans with VL.

Natural Treated and Untreated History of Malignant Ureteral Obstruction Secondary to Ovarian Cancer

Kathryn Faidley, BA; Hannah Botkin, BS; Emily Hill, MD; Bradley A Erickson, MD, MS
Department of Urology

Introduction: Ureteral obstruction from advanced gynecological malignancies (such as ovarian cancer) is common, and can lead to pain, renal impairment, and urinary tract infection. Obstruction relief can be accomplished by placement of either a retrograde ureteral stent (RUS) or an antegrade percutaneous nephrostomy tube (PCN), both of which have unique benefits and disadvantages. The goal of drainage is to reestablish renal function, which is critical for these women, as many receive renally-excreted chemotherapy. However, the natural history of these obstructed renal units is poorly established, nor has it been determined which method of drainage is superior.

Purpose: Using an institutional cohort, we sought to determine the natural history of both treated and untreated ureteral obstruction secondary to ovarian cancer. Our primary goals were to: 1) determine which method of treatment was superior in terms of renal preservation and management complications 2) determine the rate, and predictors of, spontaneous resolution of hydronephrosis without the need for ureteral reconstruction and 3) assess the long-term survivability of the obstructed renal unit.

Hypotheses: 1) Percutaneous nephrostomy tube drainage will prove to be a superior method of drainage when accounting for renal preservation and complications. 2) Resolution of hydronephrosis will occur in fewer than half of the cases. 3) Renal units will continue to decline in function over the ovarian cancer treatment course despite drainage.

Methods: We conducted an IRB-approved retrospective cohort study of patients who were diagnosed with hydronephrosis secondary to ovarian cancer and were treated at the University of Iowa Hospitals and Clinics from January 2004 to December 2019. This data set consisted of 206 patients. Data was stored in an online REDcap database. Specific analysis included hydronephrosis treatment type (PCN vs. ureteral stent), creatinine levels, changes in treatment type, and post-treatment complications (recurrent UTIs, urinary incontinence/retention, dysuria, hematuria, flank pain, and rising creatinine). We assessed for hydronephrosis resolution, which was defined as the ability for clinicians to remove the ureteral stent and/or PCN drainage without recurrent or persistent hydronephrosis or having the patient undergo reconstructive surgery. Chi-squared tests were used to compare the number of patients with stent vs. PCN that experienced each complication. Other variables of interest included degree of hydronephrosis, FIGO stage, cancer treatment received, age, and BMI. These variables were assessed (via chi-squared tests or t-tests) for their ability to predict for hydronephrosis resolution.

Results: Of the 2,580 patients that were diagnosed with ovarian cancer at UIHC from January 2004 to December 2019, 206 (8.0%) developed hydronephrosis over time. Of these 206 patients, 127 (61.7%) had their hydronephrosis treated (with either stent or PCN). Patients were untreated either because their hydronephrosis was not clinically significant (n=43) or because they were placed on hospice and/or renal drainage would not affect cancer treatment (n=34). Of the treated patients, 92 patients (72.9%) initially received a stent, while 35 (27.3%) initially received a PCN. Fewer patients experienced overall complications when initially treated with PCN (68.6%) vs. stent (84.8%) (p=0.04) with differences being most pronounced with dysuria (38.5% vs. 8.6%, p=0.001) and treatment failure (i.e. hydronephrosis persistence; 51.3% vs 2.9%, p=7.4E-07). The number of patients who experienced rising creatinine when treated with stent (34.2%) was not significantly greater than when treated with PCN (31.3%) (p=0.77). Spontaneous hydronephrosis resolution was experienced in only 30 patients (23.3%), with the median time-to-resolution being 207 (+/- 272.1) days. Earlier cancer stage (p=0.038) and worse pre-treatment calyceal blunting (p=0.008) were the only factors that predicted for resolution, while the other predictors assessed did not. Of the 99 patients that did not experience resolution with stent or PCN, only 2 (2.1%) underwent definitive reconstruction of their ureter.

Conclusions/Discussion: Overall, resolution of hydronephrosis secondary to ovarian cancer is rare. Management with ureteral stent is more common than PCN, but appears to lead to more complications. Lower stage and worse pre-management hydronephrosis (in the form of calyceal blunting) predicts for eventual hydronephrosis resolution. Very few patients without resolution undergo reconstruction, indicating a possible opportunity for improvement in care. We anticipate that patients with no evidence of disease and persistent hydronephrosis will benefit from ureteral reconstruction.

An Assessment of Provider's Knowledge in Firearm Safety and Terminology

Authors: Christian Findlay, BFA, NREMT; Karisa Harland, BA, MPH, PhD
Contributors: Priyanka Vakkalanka, ScM, PhD Candidate; Morgan Bob-Swanson, PhD Candidate
Department of Emergency Medicine, University of Iowa Hospitals and Clinics

Abstract

Background: In the United States (US) firearms are responsible for nearly 40,000 deaths each year and are the second leading cause of injury related deaths. To date, little is known about the medical community's understanding of basic firearm safety terminology and protocols. Furthermore, many of the studies on the topic of firearm safety have focused on the providers' subjective opinion in assessing their comfort with firearms safety rather than testing the providers' knowledge.

Purpose: The purpose of this study was to asses healthcare provider knowledge at the University of Iowa's Hospitals and Clinics (UIHC) in regard to basic firearm safety protocols and terminology. The study also assessed provider opinions on a 5-point Likert scale on the current state of firearm trauma within the US and whether providers have a duty to address firearms violence.

Methods: A Qualtrics survey was sent out to departments within UIHC that were highly likely to play a role in firearms counseling. These departments included the department of Emergency Medicine, Family Medicine, Internal Medicine, Obstetrics, Paediatrics, Psychiatry, and Surgery. Providers eighteen years of age and older with a professional medical degree – MDs or the international equivalent thereof, DOs, Advanced Registered Nurse Practitioners, and Physician Assistants – were eligible to participate. It should be noted that participants were permitted to skip questions they did not wish to answer, which led to a varying number of participants for each question.

Results[*]: To date, a total of 214 UIHC providers consented to participate in the survey and 151 providers have completed the entire survey. From the 151 UIHC providers that completed the survey, 29.1% were from pediatrics and 25.2% were from internal medicine. Both family medicine and obstetrician & gynecology each contributed 9.9% of the completed responses; the remaining specialties represented 26.1%. A total of 13.5.% (20/148) of the survey sample were firearm owners.

In response to the statement: "I believe firearms injuries are a public health crisis," 88.7% (173/195) of UIHC providers either strongly agreed (62.6%) or somewhat agreed (26.2%). Only 5.6% of these providers (n=11) either strongly disagreed (1.5%) or somewhat disagreed (4.1%) with the statement. In response to the statement: "I believe that physicians (as a profession) have a duty/obligation to address firearms violence," 77.4% (151/195) of UIHC providers either strongly agreed (48.7%) or somewhat agreed (28.7%). Only 9.3% of these providers (n=18) either strongly disagreed (2.6%) or somewhat disagreed (6.7%) with the statement.

In two clinical scenarios UIHC providers were asked to recognize firearm safety recommendations made by the American Academy of Pediatrics (AAP) and the American Medical Association (AMA). In a third clinical scenario providers were asked how to counsel a patient that purposely declined to follow these recommendations. A total of 69.0% of UIHC providers (127/184) recognized that "the safest home for a child is one without firearms," as recommended by the AAP. 92.3% of UIHC providers (168/182) recognized "that all guns in the home should be locked and unloaded, with the ammunition stored separately," as recommended by the AMA. However, only 28.3% of UIHC providers (51/180) were correctly able to identify the safest possible alternative in a clinical scenario where the patient declined to follow the AMA's guideline. Nearly half of all UIHC providers surveyed (47.2%, 85/180) reported not knowing how to counsel a patient that declined to follow the AMA's recommendation. Moreover, nearly a quarter of providers (24.4%, 44/180) chose an incorrect answer in the scenario where patient declined to follow the AMA's firearm safety recommendation.

Conclusion: Most providers at UIHC seem to believe there is a firearms trauma public health crisis and that physicians have a duty/obligation to address this crisis. Our survey suggests current guidelines being put forth by well-established medical organizations, such as the American Academy of Pediatrics and the American Medical Association, are reaching their intended audience. However, in this study, when a patient intentionally deviates from these recommendations most providers at UIHC were unsure how to properly counsel the patient. Moreover, our data currently indicates that many UIHC providers are deficient in knowledge regarding basic firearms protocols and terminology. Establishing basic firearms safety education will create a solid base of knowledge from which UIHC providers can establish credibility with firearm owners thus reducing the potential risk that providers may lose credibility with individuals whom they wish to counsel. The data strongly supports that firearm safety training education and utilizing a harm-reduction approach may benefit many providers at UIHC who are unsure of how to counsel patients that decline to follow the AAP and AMA firearm safety guidelines.

[*]At the time this abstract was written for the Medical Student Research Conference at the Carver College of Medicine data from the study was still being collected and analyzed.

Procedural Pain in Burn Patients - Quality Improvement Project

Zachary Fleishhacker, BS; Colette Galet, PhD; Lucy Wibbenmeyer, MD

Background. Burn pain management has been on the forefront of research in burn care due to the sequela of inadequate pain control including PTSD, suicidal ideation, and depression. Burn injury patients experience pain in three forms: background pain, procedural pain during daily wound cleaning, and break through pain. Multimodal pain therapy is used to treat burn pain. This therapy uses multiple drugs that act synergistically to reduce pain and decrease overall opioid use. Drugs used in multimodal pain control include antipyretics, anti-inflammatory drugs, benzodiazepines, antihistamines, and neuroleptics. However, opioids remain the mainstay therapy for controlling pain during procedures. Along with the known ceiling effects of opioids such as nausea/vomiting, opioid induced hyperalgesia, and addiction, surgeons staffing the UIHC burn unit have noticed that pain control often is not satisfactory for burn patients during wound care.

Purpose. The purpose of this quality improvement project (QI) was to assess our current practices regarding procedural pain control management in the UIHC burn unit. We hypothesized that procedural pain control in burn patients during wound cleaning (hydrotherapy) is not adequate as measured by pain and satisfaction scores.

Methods. Burn patients admitted to the UIHC burn unit were surveyed over the months of June-August 2020. Patients who were pregnant, incarcerated, or unable to understand and answer study questions were excluded. Demographics, comorbidities, injury related data, and admission data were collected. Pain scores (Numeric Rating Scale, NRS 1-10), sedation scores (Riker Agitation-Sedation Scale (RAS) 0-6), patient and nurse satisfaction scores (1-10), anxiety level (0-10) and event recall data (cards and events) were collected by surveying nurses and patients before, during, and after hydrotherapy. A single patient could be surveyed for up to three hydrotherapies. Descriptive statistics were obtained. Paired t-tests and one-way ANOVA were performed to assess significant differences between pre and post procedure patient pain scores and satisfaction ratings across encounters, respectively using SPSS 25.0. $P < 0.05$ was considered significant.

Results. Twenty-eight patients and 48 hydrotherapy events were surveyed; 82.1% were male, the average age was 44.8 (11-94) years, average percent body area burned (TBSA) was 11.9% (1-46.5%), and the average length of stay was 6.8 (1-24) days. Pain scores post procedure significantly increased compared to pre-procedure scores on the first encounter (n = 28, 5.4 vs. 6.3; p = 0.04) and second encounter (n = 14, 5.0 vs. 6.71, p = 0.01), but not on the third encounter (n = 6; 6.0 vs. 6.7, p = 0.1); the lack of significance may be associated with the small sample size for the last encounter. No significant difference in patient satisfaction scores regarding their pain control during hydrotherapy was observed when comparing scores obtained on the first, second, and third encounters (7.3 vs. 8.50 vs. 8.17, p = 0.18). Nurse satisfaction scores with their patient's pain control were similar across encounters (7.4 vs. 7.2 vs. 7.2, respectively, p = 0.96). Nurses were also asked to rate the ease of performing the procedure from 1-10, with 10 being the easiest. Similarly, no significant difference was observed across encounters (9.0 vs. 7.8 vs. 7.5 respectively, p = 0.09). Across all encounters, no adverse events (oxygen desaturation <92% or somnolence as measured by RAS scale <2) were observed.

Discussion. This survey highlights three areas of improvement. First, baseline pain control is unsatisfactory with the average pain score ranging from 5.39-6.0. Good clinical practice aims to achieve <3 and acceptable to the patient on the NRS. Secondly, procedural pain control (6.3 - 6.7) while not that much higher than baseline, could be improved judging by patient satisfaction ranging from 7.3 - 8.5. Finally, nurses rated low satisfaction with pain control (7.2 – 7.4) and ease of completing procedures falling from 9.0 to 7.5. This is important as poor nurse satisfaction with their patient's pain control may lead to inadequate wound care, increased moral distress, and higher rates of burnout. Altogether, these data support the implementation of changes in pain management, both background and procedural. Future goals of this QI project include reviewing timing and amount of procedural medications on pain control and amnesia. The overarching goal of this QI is implement the use of a patient-controlled analgesia (PCA) device with a midazolam/ketamine cocktail for pain control during hydrotherapy.

Return to Sport in Surgical and Conservative Management of Knee Injuries in Collegiate Wrestlers

Authors: Kory Ford, M2[1]; Jerrod Keith, MD[2]; Robert Westermann, MD[3]

[1]Carver College of Medicine, University of Iowa, Iowa City, IA
[2]Department of Plastic and Reconstructive Surgery, University of Iowa, Iowa City, IA
[3]Department of Orthopedics and Rehabilitation, University of Iowa, Iowa City, IA

Background: Wrestling is known to be a sport of relatively high injury incidence, and knee injuries account for a large percentage of those injuries. Injuries may be treated conservatively with ice, physical therapy, medications, and/or injections, or alternatively, treated surgically. It is hypothesized that knee injuries that may be treated with surgery can instead be effectively treated conservatively leading to a faster complete recovery and return to sport (RTS).

Purpose: The purpose of this study was to analyze knee injury characteristics, RTS times, and other key recovery metrics of wrestlers with knee injuries managed either conservatively or surgically in order to identify injury trends and determine the efficacy and necessity of surgery for common knee injuries in wrestlers.

Methods: Wrestlers at the University of Iowa who had sport-related knee injuries reported on the team Sports Injury Management System from 2010 to 2020 were identified. 173 injuries from 77 wrestlers were analyzed and key characteristics were recorded through a retrospective chart review. These included wrestler (age, weight class), injury (diagnosis, side, date of injury, date removed from participation, acute/chronic, mechanism, activity, if recurrent), and recovery (management, RTS, days, practices, and games missed) metrics. Variables were compared using a two-tailed t-test assuming unequal variance with significance set at $p < 0.05$.

Results: Of the 173 knee injuries identified, 128 were treated conservatively with an average RTS of 12.5 ± 24.7 days, while 45 were treated with surgery with a RTS of 100.9 ± 105.5 days which varied significantly ($p < 0.01$). 160 were acute injuries while 13 were chronic with no significant difference in RTS. There was a significantly longer RTS among 38 recurrent injuries compared to new injuries ($p < 0.05$). Injuries were stratified to compare management and RTS of similar injuries. Among the 83 ligamentous injuries (ACL, MCL, LCL, PCL), all of the MCL, LCL, and PCL injuries in this study were treated conservatively. 9 out of 11 ACL injuries were treated with surgery. Greater variation was found in meniscus and patellar injuries; out of 44 meniscus injuries, 14 were treated conservatively for a RTS of 4.0 ± 10.7 days and 30 were treated surgically for a RTS of 49.6 ± 41.9 days, which varied significantly ($p < 0.01$). 17 out of 22 patellar injuries such as prepatellar bursitis were treated conservatively with a RTS of 15.1 ± 24.8 days, whereas 5 were treated surgically with a RTS of 87.2 ± 52.9 days, which did not vary significantly ($p = 0.11$).

Conclusions: A clear trend of surgically treating ACL injuries and conservatively treating non-ACL ligamentous injuries was evident, with insufficient power to determine the efficacy of conservative treatment on ACL injuries. Meniscus injuries had a quicker RTS with conservative treatment, while patellar injuries showed no significant difference between treatments. This study can be used to help guide clinical judgement and adjust treatment algorithms for future knee injuries in wrestlers. Subsequent studies should focus and expand on areas of significant variation in treatment, such as meniscus and patella injuries, and compare management results across several institutions to incorporate varying treatment philosophies.

Title: Normative value for the 6-minute walk in pediatric patients with Fontan Physiology

Authors: Clara Garcia BS, Jen Maldonado BS-RTR, Ben Reinking MD

Introduction: Patients with single ventricle congenital heart disease undergo a series of staged surgical procedures between birth and 3 years of age which divert superior and inferior vena cava flow directly to the pulmonary arteries. This cardiovascular state, commonly referred to as Fontan physiology creates stable circulation from childhood to adulthood with good quality of life and few clinical symptoms. The absence of a sub pulmonary ventricle leads to term consequences, including hepatic fibrosis and congestive heart failure, Early changes in exercise tolerance may help guide medical therapy which could alter this natural history.

Aims: The primary aim of this study was to establish normative values for the 6-minute walk in patients with Fontan physiology. The secondary aim was to determine factors associated with total distance walked.

Methods: A single center retrospective review of age was performed to identify patients who completed a 6-minute walk at the University of Iowa Stead Family Children's Hospital between 10/1/17 and 6/1/20. Demographic data (gender, dominant ventricle, type of Fontan, presence of fenestration), serum pro-brain naturetic peptide levels, and results of the 6-minute walk were compared using descriptive statistics, students- t-test. and ANOVA

Results: Fifty-five patients completed 81 walks. The cohort was: 63% male, 67% right ventricle dominant, 91% extracardiac conduit, and 40% fenestrated at the time of Fontan 225 pg/ml as the average BNP level, and average age was 10.4 +/- 3.4 years at walk. Results of the walk are summarized below.

6 Minute Walk Data (n=81)			
	Mean	**SD**	**Range**
Resting Heart Rate (bpm)	88	18	48-130
Resting Systolic Blood Pressure (mm Hg)	103	10	92-132
Resting Diastolic Blood Pressure (mm Hg)	62	9	40-86
Resting Oxygen Saturation (%)	90	3	74-98
Peak Exercise Heart Rate	121	20	66-162
Peak Exercise Oxygen Saturation (%)	84	5	69-93
Recovery Heart Rate (bpm)	96	19	54-144
Recovery Systolic Blood Pressure (mm Hg)	109	11	82-140
Recovery Diastolic Blood Pressure (mm Hg)	65	8	40-09
Recovery Oxygen Saturation (%)	90	4	74-97
Total Distance Walked (Ft)	1619.35	302.98	450-2400
MET	3.34	0.437	1.65-4.5

Neither ventricular morphology ($P< 0.079$) nor gender ($p< 0.77$) significantly impacted walk performance.

Increasing age positively correlated with increased distance walked.

Conclusion: our study established normative 6-miunte walk values for patients with Fontan physiology.

Development of an in vivo model for Neuromyelitis Optica Spectrum Disorder in Long Evans Rats

Cheyanne R. Godwin[1], Delaine K. Quaresm[2], Oliver W. Gramlich[2,3]

[1]Carver College of Medicine; [2]Iowa City Veterans Affairs; [3]University of Iowa Department of Ophthalmology

Purpose: Neuromyelitis Optica spectrum disorder (NMOSD) and Myelin Oligodendrocyte Glycoprotein (MOG) antibody associated disease (MOGAD) are autoimmune demyelinating disorders. NMOSD and MOGAD patients present with different patterns and disease courses with optic neuritis and transverse longitudinal myelitis both leading to eventual paralysis and blindness. In NMOSD autoantibodies bind to Aquaporin 4 (AQP4) on astrocytes leading to complement mediated astrocytopathy with secondary demyelination and neuronal cell death. In MOGAD autoantibodies are generated against the myelin sheath protein MOG leading to demyelination and subsequent neuronal cell loss. Currently there is a lack of animal models that recapitulate optic neuritis and vision loss seen in NMOSD and MOGAD. Those animal models are urgently needed to develop new treatments. Our aim is to develop a novel in vivo model for NMOSD using recombinant anti AQP4 antibodies and for MOGAD using human serum with MOG autoantibodies injected into the optic nerve sheath of Long Evans rats.

Methods: Long Evans rats were anesthetized with ketamine/xylazine and received a unilateral injection of either MOGAD serum (MOG group, n=10) or recombinant AQP4 antibodies (NMO group, n=10) into the optic nerve sheath. The contralateral, uninjected eyes and a naïve group served as controls. 21 days post injection retinal structure and function was assessed using optical coherence tomography (OCT), flash and pattern visual evoked potential (VEP), and pattern electroretinogram (pERG). Post-mortem analysis included H&E and Luxol fast blue (LFB) staining to determine infiltration and myelination in optic nerves.

Results: NMO injected eyes showed significant thinning of the retinal ganglion cell (RGC) complex on OCT imaging compared to either naïve (p=0.007) or uninjected, contralateral control eyes (p=0.03). pERG P1 amplitude was reduced compared to naïve rats in NMO (p=0.007) and MOG (p=0.04) injected eyes. Likewise, the pERG P1-N2 amplitude was decreased in MOG injected eyes compared to naïve (p=0.004) and in NMO injected eyes compared to naïve (p=0.004) and uninjected (p=0.02) eyes. Flash VEP P2 latency was significantly prolonged in NMO injected eyes compared to naïve rats (p=0.03), but not in MOG injected eyes. Pattern VEP N2 amplitude was reduced in NMO injected eyes when compared to naïve (p=0.0001) and uninjected (p=0.0001) eyes, as well as in MOG injected eyes compared to naïve (p=0.0001) and uninjected (p=0.015) eyes. Post-mortem H&E histology showed increased cellularity and evidence of disorganization in the injected optic nerves and a mild reduction in LFB saturation, an indication of demyelination.

Conclusion: Our data suggest that injection of anti-AQP4 antibodies or MOG antibody positive serum into the optic nerve sheath of Long Evans rats leads to an ocular phenotype that is similar to what is observed in patients with NMOSD or MOGAD respectively. NMOSD and MOGAD patients suffer from optic neuritis with demyelination and neuronal cell death which differs in timing of onset and recovery. In our animals, we observed that RGC complex thinning and reduced pERG amplitudes which indicates RGC degeneration is more prominent in the NMO group. Likewise to patients, animals having received NMO or MOG injections demonstrate prolonged conduction speed due to demyelination. In summary, our model can be used to induce the ocular phenotype of NMOSD and MOGAD.

The Effect of SARS-CoV-2 (COVID-19) on Food Insecurity in a High-Risk Obstetrics Population

Anna Greenwood, Ailynna Chen, MPH, Deepika Raghavan, Katherine Merritt, MSc, Michael Haugsdal, MD, Craig Syrop, MD, MHCDS

Background: The Upstream Clinic is a quality improvement initiative identifying and addressing social determinants of health in high-risk obstetric (HROB) patients attending an academic medical center in Iowa. Food insecurity is a social determinant of health associated with higher risk for chronic diseases such as cardiovascular disease and hypertension as well as higher annual healthcare expenditures. In 2017, 11% of Iowans were food insecure with rural populations experiencing higher rates of food insecurity. Vulnerable populations, such as patients in HROB, are at risk of experiencing food insecurity during the SARS-CoV-2 (COVID-19) pandemic with the recession's increased economic insecurity, reduced school lunch programs, and broader demand for charitable feeding systems such as food banks and pantries. The aim of this analysis is to address the change in prevalence and interplay of rurality and food insecurity in a vulnerable HROB population prior to and during COVID-19.

Methods: Convenience sampling of patients attending HROB visits at an academic medical center was performed using validated food insecurity survey questions (Health Leads). Seasonally-matched data from March - June 2019 (pre-COVID-19) and March - June 2020 (during COVID-19) were extracted. Self-reported food insecurity was assessed at successive prenatal visits. Patients acknowledging food insecurity ("screen positive") prior to March 2020 were offered in-person counseling identifying nutritional resources in the patient's residential area; however, counseling was halted due to COVID-19 restrictions. Rurality coding of a patient's residence was assigned according to the Office of Management and Budget designations. Statistical analysis assessed food insecurity prevalence and correlation with rurality using Chi-square calculations.

Results: Screening results of pre-COVID-19 (N= 525) and COVID-19 (N=662) time frames were analyzed. Compared to the Pre-COVID-19 period, the percentage of positive screenings for food insecurity was significantly higher during the COVID-19 timeframe (COVID-19,11.5% vs Pre-COVID-19, 7.8%, p=0.04). There was no difference in screen positive rates between rural and urban counterparts during either the pre-COVID-19 or COVID-19 timeframes. However, patients from rural counties experienced nearly twice the increase in positive food insecurity screens during COVID-19 compared to the pre-COVID timeframe (13.8% vs. 6.5%, p=0.04).

Conclusion: The acute effects of the COVID-19 pandemic impacted many in healthcare and continue to highlight existing disparities in social determinants of health and health equity. Our findings in a high-risk obstetrics population demonstrate that COVID-19 has been associated with an increase in self-reported food insecurity, particularly in rural counties. With impacts on maternal health, newborn development, and chronic diseases, food insecurity represents a significant issue for healthcare outcomes and expenditures in the United States. Providers and health systems should consider the deleterious effect of this pandemic on food insecurity and our patients' long-term health and should consider ways of intervening upstream through effective screening and mitigation.

Identity-Based Mistreatment and Sexual Harassment of Medical Trainees at the Carver College of Medicine

Destinee Gwee MS4, Lauren Hock, MD, Nkanyezi Ferguson, MD, Denise Martinez, MD, and Patrick Barlow, PhD (Mentor)

Introduction:
In a time of social unrest regarding the inequity faced by Black communities in the US, medical providers and systems are reflecting on how systemic racism impacts the health outcomes of our patients. As we reflect on these issues, we also need to ask ourselves how race and other forms of identity impact the treatment and well-being of our medical trainees. Dr. Lauren Hock discusses the prevalence of sexual harassment toward female medical trainees (Hock, 2020). Previous surveys of surgical residents showed correlation between mistreatment and burnout and suicidality. These issues have not been explored in-depth in medical and PA student population.

Purpose:
The purpose of this study is to assess for the prevalence of identity-based mistreatment and sexual harassment of medical trainees (medical and PA students) at the University of Iowa Carver College of Medicine as well as the perceived impact that mistreatment had on professional development and well-being. This survey also served to identify decisions and behaviors around reporting mistreatment and any barriers to reporting that students identified.

Method:
We developed and distributed a novel survey instrument to all current and recently graduated MD, MD/PhD, and PA students (N = 639). Students were asked to report their prior personal experience with five common forms of harassment and discrimination: 1) Gender Identity, 2) Race/Ethnicity, 3) Sexual Orientation, 4) Religion, and 5) Nationality/Country of Origin as well as experiences with sexual harassment, specifically. Participants were asked to identify the frequency of their experiences as well as the source(s) of the behavior and the impact of their experiences on personal and professional well-being. We also asked about observing harassment and discrimination, and reporting behaviors when incidents occurred.

Data were analyzed using a combination of qualitative thematic coding (narrative comments), descriptive statistics such as measure of central tendency, spread, and frequency distributions, and inferential statistics for specific hypotheses. Dichotomous variables were analyzed univariately using chi-square tests of independence and fisher's exact tests, as appropriate, then logistic regressions were used to examine more complex relationships. We analyzed the continuous data with a combination of independent t-tests, analysis of variance (ANOVA), and linear regression.

Results:
A total of 231 (36.2%) students agreed to participate in the survey. The sample was predominantly white (85.2%), female (61.8%), and we had balanced representation of M2s (23.6%), M3s (24.8%), and M4s (28.5%). 45 (23.4%) and 57 (29.7%) students reported personally experiencing at least one form of discrimination and harassment, respectively, while 55 (28.6%) and 48 (25%) reported *observing* at least one form of these two types of mistreatment. Harassment based on gender identity and sexual harassment were the two most experienced forms of mistreatment, overall. Women were nearly three-times *more* likely to experience at least one form of discrimination (OR = 2.88, p = 0.018) and almost *eight* times more likely to experience harassment (OR = 7.8, $p < 0.001$). Similarly, BIPOC students were 5.14 times more likely to experience discrimination ($p < 0.001$) and 2.75 times more likely to experience harassment (p = 0.011). By contrast, White men were 97% *less likely* to personally experience any form of harassment compared to all others (OR = 0.03, 95% CI = 0.004 − 0.25, p < 0.001). Seventy-one percent of the students experiencing either harassment or discrimination reported that patients and/or patient families/visitors were the source of the behavior. Women were 5.44 times more likely to experience mistreatment from this source compared to men ($p < 0.026$).

Conclusion/Discussion:
Mistreatment in the forms of harassment and discrimination are common among medical and PA students at the Carver College of Medicine. Students that are female and/or non-white are most vulnerable to mistreatment. These results mirror recently completed surveys in our university's residency populations. While we were fortunate enough to hear the stories of mistreatment so many students experienced through this survey, several expressed that they did not feel comfortable sharing their experiences of mistreatment for fear of negative impact or retaliation. These views were shared on the last item of the survey, so we suspect the number of students who chose not to respond to the survey at all for those reasons may be higher.

Our results establish a troubling problem that must be acknowledged and addressed fully and aggressively. While the majority of mistreatment reportedly occurs at the hands of patients, there is a role for *all* members of our community from student peers to residents, faculty, and collegiate leadership in becoming actively anti-mistreatment. Professional development at all levels of our organization coupled with creating a safe and supportive environment for students to feel believed and protected when they choose to report their experiences will be key to changing culture. We plan to expand this project to a multi-site, national scale beginning in October, so that we can assess the degree to which the findings in the current sample are reflective of undergraduate medical training more broadly.

Pioneering the Use of Virtual Reality in Medical Education at UIHC: Immersively Teaching Transposition of the Great Arteries in Pediatric Cardiology

Jordan Haarsma M2, Anthony Zhang M2, Ravi Ashwath MD

Background: Virtual Reality (VR) is at the cutting edge of medical innovation and is a field with enormous potential, particularly in regard to medical education. 3D-modeling is also increasingly used in Pediatric Cardiology. Models are commonly printed for pre-surgical evaluation and/or as educational tools for trainees. However, the segmentation process to build 3D heart models is time consuming, requiring expert operators and is expensive.

The purpose of this pilot project, using headset-driven virtual reality interfaces, is a novel concept at the University of Iowa Hospitals & Clinics (UIHC). This uses a module series educating participants about one of the five cyanotic congenital heart defects: Transposition of the Great Arteries. The study evaluated the effectiveness of a module series in comparison to traditional teaching methods, with a secondary aim of developing and standardizing the process of creating more disease specific heart modules for educational use in the department.

Methods: Using Mimics© Medical 22.0, CT-scan DICOM images of a d-TGA heart lesion were segmented and converted to .ply files, a 3-D printable format. These .ply files of the heart models were exported to open-source design software Blender© for further processing suitable for VR. An educational module series for d-TGA of approximately 1-hour length was developed utilizing the Enduvo® software.

Participants (n=14) recruited from within UIHC consisted of medical students, residents, fellows, and physicians. Participants were then given a pre-test quiz, experienced the immersive VR module using an HTC-Vive headset, and given a post-test quiz with a brief survey about the entire experience, in that order. The survey questions asked for the extent of agreement to statements about the experience on a 10-point scale (10 being maximal agreement).

Results: Participants showed an increase in their knowledge score from the pre-quiz to the post-quiz (Δ +2.7/10, SD=1.3). Quantitative survey responses indicated participants perceived the experience positively. Participants agreed that the modules were easy to use (7.6/10, SD=1.8), efficient (8.8/10, SD=1.4) and more effective for their learning than conventional classroom-type lectures (8.4/10, SD=2.4), articles (9.1/10, SD=1.6), and even hands-on experience (7.4/10, SD=1.9). No participants experienced any nausea or dizziness.

Qualitative responses to the Virtual Reality experience were mostly positive. Representative positive feedback included "This was amazing. A great way to learn..." and "Mind blowing experience." Critical feedback included discomfort with headset positioning and an issue with image rendering in one module.

Medical student researchers continued building teaching resources, including similar one hour module series for the other cyanotic heart defects (Truncus Arteriosus, Tricuspid Atresia, Tetralogy of Fallot, and Total Anomalous Pulmonary Venous Return), along with a library of many more models of heart defects for independent exploration within the VR interface.
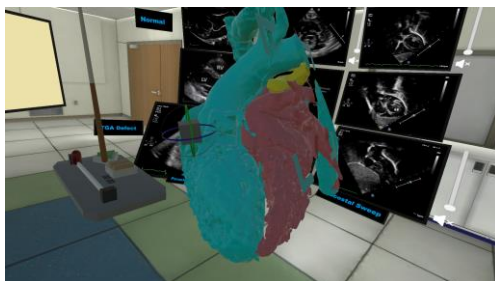

Figure 1 – Image from the Echocardiogram module within the Transposition of the Great Arteries series on the Enduvo Virtual Reality platform. Foreground: A 3-D dTGA heart model can be seen. Background: three rows of echocardiograms can be seen (left-to-right: parasternal long axis views, parasternal short axis views, subcostal sweep views; top-to-bottom: normal echocardiogram videos, labeled normal echocardiogram images, TGA defect echocardiogram videos).

Conclusions: This study is promising in increasing the real value for VR in pediatric cardiology education and potentially beyond, both in terms of efficacy and being cost effective, though the work suffers from the absence of a control condition for the knowledge evaluation. In contrast to past research indicating the need for expert operators for segmentation, this work indicates viability of less specialized staff in resource development, allowing for potential scalability and diversification of the resources built in this modality.

Title: Assessment of a three-generation pedigree with Fuchs endothelial corneal dystrophy

Authors: Josh Hagedorn, John H Fingert, MA Greiner, DC Terveen, JM Vislisel, BR Roos

Background: Fuchs endothelial corneal dystrophy (FECD) is a degenerative disorder of the cornea. It affects the thin layer of cells that line the back of the cornea called the endothelium. The role of the endothelium is to pump excess fluid out of the cornea. Disease progression occurs when these cells slowly start to die off. Over time, as the cell loss increases, the remaining endothelium is unable to sufficiently drain the corneal stroma, leading to fluid accumulation, guttae, which present as partial Descemet membrane thickening, clouding of the central cornea, decreased visual acuity, and bullae, which can be painful. Fuchs endothelial corneal dystrophy is one of the leading causes of corneal transplant in the United States. Additionally, it is estimated that over 4 percent of people 40 or older in the United States have Fuchs dystrophy.

Fuchs endothelial corneal dystrophy (FECD) has a significant genetic component to its pathogenesis and several genetic risk factors for FECD have been discovered. The first genetic risk factor for FECD, transcription factor 4 (*TCF4*), was detected by a genome wide association study. A trinucleotide repeat, (CTG)n also known as CTG18.1, is located within an intron of the *TCF4* gene. Expansion of the *TCF4* trinucleotide repeat is associated with FECD and expansion to 440 repeats confers a hazards ratio of 1.64 for a corneal transplant. Anticipation, earlier onset of disease with increasing severity in successive generations, occurs in diseases caused by trinucleotide repeat expansions (ie, Huntington's disease).

Purpose: We investigated the potential role of *TCF4* trinucleotide repeat expansion in a three-generation pedigree with a history suggestive of anticipation. The size of the *TCF4* trinucleotide repeat was evaluated in members of the FECD pedigree to determine if an expansion of the repeat might be the source of anticipation. The youngest patient in the pedigree was 27 years old with severe disease, her mother was 48 years old with moderate disease, and her grandmother was 63 years old with very mild disease.

Method: FECD was diagnosed via slit lamp biomicroscopy by a board-certified ophthalmologist with cornea fellowship training, graded using a modified Krachmer scale of 0 (no disease)–6 (45 mm of central confluent guttae with corneal edema), and examined via confocal microscopy and corneal tomography. The *TCF4* trinucleotide repeat was amplified from family member DNA samples with the polymerase chain reaction, cloned, and sequenced using standard methods. Each family member's genome has two copies of the *TCF4* gene. Analysis of these DNA sequences revealed the exact number of *TCF4* trinucleotide repeats in each family member's genome.

Results: The grandmother, mother, and daughter had 19 and 28, 19 and 26, and 24 and 26 CTG repeats in *TCF4* genes, respectively.

Discussion: All three family members with FECD had less than 40 *TCF4* trinucleotide repeats. While larger numbers of *TCF4* trinucleotide repeats confer higher risk for FECD, 20% of patients with FECD have fewer than 40 repeats as in this pedigree. Moreover, there is no expansion of *TCF4* trinucleotide repeats in successive generations of the pedigree. These data demonstrate that anticipation of FECD in this pedigree is not due to trinucleotide repeat expansion in the *TCF4* gene. The earlier age at diagnosis and severity of FECD in offspring of this pedigree may be due in part to ascertainment bias and/or other genetic and environmental factors. However, the *TCF4* trinucleotide repeat may underlie anticipation in other FECD pedigrees with patients that have larger numbers of repeats than were observed in this study. Moving forward, we have submitted all three patients for complete genome sequencing to evaluate the *SLC4A11* and *COL8A2* genes for genetic loci linked to FECD.

The Impact of Juvenile Diffuse Traumatic Brain Injury on Chronic White Matter Dysfunction

Joe Haight, Zili Luo, Alex Bassuk, Elizabeth Newell
The Stead Family Department of Pediatrics, UIHC

Abstract

Background: Traumatic brain injury (TBI) is currently a leading cause of death and disabilities in the United States. The traumatic axonal injury and dysmyelination that occur in diffuse brain injury disrupt neural networks necessary for cognition and executive function. Children under 4 years of age have one of the highest rates of TBI and require special consideration because their nervous systems are still maturing at the time of injury. Myelin, the insulating layers of membrane wrapped around axons by oligodendrocytes, is essential for normal impulse conduction. Myelination correlates with cognitive development and can be regulated by impulse activity through unknown molecular mechanisms. Although myelination is predominately driven by oligodendrocytes, astrocytes and microglia contribute to this process through their impact on oligodendrocyte function. It is currently unknown if diffuse traumatic brain injury during the critical period of myelination results in halted or disordered white matter development and/or greater axonal injury. Whereas white matter astrocytes normally support myelination, astrocyte activation has been implicated in oligodendrocyte injury and dysmyelination in inflammatory neurologic disease. Similarly, microglia activation has been implicated with disrupting oligodendrocyte maturation and myelin sheath phagocytosis.

Hypothesis: We hypothesize chronic white matter microstructural injury occurs due to demyelination, interruption of developmental myelination, and greater axonal injury and is associated with lasting white matter dysfunction and glial cell activation.

Methods: We used a mouse model of pediatric diffuse TBI that results in axonal injury and demyelination. Twenty-one-day-old mice were used to approximate the neurodevelopment of toddler-aged children. We studied glial response to white matter injury following TBI in juvenile mice using the fluid percussion injury (FPI) model. This is a well validated model of TBI that induces injury by a fluid pressure pulse delivered directly to exposed dura following craniotomy. Sham injured mice, which undergo craniectomy with no fluid percussion, were used as un-injured controls. Effects on white matter structure were tested using longitudinal immunofluorescence and evaluating white matter pathology. At 1, 3, 7, and 28 days following injury, a group of animals was perfused, and their brains processed for immunohistochemical detection of astrocyte (GFAP) and microglial (IBA-1) activation and myelin degradation (MBP). Images were then quantified using the NIH open software ImageJ.

Results: Following TBI, while the total microglia count did not significantly change, there were increased counts of activated and decreased counts of resting microglia at all time points. Furthermore, staining area of microglia was robustly increased at all time points further supporting increased microglial activation. There was a significant increase in total astrocytes 1 day post-TBI but only a marginal increase at 3, 7, and 28 days. Staining area of astrocytes was significantly increased at all time points further supporting astrocyte accumulation and reactivity. Assessment of myelination suggested decreased myelination following injury. In the cortex, there was decreased MBP fluorescence intensity at all time points and decreased area of MBP staining at 1 and 7 days post-injury. In the corpus callosum, there was no difference in fluorescence intensity, but there was decreased MBP percent area at 3, 7, and 28 days post-injury.

Discussion: Our studies demonstrate an activation of microglia and astrocytes and impaired myelin structure of the cortex and corpus callosum following a juvenile model of TBI. Inflammatory microglial and astrocyte activation may result in white matter injury due to oligodendrocyte toxicity, myelin sheath phagocytosis, and resultant demyelination following pediatric TBI. This arrested/altered developmental myelination could result in lasting white matter dysfunction and neurobehavioral impairments. The complete mechanism linking the glial activation and myelin degeneration must be examined in future studies.

Weight-based Aspirin Dosing May Further Reduce the Incidence of Venous Thromboembolism Following Primary Total Joint Arthroplasty

Christopher R. Halbur, BS, Trevor R. Gulbrandsen, MD, Christopher R. West, MD, Timothy S. Brown, MD, Nicolas Noiseux, MD

Introduction: Patients undergoing total joint arthroplasty are at an elevated risk of sustaining venous thromboembolic events (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT). Since prophylaxis has been implemented, rates of VTE have substantially decreased, however current evidence is unclear as to which prophylactic strategy is optimal. Due to the safe, effective, and inexpensive aspects of aspirin (ASA), it has been widely implemented as the prophylactic treatment of choice following hip and knee arthroplasty. Obesity has demonstrated to be a unique, confounding factor, with increased rates of VTE after total joint arthroplasty (TJA). This "obesity paradox" might be attributed to an increased platelet reactivity mechanism, despite the associated inhibitory effects of ASA. Thus, current practices may need to be modified based on various patient characteristics. The purpose of this study was to evaluate the efficacy of a weight-based ASA dosing regimen for thromboembolic prophylaxis following TJA. We hypothesized that we could decrease the incidence of VTE in postoperative TJA patients who weigh ≥120 kg, by utilizing 325 mg ASA orally twice daily (PO BID), compared to chewable 81 mg ASA PO BID.

Methods: A retrospective cohort review was performed on patients who underwent primary total hip and total knee arthroplasty at one academic institution from 1/1/2017-2/29/2020 (38 months). A weight-based ASA dosing regimen for VTE prophylaxis was implemented on 8/1/2018. This protocol was defined as patients who weighed ≥120 kg receiving 325mg ASA PO BID and patients weighing <120 kg receiving 81mg chewable ASA PO BID. Patients who underwent revision procedures, bilateral procedures, or procedures performed due to fracture or malignancy were excluded. Of the included patients, cohort 1 consisted of those who underwent TJA prior to the change to weight-based ASA dosing (19 months), and cohort 2 included those after the dosing modification (19 months). Each cohort was separated into 'standard risk': receiving ASA for VTE prophylaxis and 'high-risk' (or already taking another anticoagulant): receiving non-ASA for VTE prophylaxis. VTE and upper gastrointestinal bleeding rates were recorded for the overall cohort and for both subgroups at 42 days and 6 months post-operatively. Each occurrence of VTE or GI bleeding was chart reviewed in detail. Fisher exact and Pearson Chi-Square tests were used to evaluate significant differences in VTE incidence between the two cohorts. Significance was determined by a P value < 0.05.

Results: A total of 2,716 patients were included in the study. Cohort 1 consisted of 1305 patients, with 1411 patients in cohort 2. Incidence of VTE in the full cohorts, including high-risk patients was 1.23% and 0.35% for cohorts 1 and 2 at 42 days (p=0.01), and 1.76% and 0.57% at 6 months (p<0.01). Overall, 1097/1305 (84%) of cohort 1 and 1187/1411 (84%) of cohort 2 were standard-risk, receiving ASA for prophylaxis. For the standard-risk subgroups, the incidence of VTE was 1.09% and 0.34% for cohorts 1 and 2 at 42 days (p=0.03), and 1.55% and 0.59% at 6 months (p=0.03). Patients prescribed a weight-based ASA regimen after undergoing primary TJA had significantly fewer rates of VTE at 42 days (p=0.03; RR: 0.31 (95% CI: 0.12–0.82) and 6 months (p=0.03; RR: 0.38 (95% CI: 0.18–0.80). There was no significant difference in upper gastrointestinal bleeding events between the two cohorts at 42 days (p=0.69) nor 6 months (p=0.92). Standard-risk cohort sub-analysis consisting of patients weighing ≥120 kg demonstrated a significant difference between the cohorts with a VTE rate of 3.48% and 0% in cohort 1 and 2 (p=0.02).

Conclusions: In this large cohort study, patients prescribed a weight-based ASA regimen had significantly fewer rates of VTE after undergoing primary TJA with a relative risk reduction for VTE of 69% at 6 weeks and 62% at 6 months postoperatively. This suggests the need to factor patient weight when determining proper postoperative VTE prophylaxis with ASA. Current prophylactic protocols should be adjusted to reflect this.

Signs and symptoms of obstructive sleep apnea in men presenting to an outpatient urology clinic for male-specific health concerns

Student: Alexander Hart   Mentor: Amy Pearlman, MD

Introduction: It has been increasingly shown in the literature that urologic conditions and Obstructive Sleep Apnea (OSA) are intertwined. As a result, health care providers caring for genitourinary conditions should be well-versed in signs and symptoms suggestive of underlying or concomitant OSA. Many patients presenting for outpatient genitourinary evaluation are candidates for at-home, rather than in-house, sleep studies, and these portable devices used to assess for OSA can be particularly useful during a pandemic.

Aims: This study aimed to identify symptoms of men presenting for an outpatient urology visit that prompted referral for an at-home sleep study by a single provider. We also assessed proportion of patients referred for the at-home sleep study who ended up undergoing the test and, out of these patients, the proportion of men diagnosed with sleep apnea.

Methods: We performed a retrospective chart review of men 18-99 years old seen by a single provider in the Department of Urology referred for an at-home sleep study. Patients with a prior diagnosis of OSA were excluded.

Results: Eighteen patients were identified (mean age at time of referral 51 ± SD 13 years). Half of patents reported erectile dysfunction/concerns, just over half (56%) reported nocturia, just under half (44%) had been diagnosed with testosterone deficiency, and 39% reported low libido. Nearly all (89%) of patients snored, all reported fatigue, 56% were over the age of 50, 44% had a BMI

>35, and 78% had hypertension (STOP-BANG criteria used to screen for OSA). Conversely, only 1 patient reported at the initial consultation an observed instance where they stopped breathing or reported choking/gasping during sleep. Twelve patients had hematocrit (Hct) levels available for review at time of office visit with the urology provider (mean Hct 45.3%; SD ± 6.6%) with 17% of levels > 52% (threshold for polycythemia). Half of the patients completed the at-home sleep study, all of whom were diagnosed with OSA for which continuous positive airway pressure (CPAP) therapy was initiated. Currently 5 patients have scheduled their at-home sleep study to be completed later in 2020. Of the 9 who completed at-home sleep studies and began CPAP therapy, 4 reported improvements in either their sleep and/or genitourinary concerns, 3 have not been seen or followed up on progress following the initiation of therapy, and 2 had specific CPAP mask concerns and were offered hypoglossal nerve stimulation as an alternative therapy.

Conclusion: Men presenting with genitourinary concerns to an outpatient urology clinic may also have OSA. Half of our patients referred for at-home sleep studies reported nocturia, low libido, erectile dysfunction and/or were diagnosed with testosterone deficiency. Half of those referred, as of present time, completed sleep apnea evaluation, of whom 100% were diagnosed with OSA. Signs and symptoms commonly associated with OSA (STOP-BANG criteria), in addition to those commonly reported by men presenting to a urology clinic, should be considered when deciding on need for sleep apnea evaluation.

Variable	N	%
Age (mean)	18	51 years
Nocturia	10	56
Low testosterone	8	44
Low libido	7	39
Erectile dysfunction	9	50
Hematocrit (mean)	12	45
Snoring	16	89
Tired	18	100
Observed Apnea	1	6
Hypertension	14	78
BMI >35	8	44
Age >50 yrs old	10	56
Male Gender	18	100
Underwent study	9	50

Preoperative Predictive Factors for Neoadjuvant Chemotherapy Response in Osteosarcoma

Student: Mustafa Hashimi, BS
Mentor: Benjamin J Miller, MD, MS
Other Collaborators: Obada Hasan, MBBS, Qiang An, MBBS,

Background: Treatment of osteosarcoma has greatly improved with the advent of neoadjuvant chemotherapy. Despite these advancements, local recurrence continues to be a significant problem, causing a poor prognosis in patients. The extent of tumor necrosis after neoadjuvant chemotherapy is an important predictive factor of local recurrence and survival in osteosarcoma. However, the response to chemotherapy is not known until after the definitive resection and limits the utility of this information for operative planning.

Purposes: Our goal is to identify clinical and radiographic factors following neoadjuvant chemotherapy, but prior to the tumor resection, that may aid in predicting a poor or good response to treatment. Accurately predicting the response to chemotherapy would have the potential to improve outcomes by allowing the surgeon to make adjustments in the treatment plan prior to potential unsuccessful surgeries

Methods: Investigators identified patients who had osteosarcoma from an ongoing cohort of extremity sarcoma patients. Our population of interest included patients diagnosed with osteosarcoma and managed with neoadjuvant chemotherapy between September 1, 2010 and February 1, 2020. Patient records, including clinic notes, pathology reports, and radiology reports, were reviewed to determine underlying patient and tumor characteristics. We identified and assessed potential predictive factors including presence of pain on the Visual Analog Scale, tumor size and growth on sequential MRIs, and tumor ossification on plain radiograph. Our primary outcome was percent necrosis which was categorized as good response when necrosis is $\geq$90% and poor response when necrosis is $\leq$90% on the final histologic specimen. Bivariate methods (Fisher's exact testing) was used to investigate the association of identified clinical and radiographic factors with percent tumor necrosis.

Results: Overall, of the 43 patients who met the study criteria, 16 (37%) had a good response to treatment. In order of decreasing frequency, a good response to treatment occurred in 85% of patients who had a decrease in tumor size (11 of 13), 21% of patients who had no change in tumor size (4 of 19), and 9% of patients who had tumor growth (1 of 11), with p < 0.0001. There were 28 patients who had a post-treatment tumor size of $\leq$ 10 cm, of which 54% (15 of 28) had a good response to treatment, compared to only 7% of patients who had a tumor size of >10 cm (1 of 15), with p = 0.015. There was a good response to treatment in 36% (14 of 39) of patients who had none to minimal pain, in both patients who had moderate pain, and no patients with severe pain, with p = 0.129. There was a good response to treatment in 20% of patients who had none to minimal ossification (2 of 10), 48% of patients who had moderate ossification (10 of 21) and 33% of patients who had extensive ossification (3 of 9), with p = 0.320.

Conclusion: Among the predictive factors, only post-treatment tumor size and growth was significantly associated with a good response to neoadjuvant chemotherapy. Further investigation may determine whether pain or tumor ossification may aid in predicting neoadjuvant chemotherapy response rates in osteosarcoma. Such studies have implications regarding surgical margins, borderline limb salvageable presentations and functional preservation. We recommend further studies with a larger sample size to determine the factors associated with such an outcome.

Assessment of Femoral Version in Patients with Patellar Instability
Student: Ryan Havey
Mentor: Dr. Robert Westermann

Background: Patellofemoral instability is a deficit in anatomical structures keeping the patella in the trochlear groove of the femur, leading to patholaxity and increased risk for patellar dislocation.

Purpose: To retrospectively analyze the association between femoral version, tibial torsion, TT-TG distance, and TT-PCL distance in patients who have undergone surgery to correct for patellofemoral instability using magnetic resonance imaging (MRI).

Study Design: Retrospective cohort study

Methods: 52 patients with a history of patellofemoral instability and surgical correction were analyzed using the institutional patellofemoral registry at the University of Iowa- Division of Sports Medicine. Preoperative MRIs were used to evaluate femoral version, tibial torsion, TT-TG distance, and TT-PCL distance. For femoral version, a positive number was used to indicate anteversion while a negative number indicated retroversion. A single rater measured TT-TG and TT-PCL distance while two raters completed femoral version and tibial torsion measurements. Intraclass correlation coefficient was used to determine interrater reliability between the two raters. These four measurements were then compared using Pearson correlation coefficient to determine correlation and significance.

Results: Interrater reliability was found to be 0.975 for femoral version and 0.915 for tibial torsion. Femoral version average was 15.61 and tibial torsion average was 29.18. TT-TG average was 20.75 and TT-PCL average was 24.37. There was found to be a significant correlation between TT-TG and TT-PCL distances while no significant correlations were found involving femoral version and tibial torsion.

Conclusions: The TT-TG and TT-PCL correlate strongly and both can be used to assess for mal-alignment in patients with patellar instability. While femoral anteversion was high in this series, it appears it is a factor that needs to be assessed independently of conventional patellofemoral mal-alignment measures (TT-TG and TT-PCL) in order to comprehensively treat patients with lateral patellar instability.

Dependence on canonical MAPK signaling in drug-resistant melanoma

Student: Joseph Hentges
Mentor: Christopher Stipp, PhD

Abstract: Melanoma is the most aggressive form of skin cancer. Understanding key cellular pathways is important for improving patient outcomes with metastatic melanoma. The RAS/RAF/MEK/ERK pathway, or canonical MAPK signaling, is one that has been targeted by multiple drug therapies to slow cell proliferation. In our experiments we attempt to learn more about the importance of this pathway and the role RAC signaling may have in drug resistant melanoma cell lines. Cobimetinib (Cobi) and Vemurafenib (Vem) are currently used in clinical treatment of melanoma to inhibit MEK and constitutively active BRAF^{V600E}, respectively. Another drug, Ulixertinib (Ulix), has been developed to inhibit ERK. We used parental A375 melanoma cells and vemurafenib-resistant VRPP3 melanoma cells that were treated with a combination of Vem/Cobi (5μM/5nm) or Ulix (5μM). Cell lysates were made after an overnight period, three days, and seven days. We then performed SDS-PAGE and immunoblotting to compare levels of phosphorylated and non-phosphorylated MEK and ERK, and p90RSK, an indicator of ERK signaling activity. Our data showed that Vem/Cobi was effective at reducing pMEK and pERK in A375 but had very little effect on VRPP3. VRPP3 was more susceptible to Ulix because levels of p90RSK decreased to a very low level by seven days. Alamar Blue values for VRPP3 treated with Ulix were much lower than those treated with Vem/Cobi. In untreated A375 the level of p90RSK was much higher than the level in untreated VRPP3. This data suggests that VRPP3 is resistant to upstream inhibitors of the canonical MAPK pathway by not responding to Vem/Cobi treatment. VRPP3 is still somewhat dependent on the canonical MAPK pathway because of decreased proliferation when treated with Ulix. A CRISPR kinome screen using various melanoma cell lines has been started and will examine 763 different kinases. This screen will hopefully provide kinase candidates for the future study of resistance mechanisms in canonical MAPK in melanoma and the potential role of RAC signaling.

Dexamethasone-Eluting Cochlear Implants Reduce Intracochlear Inflammation Following Surgery

Timon Higgins, M2, Alexander Claussen, MD, Department of Otolaryngology, Brian Mostaert, Department of Otolaryngology, Marlan Hansen, MD, Department of Otolaryngology

Introduction: Cochlear implants (CIs) dramatically alter the lives of patients with hearing deficiency, and although their technology is constantly improving, improvements continue to be limited by the immunologic/fibrotic foreign body response (FBR) that occurs within the cochlea following CI. Although the FBR is a natural protective mammalian mechanism, this reaction can have detrimental consequences for CI users, including increased impedances leading to decreased CI battery life, delayed loss of residual acoustic hearing after hearing preservation CI, granulomatous reactions, or in rare cases device extrusion or failure. As such, the aim of the current study is two-fold: (1) to characterize the intracochlear foreign body response following cochlear implantation surgery and define its causes, including how stimulation of the implants affects inflammatory responses; and (2) to reduce the FBR by using cochlear implants that elute corticosteroids. Using a murine model, this study seeks to show that the use of corticosteroid-eluting cochlear implants has the potential to significantly reduce intracochlear inflammation following cochlear implantation with the goal that this will lead to improved long-term implant performance.

Hypotheses: We hypothesized that mice which underwent chronic cochlear implantation will display increased intracochlear inflammation when compared to sham surgery and acutely implanted mice. For the chronically implanted mice, we hypothesized that presence and level of electrical stimulation of the functional cochlear implant will not affect intracochlear inflammation. When comparing the cochlea of mice with normal implants to those with corticosteroid-eluting implants, it was hypothesized that those with corticosteroid-eluting implants would show significantly less inflammation and intracochlear fibrosis.

Methods: For each experimental condition and timepoint, triplicates of mice were implanted in their left ear, and paired right ear unimplanted specimens were utilized as controls. Black reporter mice with $CX3CR1^{+/eGFP}$;$Thy1^{+/YFP}$ genotype were used for all experiments in order that macrophages would express GFP and spiral ganglion neurons would express YFP. Experimental conditions included sham surgery (complete surgery minus insertion of the cochlear implant), acute insertion (full surgery, including insertion of the cochlear implant, but the implant is removed prior to closure), and chronic insertion (complete surgery with chronic placement of the cochlear implant). The timepoints for sacrifice and analysis were 4 hours, 24 hours, 96 hours, 7, 8, 11, 14, and 21 days. Beginning at 7 days, when the implants are then able to be turned on, chronically inserted mice were divided into no stimulation, low-level stimulation, and high-level stimulation groups and then stimulated according to each protocol. Additionally, four mice were implanted with non-functional, dexamethasone-eluting implants and were sacrificed at 21 days. Mice were sacrificed at each endpoint, following which their cochlea were sectioned and analyzed to determine the number of macrophages/unit volume (density) and number of macrophages/total cells (cellularity). Analysis was done in three areas of interest, the lateral wall, Rosenthal's canal, and scala tympani, across all three turns of the cochlea (basal, middle, and apical). Groups were compared using ANOVA with post hoc analysis.

Results: When comparing the chronically inserted mice with the sham surgery and acutely inserted mice, no differences in macrophage density or cellularity were observed at the 4 or 24 hours timepoints. Beginning at 96 hours, chronically inserted mice began showing an increase in macrophage density and cellularity in the basal turn scala tympani, and significant differences were seen beginning at 11 days and onward. No significant differences were observed in the lateral wall or Rosenthal's canal, nor were there any significant differences in the middle or apical turns. Amongst the different stimulation groups, no significant differences were observed in macrophage density or cellularity between the different stimulation protocols. The dexamethasone-eluting implants displayed significant reductions in macrophage density and cellularity in the basal turn in the scala tympani, Rosenthal's canal, and lateral wall when compared to the chronically-implanted mice across all stimulation groups. The dexamethasone group also displayed a significant reduction in macrophage cellularity and density in the basal turn Rosenthal's canal and lateral wall when compared to the right ear control specimens from this group.

Conclusions: (1) The most significant contributor to inflammation and intracochlear fibrosis following cochlear implantation surgery is the chronic presence of the implant, not surgical trauma. (2) The electrical stimulation of the cochlear implant is not a significant contributor to intracochlear inflammation and fibrosis. (3) Corticosteroid-eluting implants significantly reduce intracochlear inflammation and fibrosis following surgery.

Characterization of Factors Contributing to Iatrogenic Injury to Articular Cartilage during Arthroscopic Procedures

Arman Hlas, BS[1], Ino Song, MS[2], Dongrim Seol, PhD[2], Jordan A. Jensen, MS[3], Edward Sander, PhD[3], James Martin, PhD[1,2], Joseph Buckwalter, MD, MS[1,2]

[1]University of Iowa Roy J. and Lucille A. Carver College of Medicine
[2]Department of Orthopedics and Rehabilitation, University of Iowa Hospitals and Clinics
[3]Department of Roy J. Carver Biomedical Engineering, University of Iowa

Background: Arthroscopy is a commonly used, minimally invasive surgical technique for the diagnosis and treatment of articular joint injuries. While arthroscopy allows patients to benefit from reduced postoperative swelling, lower risk of complications, and faster recovery compared to open arthrotomy, arthroscopic procedures can cause joint damage due to iatrogenic cartilage injuries (IACI) and sub-optimal joint irrigation. IACI during arthroscopy are caused by mechanical forces of instrument contact at a single point along the cartilage surface. On a cellular level, these injuries cause oxidative stress and mitochondrial dysfunction, leading to chondrocyte malfunction and eventual death. The most commonly used irrigation fluid, normal saline, is additionally hypotonic with respect to the cartilage matrix, creating an unfavorable environment for chondrocyte viability and function. The significance and clinical implications of mechanical insult and osmolarity variation within the joint capsule are largely unknown. Despite these apparent risks, little work has been done to characterize or prevent such injuries.

Purpose: The goal of this study is to evaluate the effects of normal saline, a solution commonly used for joint irrigation, on cartilage health. We hypothesized that incubating articular cartilage explants in normal saline would lead to increased chondrocyte death and oxidative stress compared with incubation in culture medium.

Methods: A tissue culture model consisting of 10 mm-diameter osteochondral explants from porcine stifle joints was collected from a local abattoir. Explants were incubated in either culture medium or normal saline for 2, 6, or 24 hours (n = 4-5 per time point). After incubation, the explants were stained with dihydroethidium (DHE), a probe for cellular oxidant production, and propidium iodide (PI), a probe for cell death, and then imaged using confocal microscopy. ImageJ was used to measure fluorescent area of stain captured in each sample. Data collected was analyzed by one-way ANOVA.

Results: Incubating explants in normal saline for 2 or 6 hours did not elevate DHE or PI staining compared to culture medium controls. However, at 24 hours there was a significant increase in PI staining and a trend toward higher DHE staining in the normal saline group versus control.

Conclusion: Although further tests are needed in order to fully assess the effects of normal saline on cartilage health, our current results indicate that it induces chondrocyte death and oxidative stress, similar to mechanical insults to cartilage that we have shown lead to post-traumatic osteoarthritis. These findings suggest that the addition of antioxidants to irrigation fluids may be beneficial.

Title: The Parabrachial Nucleus
Student: Dake Huang
Mentor: Joel Geerling MD PhD

The parabrachial nucleus is a group of neurons located in the dorsolateral brainstem bordering the cerebellum. This group of neurons forms a complex, three-dimensional structure with the superior cerebellar peduncle traveling through the middle of it, splitting it into a medial and a lateral subdivision. Using this separation provided by the superior cerebellar peduncle, previous neuroanatomists have divided the parabrachial nucleus into different subnuclei based on their cytoarchitecture and location (Fulwiler & Saper, 1984; Saper & Loewy, 1980). Using cytoarchitecture and location provides ambiguity for interpretation among different groups of scientists, which does not provide a standard to study these neurons. We here provide an alternative in which different parabrachial subpopulations are identified based on their genetic identity instead of their shape, size and location. Firstly, utilizing cell-type-specific markers to segregate out different subpopulations provides a standard that all other scientists can replicate (whether a cell does or does not express the gene). Secondly, gene expression determines the functionality of the neurons and therefore provides a more relevant basis to study these neurons than cytoarchitecture. Lastly, a genetic profile of these neurons will provide other scientists a framework to target these different parabrachial neurons and delineate their distinct functions. Using the genetic profile of these neurons, we then traced out the efferent projection from the *Vglut2, Foxp2, Pdyn, and Calca* expressing parabrachial populations. We learn that while the glutamatergic neurons largely encompass the entire parabrachial efferent projection, the projection from *Foxp2 and Pdyn* neurons are largely mutually exclusive with neurons that express *Calca.*

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Authors: Dr. Cesar de Cesar Netto, Eli Auch, Caleb Iehl

Introduction: Adult acquired flatfoot deformity (AAFD) is a complex 3-dimensional (3D) deformity of the foot characterized by peritalar subluxation (PTS). PTS is typically assessed at the posterior calcaneal facet, but recent studies have called this into question. The objective of this study was to use 3D distance mapping (DM) from weightbearing CT (WBCT) to assess PTS in AAFD patients and controls. We hypothesized that DMs would identify the middle facet as a superior marker for PTS.

Purpose: To determine whether the novel WBCT 3D distance maps can objectively characterize subtalar changes in patients with adult acquired flatfoot deformity and the diagnostic value of subluxation of the middle facet of the subtalar joint.

Methods: We analyzed WBCT data of 20 consecutive AAFD patients and 10 control patients with a novel 3D distance mapping technique to objectively characterize joint coverage across the entire peritalar surface, including both articular and non-articular regions. Joint coverage was defined as the percentage of area in the DMs <4mm. Probable impingement was quantified as distances <0.5mm. The posterior facet was divided into a 3x3 grid and the sinus tarsi into a 2x2 grid for analysis. Comparisons were performed with independent t tests or Wilcoxon tests. P-values <0.05 were considered significant.

Results: Overall, coverage was decreased in articular regions and impingement was increased in non-articular regions of AAFD patients. A significant increase in uncoverage in the middle (46.6%, $p<0.001$) was found, but not anterior or posterior facets. Significant increases in sinus tarsi coverage were identified (98.0%, $p<0.007$) with impingement in 6/20 AAFD patients. Impingement of the subfibular region was only noted in 1/20 cases, but narrowing greater than 2 standard deviations was noted in 17/20 patients.

Conclusions: Objective DMs identified significant markers of PTS in the middle but not posterior or anterior facets. We confirmed prior 2D data that suggested uncoverage of the middle facet provides a more robust and consistent measure of PTS than calculations in the posterior facet.

Characterization of Non-Syndromic Hearing Loss in a Family with Suspected vGLUT3 Mutation.

Heba Isaac, BS, Camille Dunn, PhD, Marlan Hansen, M.D.
The University of Iowa, Department of Otolaryngology – Head and Neck Surgery

Abstract

Normal hearing requires the functional compliance of all parts of the auditory system. Interruptions in any part of the system can result in hearing impairments (HI). Many factors can contribute to HI with the primary causes attributed to aging, noise exposure, or genetic factors, and these factors often interact. The auditory vestibular system utilizes glutamatergic neurotransmitters that are packaged in vesicles and transported via glutamate transporter 3 (vGLUT3) to presynaptic active zone and exocytosed using specialized ribbon synapses. Therefore, vGLUT3 expression has an essential role in the function of the auditory pathway. Mutations in *SLC17A8*, the gene encoding vGLUT3, thus, can result in HI with varying severity depending on the type of genetic modification. Mutations in *SLC17A8* have been linked with DFNA25, an autosomal dominant non-syndromic hearing loss (ADNSHL) in humans. Such patients are expected to have an auditory neuropathy (AN) phenotype. Patients with AN have highly variable (and often poor) outcomes with cochlear implantation. The character of HI (age of onset, rate of progression, frequencies involved, speech understanding, etc) for patients with *SLC17A8* mutations remains poorly characterized. In addition to standard hearing rehabilitation options such as hearing aids or cochlear implants, there is lively interest in gene therapy for hearing loss because it offers the possibility to restore the expression of the defective genes. Recent studies have demonstrated that mice lacking vGLUT3 via targeted deletion of *SLC17A8* gene lacked auditory nerve responses to acoustic stimuli, although otoacoustic emissions (OAE) were present, similar to human AN phenotype. At the University of Iowa, we have the largest genetic database of patients undergoing cochlear implantation in the world. One family in the database has an identified mutation in *SLC17A8*. The present study attempted to understand the nature and progression of the hearing loss in this family with a suspected *SLC17A8* mutation and inform the potential use of gene therapy as a therapeutic alternative to conventional prosthesis.

A total of 8 family members were tested across multiple generations. To characterize the pattern of hearing loss, detailed family history was obtained through pedigrees, questionnaire, and personal interviews. Comprehensive audiometric assessments were performed in all participants. Stimuli and task-specific procedures including HHIA, SSQ-6 and TFI were performed. Genotyping and linkage analysis was performed from saliva samples obtained from cooperative family members with assessment of how the SCL17A8 P54L variant segregates with hearing phenotype.

Results showed that 5 family members were affected. The pattern of inheritance was autosomal dominant (Figure 1). The proband of the family was a 63-year-old female with bilateral severe hearing loss, and a missense mutation was identified at chromosome 12 where thymidine (T) was substituted with cytosine (C). The corresponding amino acid sequence produced threonine instead of isoleucine. The patient was found to be heterozygous for this mutation at the exon region. This variation was not found in the 3 individuals with normal hearing. This variation was reported with alternate allele C frequency of <0.001%.
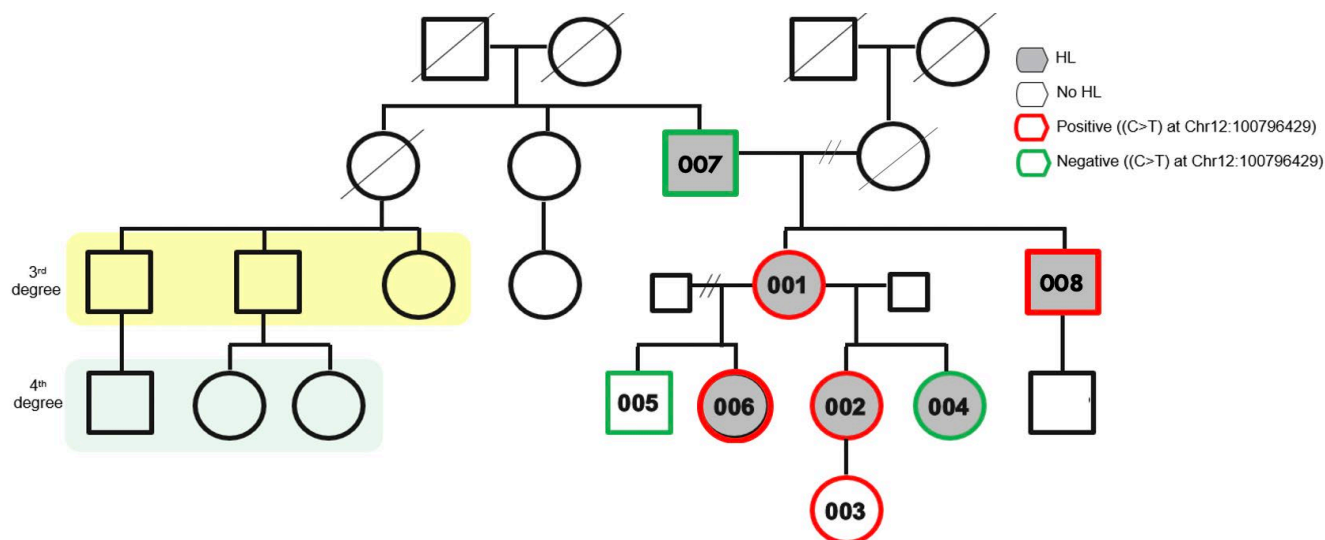

Figure 1: Pedigree of Iowan family. Squares and circles denote males and females, respectively. Red symbols represent affected individuals, and green symbols represent unaffected individuals. The proband of the family is participant 001.

Virtual Anatomy Videos for Pre-laboratory Preparation: Does Usage Correlate with Grade Outcome?

Heba Isaac, BS, Darren S. Hoffmann, PhD, Nicholas Borcherding, MD., PhD., Timothy Fleagle, DPT. Department of Anatomy and Cell Biology, The University of Iowa Carver College of Medicine.

Abstract:

Previously, we described an approach for enhancing laboratory preparation in a dental gross anatomy course using custom virtual anatomy videos to be viewed prior to cadaver dissection. Students who had access to these resources in a flipped pedagogy context performed significantly better on cumulative laboratory exams compared to historical controls and rated the virtual anatomy videos as a preferred resource for lab prep. However, because there were several unique curriculum elements in the experimental group, this study did not directly evaluate the impact of virtual anatomy videos on course outcome. Furthermore, while most video views were completed as intended (prior to dissection), there were many views that occurred later as prep for course assessments. The purpose of the current study is to determine the degree of association of virtual anatomy video usage with grade outcome. Further, we sought to identify if usage for pre-lab prep was more strongly associated with course outcome than usage for exam prep.

As described in our prior study, three consecutive years of student performance and video usage data were collected (n=240 students). In the course, each student prepared for 10 laboratory dissections. To evaluate association of video usage with course outcome, mean total video views and mean views in pre-lab and pre-assessment categories were calculated for each overall course score quartile, with one-way ANOVA. Linear regression analysis was used to evaluate the level of association of usage with overall course score (total course points = 505).

Initial grade quartile analysis demonstrated that total number of video views was significantly associated with course outcome (top grade quartile 17.70 ± 2.12 views [mean $\pm$ SEM]; third quartile 15.68 ± 1.54; second quartile 10.73 ± 1.30; bottom quartile 11.98 ± 1.27; $p = 0.057$ top vs. bottom, $p = 0.012$ third vs. bottom). Regression analysis of total video views vs. overall course score confirmed that this positive trend was significant (slope = 0.597, F = 11.92, $p = 0.0007$), however correlation was not strong due to high degree of variability in video usage ($r^2 = 0.048$).

Separating views into pre-lab and pre-assessment categories revealed that pre-lab usage was positively associated with course outcome (top grade quartile 8.28 ± 0.76 views; third quartile 8.22 ± 0.74; second quartile 5.08 ± 0.66; bottom quartile 6.12 ± 0.63; $p = 0.128$ top vs. bottom, $p = 0.008$ third vs. bottom). Slope of the regression line was higher (1.311) and correlation ($r^2 = 0.045$) was similar to results for total views. In contrast, pre-assessment usage trended toward higher views in higher grade quartiles, however there were no significant differences between the groups. Further, slope of the regression line was lower (0.648) and had a weaker correlation ($r^2 = 0.030$)

The results of this study indicate that using virtual anatomy videos to prepare for laboratory dissection is associated with positive course outcome, however there is considerable variation in the data indicating that usage does not guarantee success. Further, students should be advised that the strongest benefit of pre-lab videos is achieved through pre-lab viewing and reviewing these resources later for exam prep is less likely to result in further grade improvement.

The Effect of Weight and Body Mass Index (BMI) on Serum Progesterone Values in In Vitro Fertilization (IVF) Cycles

Student researcher: Margurite Jakubiak

Mentor and collaborators: Rachel Mejia, MD; Karen Summers, MPH; Rachel Whynott, MD

Introduction: Obesity affects 39.7-43.3% of women of reproductive age in the U.S. (1). Many adverse health outcomes are associated with obesity, including infertility and decreased success with assisted reproduction (2). One hypothesized reason for this is that weight and/or body mass index (BMI) reduces the bioavailability of hormonal medications used in assistive reproduction procedures such as in vitro fertilization (IVF). Progesterone (P4) is supplemented in IVF to prepare the endometrium for implantation and support early pregnancy. It is important to investigate how weight/BMI may impact P4 serum levels during IVF cycles to better care for obese patients.

Purpose of the study (hypothesis, aims): To determine the effect of body weight and BMI on serum P4 levels at time of pregnancy test in women undergoing cryopreserved IVF. Secondarily, to determine how serum P4 levels at time of pregnancy test affect live birth rate in a clinic that increases the dose of P4 in response to levels <15 ng/mL.

Method: This study was a retrospective cohort of women who underwent their first cryopreserved embryo transfer cycle at the University of Iowa between January 2015 and December 2018 with initial supplemental P4 dose of 50 mg IM daily. Spearman's correlation was used to assess the relationship between weight/BMI and serum P4. Chi-square, t-tests, and Kruskal Wallis were used to compare demographics, serum P4 level, and pregnancy outcomes. A power analysis determined that 281 cases would be sufficient to detect differences in live birth rate.

Results: There was a negative correlation between BMI and serum P4 level at time of pregnancy test (rho= -0.521, $p<0.001$) with BMI accounting for 27% of variance in P4 level. Weight was found to be a better predictor of P4 level, with weight accounting for 29% of variance in P4 level at time of pregnancy test (rho= -0.536, $p<0.001$). Among women weighing 200+ lbs, there was no significant correlation between P4 level at time of pregnancy test and pregnancy outcome.

Discussion/Conclusion: Both body weight and BMI negatively impacted serum P4 levels at time of pregnancy test, with weight having a greater impact. Nearly 30% of patients ≥200 lbs had P4 <15 ng/mL, a value associated with lower live birth rates in previous studies. Despite this, in a clinic that increases P4 dosage in response to low P4 serum levels, there was no correlation between serum P4 at time of pregnancy test and live birth outcomes. This suggests that increasing IM P4 supplementation to 75 mg for serum levels <15 ng/mL on pregnancy test day is sufficient to maintain favorable live birth rate.

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Patella Resurfacing During Total Knee Arthroplasty and its Effect on Patient Ability to Kneel

Alec E. James, B.S., Tim Brown, M.D., Lauren Keitel, B.S., Jesse Otero, M.D., Nicholas A. Bedard, M.D.

Background: Many patients report difficulties with kneeling following total knee arthroplasty (TKA). Current data is conflicting regarding whether patellar resurfacing at the time of TKA can improve a patient's ability to kneel. The purpose of this study was to evaluate whether patellar resurfacing leads to increased ability to kneel and improved patient reported outcomes compared to TKA patients without their patella resurfaced.

Hypothesis: We hypothesized that those who had their patella resurfaced as a part of their TKA would report a greater ability to kneel 1 year following surgery than those who did not undergo patellar resurfacing.

Methods: A retrospective review of primary TKA patients was performed to evaluate each patient's ability to kneel on their TKA. All surgery was performed by two surgeons; one of whom routinely resurfaced the patella at the time of TKA and the other who did not. All patients received the same TKA implant and were at least 1 year out from surgery. Information regarding each patient's ability to kneel was obtained via a survey specifically evaluating kneeling. Patients also completed the following patient reported outcome measures: PROMIS global health scale, KOOS Jr and the Oxford Knee Score. Patient demographics and patellar resurfacing were evaluated for their association with ability to kneel after TKA. Chi squared analysis was used to compare the resurfaced patella group with the non-resurfaced patella groups.

Results: In total 86 TKAs were performed and 83 patients were evaluated with 29% of TKAs having the patellar resurfaced and 71% not resurfaced. Mean age was 67 years at the time of surgery and 53% were female. Mean BMI at the time of surgery was 34 kg/m^2. There was no difference in the ability to kneel between the resurfaced and unsurfaced cohorts with 33% of patients in the unsurfaced and 32% in the resurfaced cohort reporting little or no difficult kneeling following TKA (p=0.9). There were no significant differences in patient reported outcome measures between cohorts. The top three reasons given for difficulty kneeling were feeling of an "unsettling sensation" upon kneeling (28%), pain accompanied with kneeling (26%), and lack of flexibility (15%). 53 out of 58 patients (91%) who had difficulty kneeling reported they did not think it was safe to kneel on their prosthesis.

Conclusion: Following primary TKA, approximately two-thirds of patients reported difficulty kneeling following surgery. Patellar resurfacing did not impact patient's ability to kneel. Interestingly, the vast majority of patients who had difficulty kneeling felt that it was unsafe to kneel on their prosthesis despite this not being taught in TKA education classes at our institution. This finding indicates a possible opportunity for intervention to increase patient's ability to kneel following TKA.

Efficacy of iliohypogastric and ilioinguinal nerve blocks for the treatment of groin and testicular pain

PI-Nicholas Jensen, M4
Mentor: Amy Pearlman, MD

INTRODUCTION

Orchialgia, defined as three or more months of bothersome intermittent or constant testicular pain, is a difficult to treat condition with many possible etiologies. Treatment may involve tighter-fitting underwear, scrotal support, ice, avoidance of provoking activities, non-steroidal anti-inflammatory medication(s), empiric antibiotic(s), neuropathic medication(s), or surgical intervention(s) by various sub-specialists. Those reporting inadequate pain relief despite conservative, oral pharmacological therapy, and spermatic cord block or persistent pain despite surgical intervention may be referred to a chronic pain specialist for further evaluation and management. Prospective studies in pediatric patients with orchialgia have shown that ilioinguinal-iliohypogastric nerve blocks may be a viable treatment option for pediatric patients with a history of orchialgia without an identifiable cause. No studies have been performed in adult patients to assess efficacy of nerve blocks in men presenting with orchialgia.

OBJECTIVE

The aim of our study was to assess efficacy of ilioinguinal and/or iliohypogastric nerve blocks for the treatment of chronic testicular +/- groin pain.

METHODS

Seventeen patients with at least three months of groin/testicular pain underwent ilioinguinal and/or iliohypogastric nerve block with the department of anesthesia at our institution between 2010 and 2019. Records were retrospectively reviewed to determine efficacy of the nerve block(s). Demographic information, surgical history, comorbidities, and concurrent medical therapy was also recorded.

RESULTS

Sixteen patients met criteria for chronic orchialgia and had adequate follow-up documentation. One (6%) patient obtained complete resolution of pain. Four (25%) patients reported resolution of pain for >24 hours, with symptoms returning between 24 hours post-procedure and their follow-up appointment. Two (13%) patients reported resolution of pain for <24 hours. Nine (56%) patients reported no resolution of pain or worsening of pain.

All sixteen (100%) patients were prescribed a concurrent neuropathic medication regimen at the time of their procedure (gabapentin, pregabalin, oxcarbazepine, amitriptyline, topiramate, or lamotrigine). Eleven (69%) patients had a previous groin or testicular surgery, including inguinal hernia repair, spermatic cord denervation, varicocelectomy, hydrocele excision, vasectomy, epididymectomy, orchidopexy, or orchiectomy. Five (31%) patients were previously treated with antibiotics for presumed epididymitis.

CONCLUSIONS

This is the first study to assess the efficacy of ilioinguinal and/or iliohypogastric nerve blocks for the treatment of adult patients with orchialgia. Results suggest that referral to a chronic pain management specialist for one or both of these interventions may not provide sustained pain relief. Clinical trials exploring alternative treatments are warranted.

Antibiotic timing in sepsis
Anna Kaldjian, M2
Karen Cyndari, MD, PhD
Heather Healy, MA, MLS
Nicholas Mohr, MD, MS

Introduction

The time-sensitive nature of antibiotic administration in the treatment of sepsis and septic shock is a controversial question. Previous meta-analyses and systematic reviews have addressed this question, but they have obtained varying results and often only compared administration before and after a single point in time rather than assessing incremental costs of delay in administration. Additionally, new data on the question have been published since the last meta-analysis was performed that warrant a new analysis.

Purpose

We are performing a systematic review and meta-analysis to determine the role of timely antibiotic administration in survival of sepsis and septic shock. We hypothesized that time to antibiotic administration in treatment of sepsis has a significant, non-linear effect on patient outcomes (mortality, length of stay, probability of ICU admission).

Methods

An initial search was performed with the assistance of a medical librarian. Databases searched were MEDLINE, Embase, Cochrane Library, and CINAHL. Abstracts of these studies were evaluated for inclusion by two reviewers. Further studies were obtained through a grey literature search, and a manual review of relevant papers in the field. Full studies of abstracts meeting our criteria are being evaluated by two reviewers, who will then extract the data from included studies. Included studies are English-language, adult human studies reporting the relationship between time to antibiotics and clinical outcomes. Studies examining candidemia, tuberculosis, comparisons between antibiotics, and studies that do not differentiate between times to antibiotic under 12 hours are excluded. The following data will be extracted: time to antibiotic administration, mortality, length of stay, probability of ICU admission, type of modelling authors assume (linear, threshold effect, dichotomous outcome, etc.), type of infection, severity of illness, setting (ED, ICU, inpatient floor), and age of patients. The quality of the studies will be evaluated using the Black and Downs checklist, and we will look for sufficient homogeneity to allow for analysis. We will look for publication bias via a funnel plot. RevMan will be used for analysis. We will do an initial analysis on papers that assume linearity, and we will pool their slopes. We will do a secondary analysis on papers that categorize relationships. We plan to calculate a pooled risk difference for hospital length-of-stay and mortality. Subgroups will be defined based on likelihood of bias, ED vs. inpatient setting, source of infection, and US vs. non-US.

Results

3252 studies were identified through our original search. After 14 duplicates were removed, 3238 abstracts were screened. 2564 of these were excluded, leaving 674 studies of which the full texts are being screened. 31 additional abstracts were obtained through the grey literature search.

Conclusion

The time-sensitivity of antibiotic administration in sepsis is currently contentious, leaving a gap in the evidence base of clinical practice. Thus, a meta-analysis summarizing recent data will provide a comprehensive analysis that will give clinicians a more solid evidence base for their treatment decisions and will thereby shape clinical practice.

Clinical Outcomes of Patients with Chronic Liver Disease and COVID-19 at UIHC and in the TriNetX Network of 48 Healthcare Organizations

Authors: Vijayvardhan Kamalumpundi, BS[1]; Adeyinka Taiwo MD[1]; Amal Shibli-Rahhal, MD, MS[1]; Elham Shams, MD[1]; Antonio J. Sanchez, MD[2]; Marcelo L. Correia, MD, PhD[1]

Institutional Affiliations:
1. University of Iowa Carver College of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Iowa City, IA, 52242
2. University of Iowa Carver College of Medicine, Department of Internal Medicine, Division of Gastroenterology and Hepatology, Iowa City, IA, 52242

Background: It has been shown in small observational studies that The Coronavirus Disease-2019 (COVID-19) disproportionally impacts people with chronic liver disease (CLDs), however there is still scarce data to support this assertion.

Objectives: Describe the characteristics and acute prognosis of patients with CLD and COVID-19 treated at the University of Iowa Health Care (UIHC), and across a global, multi-center health research network.

Methods: TriNetX, a global healthcare research database collaborating across 48 healthcare organizations, was used to query de-identified patients' records. The inclusion criteria for the experimental group was: (1) ≥ 18 y/o (2) diagnosed with both CLD and (3) COVID-19. The control group was defined as adults diagnosed with COVID-19 but without history of CLD. Liver and coagulation function tests, demographic information, and markers of COVID-19 severity (hospital admission rate, Extracorporeal Membrane Oxygenation [ECMO]/systemic therapy usage, mortality) were summarized with descriptive statistics. Systemic therapy was defined as any sort of medical device that was used outside the body to perform a vital physiologic function.

Results: We found 110 and 4868 patients who met the inclusion criteria at the UIHC and the TriNetX network, respectively. In both cohorts, the age of CLD patients was similar (*UIHC*: 47±10 y/o; *TriNetX*: 51±16 y/o vs. *UIHC Control*: 35±17 y/o; *TriNetX Control*: 49±21 y/o). In addition, both CLD populations had a markedly higher hospital admission rate (*UIHC*: 27%; *TriNetX*: 39%; vs. *UIHC Control*: 2%; TriNetX *Control*: 18%), ECMO/systemic therapy usage (*UIHC*: 30%; *TriNetX*: 21% vs. *UIHC Control*: 5%; *TriNetX Control*: 8%), and mortality (*UIHC*: 10%; *TriNetX*: 9% vs. *UIHC Control*: 2%; *TriNetX Control*: 5%) compared to the control population. However, most recent liver function tests showed no abnormalities in ALT (*UIHC*: 32 U/L; *TriNetX*: 27 U/L vs. *UIHC Control*: 22 U/L; *TriNetX Control*: 23 U/L), AST (*UIHC*: 33 U/L; *TriNetX*: 29 U/L vs. *UIHC Control*: 23 U/L; *TriNetX Control*: 25 U/L), Albumin (*UIHC*: 4.1 g/dL; *TriNetX*: 3.8 g/dL vs. *UIHC Control*: 4.3 g/dL; *TriNetX Control*: 3.9 g/dL), GGT (*UIHC*: 58 U/L; *TriNetX*: 53 U/L vs. *UIHC Control*: 25 U/L; *TriNetX Control*: 28 U/L), or Total Bilirubin (*UIHC*: 0.5 mg/dL; *TriNetX*: 0.2 mg/dL vs. *UIHC Control*: 0.4 mg/dL; *TriNetX Control*: 0.5 mg/dL), even though extreme values in both control and CLD groups were documented. Prothrombin Time (*UIHC*: 11 sec; *TriNetX*:13 sec vs. *UIHC Control*: 11 sec; *TriNetX Control*: 12.9 sec) and activated Partial Thromboplastin Time (*UIHC*: 29 sec; *TriNetX*: 31 sec; vs. *UIHC Control*: 26 sec; *TriNetX Control*: 31 sec), also showed no clinically significant increases, though substantial variability was also noted in both control and CLD groups.

Conclusion: CLD patients appear to have greater risk of severe COVID-19 and death compared to the control groups. Liver and coagulation tests were by and large normal, however extremely abnormal values were observed in both the control and CLD groups. Our results are limited by the fact that data was obtained from aggregated patient cohorts and based on procedural codes. Furthermore, TriNetX software does not allow us to observe trends in specific subgroups such as by race or inpatient/outpatient data. To address these limitations, we plan to do a manual abstraction of data from medical records to adjust for confounders and understand population-specific risk.

Outcomes of Succinate Dehydrogenase-Deficient Paragangliomas

Authors: Jacob Kaplan and Andrew Bellizzi MD

Background: Succinate Dehydrogenase (SDH), otherwise known as Complex II, is a heterotetramer found on the inner mitochondrial membrane that plays an important role in the Krebs cycle and the electron transport chain. The enzyme complex couples and catalyzes the oxidation of succinate to fumarate and the reduction of ubiquinone to ubiquinol. Paragangliomas and pheochromocytomas are known to harbor SDH subunit mutations at relatively high frequencies. Germline mutations in any of the four subunits increases the risk of developing hereditary paraglanglioma-pheochromocytoma (HPGL/PCC) syndrome – a condition inherited in an autosomal dominant pattern. Although most paragangliomas and pheochromocytomas pursue a benign clinical course, there is some data that SDH-deficient tumors pursue a more aggressive course.

Purpose: The goal of this study was to examine succinate dehydrogenase status in paragangliomas in relation to clinical factors, including recurrence-free and overall survival. These findings will be combined with Ki-67 proliferation indices from the same tumors - to determine how loss of enzyme function affects this critical index and how the index impacts disease. Unfortunately, not all succinate dehydrogenase deficient tumors have been indexed at this time and so this data could not be included in this abstract.

Methods: Patient age, gender, tumor location (head and neck, thoracoabdominal) and nature (primary vs metastatic), treatment (surgery, radiation, chemotherapy), germline mutation status, time to recurrence, vital status, and duration of follow up were determined retrospective chart review. SDH status had previously been determined by SDHB immunohistochemistry on tumors contained in a tissue microarray. Kaplan-Meier curves were plotted and survival curves compared with the log-rank test (p<0.05 considered significant).

Results: 78 patients were included in this analysis, of which 16 were SDH-deficient. SDH-deficient tumors occurred in younger patients (mean age 36 vs 51) (p=0.0007) with trends toward increased frequency in men (p=0.052) and a thoracoabdominal location (0.056). SDH-deficient tumors showed inferior recurrence free (p=0.0038) survival, though reduced overall survival was not significant (p=0.089).

Conclusion: Our study highlights the frequency of SDH-deficiency among paragangliomas (21% of our cohort). Patients with SDH-deficiency experienced a higher rate of recurrence following surgical resection of their tumors than those with intact protein. Ki-67 indexing is still in progress for the last tumors and we hope to show a relationship between this index and loss of succinate dehydrogenase. Furthermore, we hope to continue this work with additional markers to better understand the effect this mutation has on disease progression and to better predict outcome in disease. We simultaneously are working on creating a new cohort consisting of patients with pheochromocytomas – another neuroendocrine tumor – and have begun Ki-67 indexing for these slides as well.

Title: Accuracy of X-ray and magnetic resonance imaging in defining the tumor margin in primary bone sarcoma.

Student: Theodore Katz, M2
Mentor: Benjamin Miller, MD - Department of Orthopedics and Rehabilitation

Introduction: Primary bone sarcomas typically originate near the end of long bones and are often treated with limb-salvage surgery and endoprosthetic reconstruction. Modern technology allows physicians to use measurement software on electronic X-ray and MRI (magnetic resonance imaging) to plan the corticotomy and ensure the intramedullary extension of the tumor will be removed with an appropriate margin between the tumor and the remaining tissue. We sought to compare the margins predicted by pre-operative electronic measurements with X-ray and MRI to the final pathologic surgical margins in limb-salvage surgeries of bone tumors.

Methods: This study was a retrospective chart review of 39 patients with primary bone sarcoma treated operatively with limb-salvage surgery. The pathology reports of the resected tissue provided the length of the bony resection and the true margin from the tumor to the bone. Two non-blinded reviewers used electronic measurement tools to determine the expected margin from X-ray or MRI based on the length of tissue resected and compared with the gold standard i.e. pathology. The measurements on X-ray images used anterior-posterior and lateral films. MRI measurements were made on coronal and sagittal images. The averaged margin was calculated for X-ray by averaging the anterior-posterior and lateral margins, and for MRI by averaging the coronal and sagittal margins. We also determined the average margin error when the MRI image with the smallest predicted margin was used. Univariate statistical analysis was conducted on the electronic measurements to determine the variability of expected margins and overall accuracy of each imaging technique.

Results: The average absolute error of the margin measured from averaged MRI views was 0.74 cm with a standard deviation of 0.77 cm. When MRI images with the smallest predicted margin were selected, the average margin error and standard deviation was 0.71 cm and 0.70 cm respectively. The average absolute error of the margin measured from X-ray images was 1.11 cm with a standard deviation of 0.84 cm. There were 6 outliers of 66 MRI measurements and 14 outliers of 70 X-ray measurements as defined by an absolute error greater than 2.00 cm. MRI measurements overestimated the margin in 35/66 images and underestimated the margin in 31/66 images. X-ray measurements overestimated the margin in 30/70 images and underestimated the margin in 40/70 images.

Conclusions: On average MRI provided less error in margin measurements than X-ray, in addition to lower variability. Selection of the MRI series with the smallest predicted margin provided the least error. Anterior-posterior X-ray measurements were more accurate than the average view measurement or the lateral view. Surgeons should measure at least 2 cm away from the edge of the tumor on MRI imaging to have an adequate margin.

Oncologic Outcome of Low Testosterone in Male Patients with Pancreatic Cancer

Austin G. Kazarian[1], Holly K. Conger[1], Sarah L. Mott[2], Bradley T. Loeffler[2], Erin E. Talbert[2,3], Amy M. Pearlman[4], Carlos H.F. Chan[2,5]

[1]University Of Iowa, Carver College Of Medicine, Iowa City, IA, USA; [2]University Of Iowa, Holden Comprehensive Cancer Center, Iowa City, IA, USA; [3]University Of Iowa, Department Of Health And Human Physiology, Iowa City, IA, USA; [4]University Of Iowa, Department Of Urology, Iowa City, IA, USA; [4]University Of Iowa, Department Of Surgery, Iowa City, IA, USA

Introduction: Pancreatic ductal adenocarcinoma (PDA) is one of the leading causes of cancer-related death. Treatment for PDA involves an intensive combination of surgery, chemotherapy, and/or radiation that is often difficult for patients to tolerate. Recent studies have found that patients with PDA have worse quality of life (QOL) measures in all categories compared to patients with other cancer types. Testosterone deficiency is associated with chronic fatigue and weakness in addition to male sexual dysfunction. We have recently discovered that male PDA patients are rarely screened for testosterone deficiency despite reporting symptoms. Additionally, it has been shown that PDA may overexpress androgen receptors playing a role in tumorigenesis and disease progression. Our study aims to determine if male PDA patients have low testosterone levels and if testosterone levels correlated with oncologic outcome.

Purpose: To determine prevalence of low testosterone and investigate association of testosterone levels with oncologic outcomes in patients with PDA.

Methods: Serum samples were obtained from a cohort of male PDA patients enrolled in an institutional prospective repository at a National Cancer Institute-designated comprehensive cancer center from 2012-2020. Total testosterone (ng/dL) of each sample was measured using ELISA methods. Low testosterone was defined as a level <300 ng/dL per the American Urology Association guideline. Demographic and clinicopathologic variables, treatment and outcome data were abstracted. Cox regression models were used to assess the effect of patient and disease characteristics on progression-free survival (PFS) and overall survival (OS).

Results: Serum samples were available from 89 male PDA patients. Of these patients, 69.7% reported symptoms of low testosterone prior to sample collection, and nearly half (49.4%) were found to have a low testosterone level (median: 202 ng/dL; range: 123-294 ng/dL). Only 2.2% of patients had a prior testosterone level measured; none received testosterone replacement therapy. Fatigue was the most commonly reported symptom consistent with testosterone deficiency. After adjusting for metastatic disease at the time of diagnosis and treatment, testosterone level had no statistically significant effect on PFS (p=0.66) or OS (p=0.95).

Conclusion: Nearly half of the male PDA patients in this cohort were found to have low serum testosterone levels, but very few were tested in the clinical setting despite reporting symptoms. The overlapping symptoms between cancer and testosterone deficiency including fatigue and weakness may be the main reason for the lack of testosterone testing. Since there was no apparent difference in oncological outcome between PDA patients with low or normal testosterone levels, testosterone supplementation is most likely safe and may improve patients' QOL allowing them to better tolerate the intense treatment for PDA. Further prospective studies are warranted to explore the role of testosterone supplementation in improving men's health and overall well-being during PDA treatment.

Outcome of transition from daily to weekend steroids in patients with Duchenne muscular dystrophy

Morgan Kennedy, Bridget Zimmerman, Chyan Decker, Katherine Mathews

Objective: Duchenne Muscular Dystrophy (DMD), an X-linked genetic disorder of the gene dystrophin, results in males with declining muscle strength with onset of weakness before age 5. These patients are often wheelchair bound by age 12 with additional respiratory, cardiac, and orthopedic complications. The first-line class of medications for management of DMD is corticosteroids, which have serious side-effects. High doses of corticosteroids given twice per week (on the weekend only) reduce side-effects while maintaining benefits when used as the first dosing regimen in young patients. There is no published data on the effect of switching from a daily dosing regimen to weekend dosing. We explored outcomes of this intervention through a retrospective chart review.

Methods: Medical records of all DMD patients treated at the University of Iowa Neuromuscular Clinic were reviewed. We identified all patients who switched from a daily dosing regimen of corticosteroids to a weekend regimen. Additional inclusion criteria were daily corticosteroids for at least 1 year prior to switching with at least two appointments at UIHC that spanned 9 months or more after the switch. Patients late in the disease process where appropriate variables could not be tested for were excluded. Twenty patients met the inclusion criteria and key information was extracted. Unique control patients matched for age, steroid, and steroid dose on daily regimens were identified for 17 of the 20 study participants.

Results: Follow-up after the weekend corticosteroid switch (WCS) ranged from 8 months to 7.5 years with an average of 2 years +/- 1.53 SD. Age at last follow up ranged from 6 to 20 years with a median age of 15 years in the WCS group. 18 patients remained on weekend dosing after one year, while 2 elected to transition back to a daily regimen, citing progression of weakness in one case and facial swelling in the other. 10 (50%) were ambulatory at the time of WCS compared to 8 (47%) controls. 1 WCS and 2 controls lost ambulation within one year after WCS, but all were within the expected loss of ambulation timeframe based on published natural history data. Preliminary analysis of the WCS group showed that 3 (15%) patients reported worsened behavior in the year post-switch. 11 patients were of expected pubertal age (14 and above) at the time of corticosteroid switch. 5 (45%) reported increased pubertal maturation in the year post-switch. Direction of weight percentile change from the WCS to the last collected data point was analyzed. Insufficient data was available for 1 patient, 1 patient had no change in weight, 9 (45%) gained weight and 9 (45%) lost weight. All WCS patients had normal cardiac function prior to the switch. 1 (5%) had decline in ejection fraction into the abnormal range after the switch to weekend corticosteroids. 11 (55%) reported expected progression of weakness in the year post-WCS, while 6 (30%) noted stable strength with no change in functioning.

Conclusions: Initial analysis showed that switching from daily to weekend steroids resulted in desirable outcomes for a subset of patients including increased pubertal maturation (45%) and weight loss (45%) with few (15%) behavioral concerns. We note that weight loss is typically difficult for this patient population, which is consistent with our observation that an equal proportion of the study group gained weight despite the switch. Weakness did not appear to progress more rapidly than expected for natural progression of DMD. This information may help clinicians discussing corticosteroid dosing regimen options with patients having side effects on daily steroids. Future directions for this project include quantitative analysis of height and manual muscle testing data and case-control analysis of all variables for the 17 control-matched patients.

Determining the neuroprotective role and mechanisms of Nicotinamide Riboside and NAD+ using rodent models of chemotherapy-induced peripheral neuropathy

Student: Faizan Khawaja

Mentor: Donna L. Hammond, PhD

Background: Chemotherapy induced peripheral neuropathy (CIPN) is a serious side-effect caused by microtubule targeting agents such as Paclitaxel, a commonly used treatment for breast, lung, and ovarian cancers, among others. The symptoms of CIPN can be deleterious to quality of life, causing pain, tingling, hypersensitivity to hot and/or cold temperatures, and numbness. In severe cases, CIPN may necessitate reductions in dose or even the discontinuation of treatment, thus becoming a challenge to patients and clinicians alike.

Multiple mechanisms may contribute to CIPN, including mitochondrial dysfunction, imbalances in NAD^+ bioenergetics, and activation of apoptosis pathways, all culminating in a characteristic dying back of the terminals of sensory afferents in the skin. Nicotinamide Riboside (NR), a naturally occurring vitamin B3 precursor of NAD^+, can prevent and reverse Paclitaxel-induced behaviors associated with CIPN in rodent models – mechanical hypersensitivity of the hind paws and place-escape avoidance in female rats (Hamity, et al. 2017). It can also prevent paclitaxel-induced loss of intraepidermal nerve fibers in the skin or the hind paw (Hamity et al., 2020). As of yet, the mechanism by which NR can protect against neurodegeneration and alleviate CIPN remains undetermined. The goal of this study was to determine whether (1) paclitaxel alters transcript for the enzymes in the salvage pathway for synthesis of NAD^+ or the apoptosis pathway, (2) NR by itself alters these enzymes, and (3) NR can prevent paclitaxel-induced changes in these transcripts.

Methods: Female Sprague-Dawley rats were randomly assigned to one of four treatment groups. Paclitaxel i.v. + NR p.o.; Paclitaxel i.v. + water p.o.; Cremophor vehicle i.v. + NR p.o.; and Cremophor vehicle + water p.o. Rats received daily treatment with 200 mg/kg NR for one week before administration of paclitaxel, which continued for another 14 days. Rats were then euthanized and dorsal root ganglia (DRG) were harvested. Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was used to quantitate copy numbers for nicotinamide riboside kinase 1 (*nmrk1*), the enzyme by which NR enters the NAD^+ biosynthetic pathway, and nicotinamide mononucleotide adenylyl transferase (*nmnat2*), the enzyme responsible for conversion of nicotinamide mononucleotide into NAD^+ and thought to play a role in axon degeneration. For the apoptosis pathway, cDNA from the same DRGs was processed for anti-apoptotic members of the *BCL* apoptosis regulator family: *bcl2*, *bcl-xl*, and *bcl2l2 (bcl-w)* which is thought to be particularly critical for paclitaxel's effect. The experimenter was blinded to treatment conditions. Data were normalized to *hprt*, a housekeeping gene previously determined to be stably expressed across all treatment conditions.

Results: Data collected to date indicate that treatment with paclitaxel does not significantly alter the expression of *nmrk1* compared to vehicle-controls; however, 14 days treatment with NR resulted in a two-fold increase in expression of *nmrk1*. Levels of *nmnat2* were unchanged by either paclitaxel or NR treatment, alone or in combination.

Discussion/Conclusion: These intriguing data suggest that NR may be able to induce its entry into the NAD^+ salvage pathway, increasing NAD^+ levels by a feed-forward mechanism. Of note, loss of NAD^+ is thought to contribute to the degeneration of sensory afferents after injury, supporting the idea that agents preventing the loss of NAD^+ are neuroprotective. Results with the three antiapoptotic genes are pending. It will be of interest to determine whether paclitaxel decreases the expression of these genes and, if so, whether the effect can be prevented by NR. The results of these studies will provide much needed information about the mechanisms by which paclitaxel causes a dying back of peripheral afferents, as well as determine whether the ability of NR to prevent this effect is related to restoration or enhancement of NAD+ levels in neurons and/or anti-apoptotic genes.

Modeling Diabetes: Hyperglycemia Affects TGFBI Expression and Glycation in the Extracellular Matrix of the Posterior Cornea

Kenten Kingsbury, BS, Jessica M. Skeie, PhD, Timothy Eggleston BBA, BSE**,** Hanna Shevalye, BS, Gregory Schmidt, MBA, CEBT, Esther Baker, BA, MA, MBA**,** Mark A. Greiner, MD.

Problem: Diabetes is a risk factor for premature failure of corneal transplants that use the posterior corneal tissue. Previous work from Skeie *et al.* revealed that transforming growth factor-beta induced (TGFBI), an extracellular matrix (ECM) protein, was increased in non-insulin dependent diabetic corneal ECM. Another study noted the high likelihood that TGFBI is a target of increased posttranslational modification through the formation of advanced glycation end products (AGEs) in the onset of diabetes managed without insulin. If TGFBI and AGEs are found to colocalize as a result of hyperglycemia, a major and essential component of diabetes, measures may be developed to track diabetes severity and improve surgical outcomes using diabetic donor tissue.

Purpose: Localize and semi-quantitate the presence of AGEs on the ECM protein TGFBI in a hyperglycemic corneal endothelial cell (CEC) culture model.

Methods: Immortalized human CECs were cultured in four environments of increasing glucose concentration (5.5 mM, 13.0 mM, 30.5 mM, and 105.5 mM). Cell were cultured for two weeks prior to analysis via immunohistochemistry and western blot assays.

Results: Immunohistochemistry revealed that with rising hyperglycemic levels there was an increase in deposition of TGFBI and AGEs in the ECM of immortalized CEC ECM. Merged fluorescent images revealed the colocalization of TGFBI and AGEs. Western blotting results quantified an increase in TGFBI in the ECM fraction of the CECs until 105.5 mM glucose, where the level appeared to decrease slightly. Quantification of AGEs showed a marked increase with increasing hyperglycemia.

Conclusion: Hyperglycemia, an essential feature of diabetes mellitus, can initiate increased TGFBI deposition in the ECM of the posterior cornea endothelium, along with an increased amount of associated glycation events. These results may lead to development of metrics and treatments to improve diabetic donor tissue quality and performance.

Identifying Antidepressant Gene Expression Signatures from an L1000 Dataset
Brian Kinnaird, M2 student; Kang-Pyo Lee Ph.D. (collaborator); Mark J. Niciu M.D. Ph.D (mentor)

Background, rationale, or introduction: Major depressive disorder, which affects about 16% of the world population at some point in their lives, is associated with serious consequences for health and quality of life. Because many commonly-used antidepressants can take weeks-to-months for antidepressant efficacy and are ineffective in up to one-third of severely depressed patients, new or repurposed antidepressant medications are needed. As global gene expression changes in response to antidepressants have been studied in non-human organisms and peripheral human tissue but not in the human brain, there is a critical need to study specific transcriptional effects in human neural cells to improve the understanding of antidepressant mechanisms of action and develop antidepressant treatment response biomarkers. Well-validated, neurobiologically-informed biomarkers could be powerful tools in antidepressant drug development.

Study Aim: To investigate whether there are characteristic, identifiable molecular antidepressant response signatures that depend on the specific target engagement, i.e., serotonin transporter for selective serotonin reuptake inhibitors.

Method: Gene expression databases were downloaded from the Gene Expression Omnibus, a publicly accessible repository of high-throughput L1000 assay gene expression data released by the Library of Integrated Network-based Cellular Signatures (LINCS) consortium. These data were probed for human transcriptomic data at physiologically-relevant doses of each antidepressant compound selected for study. Using the open-source Jupyter Notebook as a web-based environment for cloud computing, commands employing the Python coding language were used first to concatenate relevant data spread across five separate databases into a single milieu. Then, iterations of the dataset were progressively filtered by antidepressant class, i.e. selective serotonin reuptake inhibitors (SSRIs), dosage, exposure time, cell line treated, and corresponding gene expression Z-scores. A Z-score greater than or equal to 2 was considered a significant upregulation, and less than or equal to -2 was considered significant downregulation. For each SSRI, upregulated and downregulated genes were programmatically sorted by neuronal-like cell line (one was terminally differentiated to be neurons; the other was stem cells derived from fibroblasts but not terminally differentiated). Genes that were upregulated or downregulated by a majority of the available SSRIs were catalogued and their known functions, when available, were compiled.

Results: Data were analyzed for five SSRIs (escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) from a series of trials in which neural progenitor cells were treated at 10 μm doses for 24 hours. Across the more than 12,000 genes probed, 10 unique genes were upregulated (Z-score ≥ 2) by at least three of the five SSRIs. Identified functions of these genes include axon proliferation (e.g., *MAP7* or microtubule-associated protein 7), cell growth and survival (e.g., *TM4SF1* or transmembrane 4 L six family member 1), and cell cycle regulation. Additionally, 11 genes were downregulated (Z-score ≤ -2) in at least three of the five SSRIs, including those involved in DNA replication and repair (e.g., *PCNA* or proliferating cell nuclear antigen), inhibition of DNA transcription, cytoskeletal dynamics (e.g., *PFN1* or profilin 1), and cell adhesion and signaling.

Discussion: In the dataset examined, 10 and 11 genes were found to be upregulated or downregulated, respectively, by at least three of five SSRIs tested. These results demonstrate the plausibility of characteristic, identifiable molecular antidepressant response signatures that warrant further investigation. The study was limited by significant processing times for certain computing operations as well as the variability inherent in the dataset due to the methods used to generate gene expression Z-scores. Some potential next steps include exploring SSRI transcriptomic commonalities for not just the exact same genes, but those closely associated with one another (e.g., by function); and exploring molecular antidepressant response signatures in compounds with different mechanisms of action, such as dopaminergic (e.g., bupropion) and glutamatergic (e.g. ketamine and its bioactive metabolites) antidepressants. Experimentally, this will involve differentiating iPSCs into human corticospheroids and using single cell RNA expression data to determine the antidepressant propensity of individual neurons exposed to both traditional and rapid-acting antidepressants, e.g. racemic ketamine and bioactive ketamine metabolites such (2R,6R)-hydroxynorketamine.

Assessment of Virtual Medical Education During COVID-19

Michael Klemme, Anne Nora, Melissa Chan, Sarah Shaffer

Purpose

Identify strengths and weaknesses of virtual medical education to improve future clerkships, as well as appreciate how virtual education during the pandemic impacted students' trajectory and residency choice.

Background

Virtual learning has proven effective in supplementing medical education. However, little was known about directly replacing clinical rotations with online learning. This survey sought to qualitatively evaluate how the transition to virtual education transformed clinical training for medical students during the COVID-19 pandemic.

Methods

Surveys were sent out through an anonymous link to clerkship directors and clinical medical students. Results were reviewed and categorized based on overarching themes with the intent to summarize and identify strengths and weaknesses of virtual medical education.

Results

Students were challenged by the loss of clinical experiences and lack of patient and interprofessional interaction during virtual clerkships. While zoom lectures were inadequate at replacing in-person learning, virtual surgical videos with annotations were helpful. 70% percent of students experienced decreased motivation and 60% rescheduled Step 2 CK. Seventy-two students reported spending more quality time with family and friends. Nearly 50% of M3s and 20% of M4s noted concern about the impact of shortened clinical rotations on their specialty choice. Clerkship directors believed education, while challenging, continued unhindered despite lacking patient care.

Discussion

The months students spent virtually during the COVID-19 pandemic revealed few positives and many negatives, which may influence their career trajectory. Educators believe students' clinical decision-making will have the largest deficit. Appreciation of this impact should be used to help guide decisions to augment future virtual and clinical education.

An exploratory survey of the cell density of progenitor populations in proximal to distal native airways of the ferret lung transplant model.

Camilla Koczara, M2
Dr. Kalpaj R. Parekh, MBBS, Department of Surgery
Bethany Ahlers, Tom Lynch, Vitaly Ievlev, and Albert Pai

Rationale: Lung transplantation is an important, often lifesaving, therapeutic procedure for patients with end-stage lung disease. However, long-term patient outcomes are threatened by devastating chronic lung allograft dysfunction (CLAD) diseases that develop in a majority of lung transplant recipients. Obliterative Bronchiolitis (OB) is the most common of these chronic rejection pathologies, affecting 50% of transplant patients within 5 years and 76% of patients within 10 years. OB remains the chief cause of death following the first year after transplant and is the most frequently cited indication for re-transplant in patients. Therefore, understanding the mechanisms of OB pathogenesis is critical for the development of preventative and curative measures for the majority of lung transplant recipients.

Objectives: The mammalian lung possesses a unique cellular architecture of stem/progenitor cell niches throughout the lung. On the surface of the conducting airways in the surface airway epithelium (SAE), basal cells serve as the primary source of multipotent stem cells (SCs)s. More proximally in the airway, embedded between surface airway epithelium (SAE) and tracheal cartilage are submucosal glands (SMG), which are another source of progenitor cells. The Parekh lab uses ferrets as a model for lung transplantation due to the key similarities in distribution and abundance of stem cells between ferret and human lungs and the fact that ferret lung allografts develop similar pathology as seen in a human allograft. Using this ferret model, it has been shown that the depletion of airway stem cells leads to the development of OB in allografts. To better understand their presence and purpose, proximally to distally in chronic lung transplant rejection, this study quantifies these stem cell populations in the ferret model to determine in which locations these cells contribute to the bulk of lung damage repair.

Methods: The surface airway epithelial (SAE) and submucosal gland (SMG) stem cells were extracted from four wildtype male and four wildtype female ferrets (N=8) using a series of digestive steps aimed at liberating the two distinct cell populations. These cells were isolated from the main bronchus, lobar bronchus, and distal bronchus segments of the Left Upper Lobe (LUL), the Left Lower Lobe (LLL), the Right Upper Lobe (RUL), and the Right Lower Lobe (RLL). Fluorescent-activated cell sorting (FACS) was utilized to determine the abundance of the SMGs and SAEs from each bronchus in each respective lobe. The differences observed in each location were then analyzed using Prism software.

Results: Wildtype ferret lungs reveal significant differences in SAE and SMG populations as one navigates proximally to distally in the airway. The main bronchus SAE population (cells/g of airway tissue) is significantly smaller than that of the lobar and distal bronchus SAE populations (N=20; p<0.05). And within the distal bronchus segments, the SAE cell population was far greater (cells/ g of airway tissue) than that of the SMG cell population (N=20; p<.001). No significant differences in the number of cells per gram of tissue were found between female versus male ferrets, upper lobes versus lower lobes, and right lobes versus left lobes (N=20; p>0.5). Lastly, in comparing the ratio of SAEs to SMGs in each location, it was revealed that proximal to distal in the ferret airway, the relative SMG population size declines (cells/g of airway tissue), as the relative SAE population conversely increases (N=14; p<.001).

Conclusions: SAEs and SMGs compartments differ significantly, proximally to distally in the native ferret model. Establishing this control criterion for SAE and SMG cell quantities in both the proximal to distal airways in the ferret model is critical for fully understanding their self-renewing capabilities in the ferret transplant model, and by extension the human lung.

Maximizing Emergency Department Efficiency: An Analysis of Team Triage at UIHC
Steven Leary, Andrew Nugent, MD

Prior studies have shown that a provider in triage model can improve measures of emergency department (ED) efficiency and help combat the nationwide issue of an increasingly higher number of ED visits each year. In August 2017, the UIHC ED instituted Team Triage in hopes of replicating these results. Since that time, there have been a total of 4 iterations of Team Triage each with the same goal of maximizing efficiency. We performed a retrospective analysis of patient care data from October 2014 to August 2020 to determine which iteration, if any, significantly impacted measures of ED efficiency including wait times, total left without being seen, and length of stay among others. We also aimed to identify specific areas in which Team Triage could be improved so as to guide future changes to ED operations.

We gathered patient care data using the reports function in the Epic electronic medical record system. It was then stratified by the different iterations of Team Triage and by the acuity of patients seen by Team Triage. We found that Team Triage did not significantly improve any measure of ED efficiency regardless of patient acuity. However, the number of admitted patients boarding in the ED also increased over this same time period making it a potential confounder of our results. This remains an ongoing project and our data is currently being used to form a fifth iteration of Team Triage as well as guide other changes to ED operations.

Correlation of POCUS Measures of OSA with Apnea- Hypopnea Index (AHI): An Exploratory Study.

Authors: Ethan Lemke, Matthew Behrens
Mentor: Rakesh Sondekoppam M.D.

Background: Obstructive sleep apnea (OSA) is characterized by recurrent collapse of the pharyngeal airway during sleep, resulting in reduced airflow (hypopnea) or complete cessation of breathing (apnea). Identification of OSA is crucial to prevent potentially life-threatening cardiopulmonary complications in the perioperative environment. Despite this, a large proportion of individuals have undiagnosed OSA at the time of surgery. Current screening tools are mainly questionnaires that are sensitive but not specific, resulting in many false positives and possibly unnecessarily increasing resource utilization, cost burden, and legal implications. The gold standard for diagnosing OSA is a polysomnography (PSG) - or sleep study - which can be expensive and not widely available. These highlight the need for an objective and relatively easier way to diagnose OSA at the bedside using the point-of-care ultrasound (POCUS). This noninvasive tool can also be used to evaluate a patient's airway, which may be useful for both OSA screening and airway management.

Purpose: The purpose of our study was threefold: 1) to evaluate POCUS measures of OSA and correlate them with the severity of a patient's OSA based on their PSG apnea-hypopnea index (AHI). 2) To find which measure or combination of measurements from POCUS can diagnose the incidence and severity of OSA. And, 3) to develop a protocol for using POCUS to screen for OSA.

Methods: This prospective observational study was approved on May 23, 2020 by the University of Iowa Institutional Review Board (IRB #202001068). Patients between 18-85 years old undergoing surgery with a history of PSG confirmed OSA within the last 4 years were approached to participate in this study. A consent to obtain information sheet was completed as needed for subjects whose PSGs were not done at UIHC. The STOP-Bang questionnaire was completed after surgery, prior to scanning by the research team. Subjects were scanned when patients were awake and the images stored to perform predefined measurements on parameters deemed important for the diagnosis and quantification of OSA. These included tongue base thickness in the sagittal plane with and without Muller maneuver (TBT-S and TBT-S MM), upper airway length with and without Muller maneuver (UAL and UAL MM), tongue cross sectional area (T-CSA), skin-hyoid distance (SHD), retroglossal diameter (RGD), transverse diameter of the pharynx (TDP), retropalatal diameter (RPD), tongue base thickness in the coronal plane (TBT-C), distance between lingual arteries (DLA), and right/left lateral parapharyngeal wall thickness (R/L LPWT).

Results: To date, 118 patients have been enrolled in the study. Of those 118 enrolled, PSG data has been received for 63 subjects - 5 of which were unable to be scanned. This left 58 subjects for preliminary data analysis, with a mean AHI of 22.56 events/hour. The average time to complete the US scanning was 8 minutes and 57 seconds, with a range of 4 to 22 minutes. Conclusion: At the time that this abstract is due, data has not yet been analyzed to examine the possible relationships that may exist between the subject's reported AHI and POCUS measurements.

Predictive Power of Quantitative Ultrasound Measurements in Children with High-Grade Hydronephrosis

Tomas Lence, Dr. Christopher Cooper
Carver College of Medicine, Iowa City, IA, USA

Background

Prenatal hydronephrosis (HN) is diagnosed in 1-5% of all pregnancies. The Society of Fetal Urology (SFU) grading system classifies HN into low and high-grade disease, but is a subjective grading system with significant inter-observer variability. Most cases of low SFU grade HN either resolve or remain stable and maintain renal function. Higher grades of HN are associated with an increased probability of a ureteropelvic junction obstruction (UPJO) which left untreated results in a loss of kidney function. UPJO is an indication for surgical correction via a pyeloplasty to relieve the obstruction and restore low pressure flow of urine from the kidney into the ureter and bladder. However, many patients with high grade HN do not have a UPJO. Therefore, the challenge is to determine which patients with high grade HN are most likely to have a UPJO necessitating a pyeloplasty.

Pyramidal thickness (PT) has been identified as a potential marker on ultrasound (US) imaging that can differentiate obstructive from non-obstructive high grade HN. In the only previous study evaluating PT for this purpose it was found to have 98.1% sensitivity and 89.7% specificity in predicting pyeloplasty, making it more reproducible and predictive than either the SFU grading system or other ultrasound parameters.

Objective

We evaluated the predictive ability of PT alone and in combination with several other objective ultrasound measurements in identifying children with high grade hydronephrosis that required pyeloplasty. The predictive ability of these measurements was compared to several other grading systems.

Patients and Methods

We retrospectively analyzed the charts of children who presented to the University of Iowa Hospitals and Clinics with hydronephrosis from 2006-2018. Inclusion criteria was isolated high grade HN. We excluded patients with hydronephrosis due to other known causes such as vesicoureteral reflux posterior urethral valves. We obtained demographic data, ultrasound (US) measurements including the anterior-posterior renal pelvis diameter (APD), renal length, pyramidal thickness (PT), as well as the SFU and Urinary Tract Dilation (TUD) grades, and available nuclear renal scan data. Patients were divided into those requiring pyeloplasty (due to increasing hydronephrosis and/or decreasing relative renal function) and those followed conservatively. For the pyeloplasty group, ultrasound measurements used were obtained from the last ultrasound prior to surgery and around 3-months post-operatively. Conservatively treated patients' data was obtained from the ultrasound with the worst HN. Both groups of patients had data recorded from their last follow-up visit as well. Comparative statistics were utilized to analyze differences between these groups..

Results

88 boys and 22 girls with 125 hydronephrotic kidneys (15 patients had bilateral HN) were evaluated. 62 and 63 kidneys had SFU grade III and IV HN, respectively. 63 kidneys underwent pyeloplasty.
The average PT of the conservative group (3.49 ± 1.18 mm) was significantly larger than the pyeloplasty group (2.57 ± 1.10 mm)($p < 0.001$). The average APD in the conservative group was significantly smaller(1.09 ± 1.02 cm vs. 1.99 ± 1.02 cm;$p < 0.001$) as was the average renal length of the conservative group (5.69 ± 0.93 cm vs. 7.32 ± 1.40 cm; $p < 0.001$) compared to the pyeloplasty group, respectively.

Conclusion

There are significant differences between the conservative and pyeloplasty groups in APD, PT, and renal length measurements. These measurements can be used to develop a new, wholly-objective grading method that decreases the inter-rater variability notorious in the SFU and UTD grading systems. Development of a weighted scoring system incorporating these measurements to more accurately predict a patient's likelihood of requiring pyeloplasty is underway.

Authors: Gage T Liddiard, Catherine Marcinkiewcz
Title:

Introduction:

Alzheimer's Disease and Dementia are both enormous healthcare burdens, both monetarily in the form of $277 billion, and emotionally. Their prevalence is also increasing, and almost all of us today know directly, or know of someone who is affected by these diseases. Thus, it is of the utmost importance that we begin to develop an understanding of these diseases' progression so that we may develop treatments to aide those affected.

The Marcinkiewcz lab is interested in understanding the lifelong progression of Alzheimer's disease, specifically in the accumulation of Tau proteins that eventually yields the patterned and system-wide cell destruction and death responsible for the symptoms commonly associated with the disease. Our main goal is to find the early-affected brain regions that experience this accumulation, and to understand the effects that are mediated via this localized accumulation. These key brain regions are the Dorsal Raphe Nucleus, associated with serotonin and mood, and the Locus Coeruleus, associated with anxiety and sleep-related behaviors. Alzheimer's Disease and Depression can be thought of as sharing many of the same symptoms, and a history of depression is a known risk factor for later development of this disease. Add onto that the close relationship of anxiety and depression, as well as the history of sleep disturbances in Alzheimer's patients and it's easy to see why these brain regions might be some of the first involved in Alzheimer's disease.

As Alzheimer's progresses, the proteins involved in the pathologic process, namely beta amyloid and Tau, begin to build up and disrupt the normal function of the brain. Focusing on Tau, which is the main microtubule assembly protein in mature neurons, this protein becomes pathologically hyperphosphorylated, and less soluble. This leads to aggregation and disruption of the normal function of the neuron, and eventually to cell death. In the early stages that we are exploring this disruption, specifically in the hippocampus, can lead to neuronal disruption in the form of loss of synapses, decreased long-term potentiation, altered basal synaptic transmission, microgliosis in white matter, and neurodegenration. It is this same type of disruption that we theorize might be occurring in the Dorsal Raphe Nucleus and the Locus Coeruleus that leads to a "depression-like phenotype" that is thought to be a precursor to Alzheimer's disease.

Methods/Future Directions:

In order to recreate this early accumulation of Tau proteins in both the Locus Coeruleus and the Dorsal Raphe Nucleus we will be using stereotactic viral injections of P301L mutant Tau protein that targets both of these regions. This mutation is found to yield an aggressive neurodegenerative form of Tau, and creates a pathology modeling frontotemporal dementia. After the injection and the one month required for viral expression, we should be able to observe Tau expression, as well as analyze the mouse's behavior to observe for any phenotypic changes in said behavior. Due to the Dorsal Raphe Nucleus's involvement with serotonin we hypothesize to see a depression-like phenotype from this tau-mediated disruption. Due to the Locus Coeruleus's involvement in Norepinephrine signaling, we hypothesize to see an anxiety/sleep related phenotype. Our lab has currently injected into the Dorsal Raphe and has recorded behavioral Data. Analysis of this behavior is ongoing. Our lab has also injected into the Locus Coeruleus and is in the waiting period for the expression of the virus.

For our future directions we plan to coordinate with Dr. Gordon Buchanan to conduct a sleep-study in these Locus Coeruleus animals, and to perform EEG recordings 2 weeks post-injection to observe behavioral phenotypes even earlier than the ones currently being assessed. We also plan to explore the trans-synaptic transmission of Tau protein and to observe how it spreads from one brain area to another.

Combined Biomechanical and Clinical Analysis of the influence of Rotator Cuff Condition and Glenosphere Lateralization on Functional and Mechanical Outcomes in Reverse Shoulder Arthroplasty

Pre-M1 Student: Shannon Linderman, Mentor: Donald D. Anderson, PhD
Collaborators: Joshua Johnson, PhD; Brendan Patterson, MD, Department of Orthopedics & Rehabilitation

Background: Repair of the subscapularis following reverse shoulder arthroplasty (RSA) has mixed clinical results. Glenosphere lateralization increases the muscle moment arm and force required to externally rotate the humerus, and effectively moves the subscapularis insertion site laterally and inferiorly. This repositioning of the insertion site also increases tension across the joint, which can challenge the expected range of motion (ROM) gains from glenosphere lateralization in RSA. Poor rotator cuff (RC) muscle quality is associated with increased musculotendinous stiffness, and the subsequent effect of compromised tissue repair on RSA functional outcomes remains unclear. The objective of this study was to investigate the influence of RC condition and glenoid component lateralization on mechanical and functional outcomes in RSA using a new integrated clinical assessment, imaging, and biomechanical modeling approach.

Aims: (Aim 1) Computationally determine the mechanical influence of RC condition and glenoid component lateralization on external rotation (ER) range of motion (ROM), torque, and subluxation risk in RSA.
(Aim 2) Establish a retrospective RSA registry to assess relationships between pre and post-operative shoulder function (ROM and strength) and RC condition.

Methods: (Aim 1) A validated finite element (FE) model incorporating the Zimmer Trabecular Metal RSA system was utilized. The deltoid and subscapularis tendon were tensioned prior to shoulder ER. Baseline subscapularis stiffness was varied by 20% and 40% to evaluate its influence. Effects of three glenosphere lateralization offsets (2, 4, 10 mm) and associated increased subscapularis tension on impingement-free ROM, torque, and subluxation were assessed in this generic FE model during ER (0°-50°) for nine test cases.
(Aim 2) A registry was established to retrospectively analyze relationships between shoulder function and RC condition in our patient cohort (n= 98). RC condition was assessed from pre-operative CT reconstructions (axial reorientation perpendicular to scapular plane, n=11) by measuring cross-sectional area (CSA) of RC muscle bellies, categorizing fatty infiltration (FI – Goutailler classification) and grading muscular atrophy (Warner classification). Correlations between RC condition imaging assessments and retrospectively collected, visually approximated and/or qualitative pre and post-RSA functional shoulder measures (strength and ROM) were performed. A quantitative clinical strength and ROM assessment protocol using hand-held goniometer and dynamometer was designed and assessed for feasibility to integrate into an outpatient clinic workflow

Results: (Aim 1) Impingement-free ROM increased with glenosphere lateralization (35°, 40°, 45° for 2 mm, 4 mm, 10 mm lateralization, respectively). A 20% increase in subscapularis stiffness was associated with a 10-18% increase in pre-impingement torque, while a 22-37% increase in torque was observed for a 40% stiffness increase. Pre-impingement torque increased by 14-23% when lateralization was increased from 2 mm to 4 mm, while a 96-120% torque increase occurred for a 10 mm lateralization. Maximum post-impingement subluxation varied minimally with changes in subscapularis stiffness (<0.5 mm within the same glenosphere offset).
(Aim 2) Mean subscapularis CSA normalized by subject height was 6.60 ± 2.78 cm^2/m with a mean FI grading of 1.5 ± 0.93. 60% of assessed patients were able to achieve at least 50° ER at 2 and 6 months post-op respectively, compared to the model simulated 50° ER (Mean pre-op ER $47.5 \pm 12.1°$, Mean post-op 6-month ER $48.33 \pm 3.2°$, range 15-60 °). However, no significant correlation between subscapularis or infraspinatus FI and CSA and visually assessed and qualitative pre or post-operative ER and IR ROM and strength was noted. Highest degrees of muscular atrophy were weakly associated with lowest pre-operative ER strength and lowest CSA, while weak positive relationships between FI and atrophy, and weak negative relationships between CSA and FI were observed. A quantitative protocol to measure shoulder ROM (flexion/extension, abduction/adduction, internal/external rotation) and strength (internal rotation, external rotation, and abduction) was demonstrated to take on average 8 minutes to implement in the clinic.

Discussion: Increased subscapularis stiffness does not limit impingement-free ROM or substantially decrease post-impingement subluxation. Glenosphere lateralization improves impingement-free ROM and decreases post-impingement subluxation. Mechanical gains achieved through lateralization may be hindered by increased torque demands, especially when a stiffer subscapularis is repaired. As lateralization increases subscapularis tension, greater torque is required to externally rotate the shoulder. Subscapularis repair with the simulated baseline stiffness requires relative increases in torque that the reconstructed shoulder may not be able to physically produce to rotate the glenohumeral joint, particularly at 10 mm lateralization. These model results suggest subscapularis repair may not be indicated where a lateralized glenoid component is utilized and subscapularis quality is compromised. The generic FE model appears aligned with in-vivo patient produced post-operative ROM and force. Successful integration of the new clinical assessment protocol into clinic workflow will be essential for collecting quantifiable data needed for future patient-specific modeling such as effects of subscapularis repair on joint contact stresses.

A Just Enough Interaction Segmentation Tool Improves Consistency and Efficiency for Radiotherapy Contouring of Meningiomas

Weiren Liu, Zhi Chen, PhD, Honghai Zhang, PhD, Dongxu Wang, PhD, Kristin Plichta, MD, PhD, Mark Smith, MD, Milan Sonka, PhD and John M Buatti, MD

Purpose/Objective(s): Standard manual contouring of meningiomas is time consuming and introduces substantial inconsistencies. A user-friendly segmentation tool could reduce physician workload and improve reproducibility

Materials/Methods: Sixteen cases of treated meningiomas were used for development of a 3-dimensional LOGISMOS (Layered Optimal Graph Image Segmentation for Multiple Objects and Surfaces) based solution for segmentation. The automated LOGISMOS method is started by placing a sphere encompassing the tumor. Starting from the center of the sphere, columns of graph nodes are constructed. LOGISMOS segmentation finds the optimal set of graph nodes on the boundary with minimum total cost. Prior knowledge such as the shape and anatomy of the target constrains segmentation. If needed, errors in automated segmentation are corrected by the user interaction with the algorithm rather than manually slice-by-slice. This process uses our just enough interaction (JEI) approach that considers the expert hints pointing to the correct boundary locations to modify segmentation cost functions and search for a new optimal solution.

The 16 cases were manually contoured, then contoured using the JEI-LOGISMOS segmentation tool by two central nervous system experts. Cases were randomly displayed for both manual and JEI-LOGISMOS analyses in several sessions to avoid bias. Segmentation accuracy indices were determined as continuous variables: mean ($\pm$ standard deviations) or median (and interquartile ranges IQR) where appropriate. Computer-analysis accuracy was evaluated using point-wise 3D surfaces distance errors and volumetric linear regression. To assess reproducibility, Dice coefficient along with 3D relative volume difference (RVD) were obtained. To evaluate the efficiency of the automated method, time required for automated contouring with JEI and manual contouring was compared using Wilcoxon signed-rank test.

Results: Our 3D LOGISMOS segmentations with JEI of both experts achieved sub-voxel precision (voxel size ~1 mm) for meningioma tumor surfaces (JEI signed error: 0.86 $\pm$ 1.82 mm for expert 1, 0.24 $\pm$ 1.26 mm for expert 2) and provided accurate volume measurements in comparison to manual contouring (volume regression: $R^2 = 0.93$, $p < 0.001$ for expert 1, $R^2 = 0.96$, $p<0.001$ for expert 2;). The inter-observer variability of automated contouring showed better reproducibility compared to manual contouring (Dice: 87.4% vs. 83.6%; RVD: -1.1% vs. 14.9%). Median time required for contouring one case was significantly reduced for both experts (-204 seconds, $p = 0.01$, 46.5% faster for expert 1 and -228 seconds, $p = 0.04$, 35.8% faster for expert 2.)

Conclusion: Automated contouring using a JEI approach following the automated 3D LOGISMOS segmentation improves reproducibility and efficiency of contouring for meningiomas. Volumes obtained using manual tracing and JEI-LOGISMOS were highly comparable.

Assessment of Mitochondrial Health and Initiation of Gene Therapy in Iris Pigment Epithelial Cells from a Donor with MELAS

Lola Lozano, Nathaniel Mullin, Erin R. Burnight, Robert F. Mullins, Edwin M. Stone, Budd A. Tucker

Mitochondrial diseases are devastating disorders that preferentially affect the body's most metabolically active tissues, which are abundant in these energy-producing organelles. The visual system is one of the most active in the body[1]. As such, it is affected by a collection of diseases that predominantly result from mutations in the mitochondrial genome (mtDNA). The A3243G mutation resides within the *MT-TL1* gene which encodes for the mitochondrial tRNA Leucine1[2]. One disease that results from this mutation is Myopathy, Encephalopathy, Lactic Acidosis, and Stroke-like Episodes (MELAS)[3]. No treatment currently exists for the vision loss experienced by patients afflicted by this disease or for the other degrading systemic effects [4].

The main aim of this study is to measure the health status of mitochondria in Iris Pigment Epithelial (IPE) cells from a donor with MELAS compared to healthy, control IPE cells. An additional aim is to design and begin construction of a gene therapy strategy that will successfully deliver a wildtype copy of the *MT-TL1* gene to the mitochondria and replace the mutant variant.

In order to assess the health of mitochondria in living cell cultures, we measured their ability to maintain a healthy, hyperpolarized membrane potential over time while in the presence of a drug that inhibits mitochondrial functioning. After administering a photosensitive dye and the cytotoxic drug, relative fluorescence values were measured on a microplate reader as a proxy for membrane potential maintenance. Unexpectedly, we found higher levels of fluorescence values indicative of greater mitochondrial membrane potential maintenance in the MELAS donor's cells compared to the healthy, control IPE cells.

Additionally, we designed and constructed a transgene cassette plasmid to deliver a wildtype copy of the *MT-TL1* gene to mitochondria. Because it is highly suspected that mitochondria lack an import mechanism for nucleic acids (DNA, RNA, etc.)[5], we adopted the recently successful strategy of delivering the DNA via viral particles with surface proteins modified to express mitochondrial targeting sequences[6]. Once the viral particles are assembled, they will be applied to living cells from the MELAS patient and subsequently evaluated for their efficiency as replacing the mutant *MTTL1* gene in mtDNA with the wildtype copy.

The surprising finding of increased mitochondrial membrane potential maintenance in MELAS-donor cells exposed to a cytotoxic drug, might be suggestive of increased mitochondrial resilience in the presence of environmental stressors. This resiliency may be the result of compensatory mechanisms activated in diseased mitochondria. This speculation is further supported by other findings in the lab which revealed MELAS donor IPE cells contain higher levels of total mtDNA copies as well as lower levels of mutant mtDNA copies to wildtype mtDNA copies compared to cells from other eye tissues within the same MELAS donor. Additional research is needed and ongoing in the lab in order to further investigate and verify this speculation.

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Genome Sequencing Reveals Distinct MRSA Subtypes
at Different Age Groups in Cystic Fibrosis

Lucas Maakestad

Mentor: Anthony Fischer, MD, PhD

Collaborators: Harry Porterfield, Andrew Thurman, Christian Zirbes, Nicholas Pitcher, Zoe Kienenberger, Alexis Hansen, Valerie Reeb, Brad Ford, Daniel Diekema

Background: Methicillin resistant *Staphylococcus aureus* (MRSA) is a prevalent and consequential pathogen in cystic fibrosis (CF). MRSA is associated with worse lung function and increased mortality. MRSA phenotypes vary between patients, suggesting underlying genetic heterogeneity of MRSA in CF. Whole genome sequencing (WGS) may reveal differences in bacterial genomes that increase the risk of poorer outcomes.

Hypothesis: Some subtypes of MRSA are associated with poorer outcomes in patients with CF.

Method: We obtained 97 unique MRSA isolates from 74 individuals with CF from 2017. We collected DNA from MRSA and sequenced whole genomes using the Illumina platform. We determined the sequence type (ST) and the phylogenetic relationship between isolates. We aligned genome assemblies to a set of accessory genes from 25 reference genomes. We clustered the MRSA isolates by their accessory gene content and correlated each cluster with age and FEV_1.

Results: In this CF cohort, unrelated individuals had genetically distinct MRSA strains. The most prevalent MRSA ST were ST5 (N=54), ST105 (N=14), and ST8 (N=14). We classified the MRSA isolates into three clusters based on their accessory genome content. The first was dominated by ST5 and ST105, and the second by ST8. The ST5/105 cluster was more common among older patients who had lower FEV_1. All MRSA within this cluster encoded the enterotoxin gene cluster toxins and generally encoded SCC*mec* type II. The ST8 cluster sometimes encoded Panton Valentine Leukocidin and was positive for SCC*mec* type IV.

Conclusion: MRSA sequence types in patients with CF are predictive of accessory gene content. Two major clusters of MRSA were identified in this cohort. The cluster represented by ST5 and ST105 MRSA was the most prevalent and was found in older patients who had lower lung function. ST8 MRSA was more common in younger patients, and thus has the potential to rise in prevalence as these patients age.

<p style="text-align:center">The Utility of Bioimpedance Analysis in Primary Total Joint Arthroplasty</p>

Michael C. Marinier, BS; Jacob M. Elkins, MD, PhD

Department of Orthopaedics and Rehabilitation, University of Iowa Hospitals and Clinics

Introduction

Bioimpedance Analysis (BIA) is an emerging tool for identifying patients' body composition including their body fat mass, skeletal muscle mass, and body water balance. While BIA has been introduced in medical specialties such as oncology and critical care, it has yet to be embraced in orthopaedic surgery. Introducing this technology in orthopaedic practice holds great attraction due to the potential to establish indicators of elevated risks and adverse outcomes. Nutritional status, routinely represented by serum markers and body mass index (BMI), has long been associated with poor outcomes following total joint arthroplasty (TJA), however identification of an appropriate and proven diagnostic assessment has remained elusive. BIA offers many advantages over current assessments, and it may be able to advance current practices for patients seeking TJA by providing detailed, patient-specific insights that lead to more tailored recommendations.

Purpose

This study aimed to identify any changes in body composition in patients following TJA, while also assessing the feasibility of incorporating BIA into orthopaedic practice. In addition, this study will serve as pilot data for future studies.

Methods

This prospective cohort study recruited patients scheduled to undergo primary TJA (hip, THA or knee, TKA). Patients were subjected to three BIA scans (InBody 770; InBody USA; Cerritos, CA) at their surgical work-up visit (day -17.73 ± 9.00), post-operative week 3 (±1 week), and post-operative week 6 (±1 week). In addition to undergoing BIA scans, patients' maximal hand grip strength (HGS) was also recorded during each visit. Changes in skeletal muscle mass (SMM) were used as the primary outcome. UIHC IRB approval was obtained prior to study initiation.

Results

Over a 10-week enrollment period, the study enrolled 87 patients (63.05 ± 9.57 years old) composed of 43 males and 44 females scheduled for 42 THAs (33 posterior versus 9 anterior approach) and 45 TKAs. 26 patients were designated as control, 24 as obesity class I, 13 as obesity class II, and 22 as obesity class III at enrollment. To date, 83 patients have undergone their scheduled procedure (2 cancelled procedure, 2 yet to have procedure), 62 patients have completed their week 3 scan (study day 19.9 ± 3.2), 35 patients have completed their week 6 scan (study day 43.6 ± 4.3), and 6 patients have been lost to follow-up. Table I summarizes changes in SMM (kg and %) for each procedure. Table II illustrate selected risk factors that were identified to have a statistically significant correlation with changes in SMM.

Surgery	TKA			All THA			Anterior THA			Posterior THA		
Change	kg SMM	% SMM	n	kg SMM	% SMM	n	kg SMM	% SMM	n	kg SMM	% SMM	n
Week 3	-1.06 ± 1.23	-0.55 ± 0.81	33	-0.59 ± 1.29	-0.30 ± 0.91	29	-0.36 ± 1.00	+0.13 ± 0.46	7	-0.67 ± 1.38	-0.43 ± 0.98	22
Week 6	-0.56 ± 0.91	0.00 ± 0.01	20	-0.21 ± 0.88	0.00 ± 0.01	15	-0.86 ± 1.60	+0.01 ± 0.01	2	-0.11 ± 0.78	0.00 ± 0.01	13

Table I: Table of means with standard deviations for changes in SMM relative to surgery and surgical approach. \

Risk Factor	SMI_o	SMM_o	DLM_o	LBM_o	HGS_o	Φ_o	BMI_o
Week 3	-0.577**	-0.615**	-0.612**	-0.607**	-0.358**	-0.383**	-0.268*
Week 6	-0.363**	-0.336*	-0.333	-0.315	-0.363*	-0.457**	-0.105
*denotes p-value of less than 0.05 and **denotes p-value of less than 0.01							

Table II: Table of Pearson's correlations (r) for changes in SMM (kg) relative to selected risk factors: SMI = appendicular skeletal mass, SMM = skeletal muscle mass, DLM = dry lean mass, LBM = lean body mass, HGS = average hand grip strength, Φ = whole body phase angle, and BMI = body mass index. All risk factors based on values at initial presentation.

Conclusion

BIA is a powerful tool that allows for rapid (less than 1 minute) non-invasive assessments of body composition. This study illustrates promising pilot data in a specialty naïve to this emerging technology. While it was initially hypothesized that increasing BMI would lead to increasing losses of SMM, this was not determined to be a strong, significant correlation. In fact, the better predictors were determined to be measures of lean tissue and strength. This may indicate patients who are more habitually active prior to surgery experience larger decrement of muscle mass during the intensive recovery period after surgery. However, for both THA and TKA patients, percent SMM is seen to be nearly recovered despite SMM (kg) loss at post-operative week 6. In addition, measures unique to BIA, such as whole-body phase angle (Φ) and other measures of body water balance, are completely novel to orthopaedics and may be a better indicator of post-surgical outcomes than BMI. This is an exciting avenue of ongoing and future research.

Limitations of this study include small sample sizes in certain cohorts (obesity class II, direct anterior THA, etc.) and lack of long-term follow-up. However, the study team believes that this pilot data shows promising results for the incorporation of BIA in orthopaedic practice, as well as improving on current BMI-based surgical guidelines. Future studies include validation of BIA with DEXA, tailoring nutritional supplementation and physical therapy based on BIA results for TJA patients, tracking changes in body composition for experiencing revision TJA and/or periprosthetic infections, as well as utilization of this technology in many other orthopaedic sub-specialties.

Comparison of Postoperative Pain and Morphine Consumption between Hip Arthroscopy with and without a Perineal Post – Abstract

Student: Nolan Mattingly
Mentor: Michael Willey

Introduction:
Hip arthroscopy without the utilization of a perineal post has become increasingly popular, but the analgesic requirements of this approach have not yet been reported. Furthermore, there exists no gold standard for postoperative pain management following hip arthroscopy without the use of a perineal post.

Purpose:
To compare postoperative pain and early recovery between patients that underwent hip arthroscopy with and without a perineal distraction post.

Methods:
We retrospectively reviewed a consecutive series of patients who underwent hip arthroscopy before (n=100) and after (n=100) adoption of the postless method. Patients who underwent concurrent periacetabular or femoral osteotomy were excluded. Demographic information, procedure variables, and VAS pain scores were recorded. All administered analgesic medications were converted to morphine milligram equivalents (MME) for direct patient comparison. Descriptive statistics were calculated, and a Students T-test was used to compare means.

Results:
The overall mean ± SEM age was 26 ± 0.70 years (Post, P: 57 females; No Post, NP: 68 females). Total operative time (P 100 ± 1.79 vs NP 89.11 ± 2.5, p=0.0003), traction time (P 45.84 ± 1.06 vs NP 40.95 ± 1.11, p=0.0016), and total operating room time (P 148 ± 1.93 vs NP 137.34 ± 2.58, p=0.0005) were found to be shorter in the NP group. There was no significant difference in total MME consumed (P 63.92 ± 1.83 vs NP 60.56 ± 1.55, p=0.1620). No significant differences between first and last PACU VAS pain scores were found (First: P 5.68 ± 0.3 vs NP 6.09 ± 0.28, p=0.321; Last: P 3.67 ± 0.17 vs NP 3.97 ± 0.17, p=0.2139). Time to discharge was significantly shorter in the NP group (P 207.23 ± 5.88 vs NP 167.54 ± 4.79, p<0.0001). No overnight admissions or complications occurred.

Discussion:
Adoption of the postless technique was not associated with prolonged OR or operative time. Both groups had similar pain postoperatively, however, the time from surgery to hospital discharge was shorter in the postless group. These measures can help surgeons decide if conversion to postless distraction in hip arthroscopy is warranted.

Title of Presentation: Firearm Related Injuries to the Hand and Upper Extremity in a Rural, Midwestern State
Presenter: Matt McIlrath
Mentors: Joseph A. Buckwalter V, MD, PhD and Ignacio Fleury, MD

Introduction

The US gun debate remains a hot topic across the Nation. Unfortunately, these discussions focus predominately on person-to-person violence in Urban landscapes, failing to recognize the prevalence of unintentional firearm injuries in rural communities; a uniquely preventable cause of significant disability and economic loss. Additionally, existing firearm injury-related databases are limited due to lack of anatomical specificity of injury. This makes it difficult to extract and understand the implications of gunshot wounds affecting various anatomical locations.

Purpose

The concept of a firearm database that focuses specifically on rural, upper extremity injuries is novel and will assist in understanding this cohort and targeted interventions needed to mitigate occurrence. In this report, we create the aforementioned database and discern variables at play within this cohort as they differ from those of urban areas. Secondly, we will compare our database to State and National databases to identify improvements in recording these injuries, providing depth to our understanding of specified firearm occurrences. Overall, we intend for our results to guide firearm educational interventions and public policy aimed at prevention.

Methods

This study took place at a Rural Midwestern level 1 trauma center and included all upper extremity gunshot wound patients from January 2002- December 2019. Data acquired included demographics, injury mechanism/description/location, firearm used, temporal associations, toxicology, and hospital stay/disposition details.

Results

In total, 55 patients, average age of 33.32±12.99, presented with upper extremity gunshot wound, including 45 males with zero fatalities. 38 of these presentations were unintentional gunshot wounds (58.18%), followed by assaults comprising 19 of these presentations (34.55%). Law enforcement related and self-inflicted injuries contributed minimally. Handguns were the most frequently the culprit (43.64%). 4 injuries occurred while hunting, with 12 (21.82%) total during November or December, the active deer hunting months. Alcohol was detected in 11 of the patients (20%), while other drugs of abuse were detected in 20 (36.36%).

Conclusion

Males sustaining unintentional gunshot wounds predominate this cohort, oftentimes involving drugs and alcohol. Occurrence was higher during deer hunting season, a hobby that many Rural Midwesterners partake in. Our findings signify a vulnerable cohort who may benefit from better directed interventions. Rural-urban differences must be addressed to optimize prevention through education and public policy.

Title: Management of Airway Obstruction and swallowing disorders in Pediatric Population

Student: Ethan Meiburg, BA

Mentor: Dr. Sohit Kanotra, MD

Background:

Pediatric airway obstructions and swallowing disorders can be caused by various etiologies, both congenital and acquired. Various presenting signs and symptoms can help to point the physician in the right direction in order to develop a treatment and management plan. As a top otolaryngology hospital, Univseristy of Iowa Hospitals and Clinics, is a great option to review these cases and extrapolate data to learn more about their treatment, prognosis, presenting signs and symptoms, management and more.

Purpose:

The purpose of this study is to find etiologies of airway obstructions in the pediatric population at a tertiary care center. This review will allow for retrospective analysis of these ailments to look for the best treatment, diagnostic tests, management, prognosis, and other possible outcomes for patients presenting to this care center.

Methods:

This study is a retrospective chart review on pediatric patients (0-18 years) presenting to the otolaryngology clinic at a large tertiary care center. The chart review involves finding the etiology behind the children's airway obstruction and/or swallowing disorder and collecting variables related to the condition, such as preoperative swallow study information, complications, and presenting signs and symptoms. This information will be stored in a built database on REDCap.

Results:

Due to COVID-19 related issues, this project took a while to commence and is currently still being worked on. Therefore, there are no conclusive results at this moment in time.

Conclusions:

As mentioned in the results, data is still being collected, therefore no conclusions can be made at this time. There is a need to continue working on this project so that the etiologies of these disorders are discovered along with their associated variables. This will allow future physicians to better understand the etiological basis of airway obstructions and swallowing disorders in the area of this tertiary care center. It will also allow these physicians to make a more informed decision towards treatment and management options for the patients who are presenting with these problems.

Evaluation of an online continuing medical education module to improve provider knowledge of delirium screening in the Emergency Department

Sarah C. Minion, MS[1]
Brooks Obr, MD, MME[2]
Ryan Carnahan, PharmD, MS[3]
Sangil Lee, MD, MS[2]

[1]Carver College of Medicine, University of Iowa, Iowa City, Iowa

[2]Department of Emergency Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa
[3]Department of Epidemiology, College of Public Health, University of Iowa, Iowa City, Iowa

ABSTRACT

Background: In the emergency department (ED), delirium affects 7 to 10% of elderly patients but is diagnosed in only about 16.6% of those patients.[1] Delirium detection may be improved by increasing screening; however, provider time constraints, insufficient training, and the lack of a universally used diagnostic assessment tool impede implementation.[2, 3] Provider training on appropriate brief cognitive assessment tools may improve this.

Methods: This study was conducted at the University of Iowa Hospitals and Clinics (UIHC) from December 2019 to August 2020. All physicians, nurses, advanced practice providers, and students, listed in ED listservs plus rotating residents and medical students were invited to participate. This study involved an online delirium screening education module with a pretest and posttest, and an end-user survey to assess participant reactions. We compared test differences using a Wilcoxon Matched-Pairs Signed-Rank test and performed mean (SD) calculations on the 6-point Likert scale survey results.

Results: Of 31 total participants, we had 28 participants complete the module pretest and posttest. Twenty-two participants completed the end-user survey. Module participants significantly increased scores between the pretest (median: 40% [IQR: 30%, 60%]) and the posttest (median: 100% [IQR: 80%, 100%]). Survey participants communicated overall positive reactions to the module and indicated that they had started to implement delirium screening in their practices.

Conclusions: We found that the implementation of a brief educational module on delirium screening in the ED improved provider knowledge and received positive reactions. Future research should seek to determine whether educational modules improve delirium screening in practice and whether this improves outcomes in ED patients with delirium.

M1 Student: Timothy Morris
Faculty Research Mentor: Hasan, David M.D.
Affiliations: Department of Neurosurgery, University of Iowa Carver College of Medicine

Contrast Enhancement and Microbleeds in the Wall of Unruptured Intracranial Aneurysms: A 3T MRI Study

Background: Unruptured intracranial aneurysm (IAs) is a medical condition that can prove to be fatal if it progresses into a subarachnoid hemorrhage. The current method to detect instability of unruptured IAs is by using MR-quantitative susceptibility mapping (QSM) to identify microbleeds (MBs) that are present in the walls of aneurysms. A potential biomarker to detect inflammation and instability in the walls of unruptured IAs may be contrast enhancement seen on high-resolution vessel wall imaging (HR-VWI).

Purpose: We aim to objectively analyze the relationship between HR-VWI and QSM findings. If HR-VWI can serve as another biomarker for inflammation and instability of IAs, having this technique will allow physicians another way to easily identify risk of rupture. This can ultimately reduce the number of undetected, high risk, unruptured IAs that patients might have unbeknownst to themselves. HR-VWI may prove to be a more effective method to evaluate risk than the current standards.

Methods: Patients who were diagnosed with unruptured IAs prospectively underwent QSM and HR-VWI on a 3T Siemens MRI. If there were MBs identified on the walls of IAs after QSM analysis, the unruptured IAs were considered unstable. The contrast enhancement ratio was calculated using the T1 post-contrast images by comparing the maximal signal intensity in the aneurysmal wall and to the pituitary stalk (CR_{stalk}). Multiple t-tests were performed to analyze the correlation between several IA morphologic variables (size, length of neck, aspect ratio, size ratio), PHASES score, CR_{stalk}, and presence of MBs. A ROC curve was created to determine the best cutoff for CR_{stalk} values in distinguishing stable and unstable IAs.

Results: A total of one-hundred and twenty-three patients with 178 unruptured IAs underwent HR-VWI. 97 unruptured IAs were excluded due to QSM artifact (54), fusiform morphology (19), size smaller than 2 mm (9), location in the cavernous segment of the internal carotid artery (8), and poor HR-VWI quality (8). Of the 81 unruptured IAs analyzed, 66 were stable (without MBs) and 15 were considered unstable (with MBs). Unstable, unruptured IAs were larger (8.4 ± 5.5 mm vs 5.5 ± 2.3 mm, P=0.007), showed higher CR_{stalk} (0.6 ± 0.2 vs 0.5 ± 0.1, P=0.05), and scored higher on PHASES (6.9 ± 3.5 vs 4.8 ± 2.6, P=0.02). There was a trend for unstable, unruptured IAs having a higher aspect ratio (2.1 ± 1.3 vs 1.9 ± 0.9, P=0.56) and higher size ratio (3.3 ± 1.6 vs 2.6 ± 1.2, P=0.11); however, these were not statistically significant. The ROC curve determined the best CR_{stalk} cutoff to distinguish stable and unstable MBs is ≥ 0.55 with a sensitivity of 82% sensitivity and specificity of 67%.

Conclusion: It has been shown that aneurysmal wall enhancements and MBs have a strong positive association. The presence of MBs within the wall of the aneurysm have been correlated with other determinants of aneurysmal rupture risk. We determined that a CR_{stalk} of greater than or equal to 0.55 is a more appropriate threshold than the ranges of previous studies. Using contrast enhancement through HR-VWI serves as a biomarker for aneurysmal instability in clinical practice.

Pregnancy Complications in the Super Morbidly Obese

Catalina Mulanax[1]; Gabrielle Gray[2]; Debra S. Brandt PhD[2]; Mark K. Santillan MD, PhD[2]; Donna A. Santillan PhD[2]

[1] University of Iowa Carver College of Medicine
[2] University of Iowa Hospitals & Clinics, Department of Obstetrics & Gynecology

Introduction: Obesity is an increasing problem in the United States. At the University of Iowa Hospitals & Clinics (UIHC) during 2015, only 44.6% of pregnant women who gave birth had a normal pre-pregnancy weight. Obesity in pregnant women can result in dangerous complications such as premature birth, cesarean delivery, gestational diabetes, and preeclampsia. In addition to negatively affecting the mother's health, being obese while pregnant can put her baby's health in jeopardy both in the short and long-term. Little is currently known about pregnancy outcomes in the morbidly (BMI>40) and super obese (BMI>50) pregnant patients which makes it difficult to adequately counsel patients.

Purpose: The purpose of this study (IRB#202004178) is to investigate the complication rates and pregnancy outcomes of women with body mass index (BMI) over 40 from UIHC. Our hypothesis is that morbidly obese (BMI>40) and super obese (BMI>50) pregnant women will have an increase in adverse outcomes for both them and their newborns compared to obese women (BMI 30-35).

Methods: A retrospective cohort study was performed comparing pregnancy outcomes of women with a BMI over 30 who delivered at the University of Iowa Hospitals and Clinics between January 2009 and July 2020. Data was extracted from the electronic health record (Epic). Women were included if they were at least 18 years old, singleton pregnancy, BMI≥30 at the beginning of pregnancy, and delivered at UIHC (N=6459).

Results: There is a statistically significant increase incidence for gestational diabetes (P<0.001), preeclampsia (P<0.001), hypoglycemia (P<0.001), number of days spent in the hospital after delivery (P<0.001), birthweight (P<0.001), and a composite poor neonatal outcome (P<0.001). Both the 1-minute and 5-minute APGAR scores were worsened with increasing BMI (P<0.001). Pre-term birth decreased with increasing BMI (P=0.02). No statistically significant differences were observed in admission to NICU, neonatal death, neonatal respiratory distress, and neonatal pulmonary hypoplasia.

Conclusion: A better understanding of the adverse outcomes of pregnancy for women with severe morbid obesity is essential to develop more effective treatments and accurate counseling for these patients.

Title: Correlation between Progesterone IUD use and Dermatological Conditions
Presenter: Ananya Munjal MS
Mentor: Jennifer Powers MD
Collaborators: Stephanie Radke MD MPH, Patrick Van Eyck PhD

Background

Fertility and menstruation are largely controlled by hormones, one of which is progesterone, a steroid hormone that prepares the endometrium for the potential of pregnancy after ovulation. Progesterone prepares the endometrium for the potential of pregnancy after ovulation, and thus when the body produces high levels of this hormone, ovulation will not occur. Progesterone is widely clinically utilized as a contraceptive method for women through the use of implanted intrauterine devices, or IUDs. Anecdotally, patients with IUDs feel that they are at heightened risk for dermatological conditions including: acne vulgaris, folliculitis, hirsutism, and alopecia. These hormonal implants have androgenic activity in the human body, and these androgens have the potential to cause a variety of hormonally-induced dermatologic conditions through stimulation of sebaceous glands.

Purpose/Hypothesis

This study aimed to determine whether individuals with hormonal IUD implants have an increased incidence of developing the dermatological conditions of acne vulgaris, folliculitis, hirsutism, and alopecia as compared to individuals with non-hormonal copper IUD implants. We hypothesized that the use of progesterone-based IUDs would be more greatly correlated with the development of these dermatologic conditions as compared to the use of non-hormonal IUDs. The purpose of this research study was to establish a better risk prediction for the diagnosis of these dermatological conditions after IUD implants.

Methods

This study assessed the potential adverse dermatological effects (acne vulgaris, folliculitis, hirsutism, and alopecia) of progesterone IUDs, using women with non-hormonal (copper) IUD implants as a control. Data from medical records of patients admitted to the University of Iowa Hospitals and Clinics was analyzed using a database in TrinetX, a health research network. A retrospective cohort study was designed using patients with hormonal IUDs implanted after January 1st 2012 and a subsequent new diagnosis of acne vulgaris, folliculitis, hirsutism, or alopecia as determined by ICD-10 codes. This study tracked an eight year period with any instances of these dermatological conditions until January 1st 2020. No exclusion criteria were applied.

Results

A total of 13,780 women between the ages of 18 and 60 were included in this study, and new instances of dermatologic conditions were compared between women with levonorgestrel-releasing intrauterine contraceptive implants and non-hormonal implants. The odds ratios for the instance of dermatologic conditions post-hormonal IUD implantation were as follows: acne vulgaris OR=1.60, folliculitis OR=1.92, hirsutism OR= 1.64, and alopecia OR= 1.52. Statistical analysis of significance is pending.

Conclusions

Our results show a potential positive association pending further analysis between the prevalence of acne vulgaris, folliculitis, hirsutism, and alopecia after implementation of a hormonal IUD as compared to the prevalence of these condition after implementation of a copper IUD. This information can be utilized in a clinical setting to better inform women of the potential adverse effects of their contraceptive choices and can aid physicians in better identifying high-risk groups for better clinical decision making.

Pinpointing the genetic basis of Ehlers-Danlos Syndrome – Hypermobility Type

Bryn Myers, Dr. Benjamin Darbro

Background

Ehlers-Danlos syndrome – Hypermobility Type (EDS-HT) is the most common heritable disorder of connective tissue [1]. The syndrome is characterized by joint laxity and chronic pain and is diagnosed using a point-based measure of joint mobility known as the Beighton score. Estimates of EDS-HT prevalence have ranged between 1:5,000 and 1:20,000 people, but the true number is unknown and likely higher than expected given the disorders' clinical variability and low diagnosis rate [1]. As chronic pain is a serious and frequent complication of EDS-HT, affected individuals are often incorrectly diagnosed with chronic fatigue syndrome, fibromyalgia, depression, hypochondriasis, and/or malingering prior to recognition of joint laxity and establishment of the correct underlying diagnosis [1]. A genetic test does not yet exist, but would be pivotal in the accurate and efficient diagnosis of EDS-HT.

Aims

It is the aim of this study to analyze exome sequencing data from EDS-HT-affected families to identify the genetic determinants of this condition whether they be a specific gene or a network of genes with related function.

Methods

Subjects were recruited for this study through the patient population of the Connective Tissue clinic at the University of Iowa in the Division of Medical Genetics and Genomics. Adult and pediatric patients who had a diagnosis of EDS-HT with a Beighton score of 8 or 9 out of a possible 9 were included as affected subjects [2]. Once these subjects were identified, their family members were also asked to participate as controls. Each recruited family consists of a trio of the affected proband, one unaffected family member (with a Beighton score < 3), and one additional affected family member. Each subject provided a blood sample for exome sequencing. Exome sequencing data was analyzed using GATK Best Practices and further annotated and filtered in VarSeq (Golden Helix, Bozeman, MT). Variants were quality controlled and filtered for minor allele frequency (<5%), functional significance (missense and loss of function variants) and familial inheritance. Genes that exhibited variants across multiple families were then used for pathway analysis in Ingenuity Pathway Analysis software (Qiagen, Hilden, Germany).

Results

Collagen biosynthesis genes as well as ZNF358 and PDZD2 genes are promising candidates for the pathogenesis of EDS-HT as they are present in many of the triads, are involved in extracellular matrix function, and withstood our stringent quality control filtering. Mutations in ZNF358 and PDZD2 genes are dominantly inherited in 3 of the 7 the families, following the typical inheritance pattern of EDS-HT. Analysis of DNA variations, depth of coverage, and quality control metrics that include quality per depth and mapping quality showed that all the mutations were good quality [3]. Additionally, the Gnomad database shows that these candidate genes are intolerant to functional variation (ZNF358:Missense Z-score=2.58, pLI = 0.79) and PDZD2:Missense Z-Score=1.69, pLI=1) [4]. Pathway analysis carried out by IPA software was done using a master list of all the quality-controlled, filtered variants discovered to be present in two or more of the analyzed families. Two pathways were found to have significant enrichment: the G6P signaling pathway and the hepatic fibrosis pathway. We then took all the genes that met the criteria for quality and performed a pathway analysis that revealed high interconnectivity amongst genes that are involved in collagen synthesis and remodeling. Using this enrichment data, a network of possible-disease-causing genes was built.

Conclusion

EDS-HT is a challenging genetic condition to study and diagnose as it is likely multi-factorial with a high degree of locus and allelic heterogeneity. We hypothesize that there are many genes or combinations of genes that may yield the EDS-HT phenotype, and these genes are functionally related to one another. It is possible that certain mutations may be additive or synergistic in the production of the hypermobility phenotype. The functional network proposed in this study is an example of genes that may lead to the EDS-HT phenotype if mutated; future studies that include larger study population are required to confirm the hypothesis.

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Title: Identifying Social Determinants of Health in a Gynecologic Oncology Population
Author: Anne Nora
Mentor: Michael Haugsdal, MD

INTRODUCTION:

Social determinants of health (SDoH) are the factors that affect a patient's health quality and outcomes and contribute to health disparities. Evidence suggests that clinical care contributes only 20% to patients' health outcomes, while the remainder is under the influence of upstream factors. The upstream approach to healthcare aims to address SDoH before they contribute to less ideal outcomes downstream. Several SDoH may contribute to outcomes for cancer patients. This Upstream Gynecologic Oncology Initiative seeks to identify which SDoH affect a population of patients with gynecologic malignancies.

HYPOTHESIS:

This study hypothesizes that the health quality and outcomes of patients receiving care for gynecologic malignancies are affected by specific SDoH among the categories of housing, food, transportation, finances, health literacy and social support. This study aims to identify the frequency of these six social factors among the outpatient gynecologic oncology population at the University of Iowa.

METHODS:

This needs assessment is the first stage in a quality improvement project assessing the SDoH affecting women with gynecologic cancers. Two hundred twenty-two patients receiving out-patient care for gynecologic malignancies completed an anonymous needs assessment survey. Validated survey questions regarding housing, food, transportation, finances, health literacy and social support were used to identify needs. Responses were considered positive if any degree of need was reported.

RESULTS:

Responses demonstrated the most substantial need in the categories of social support (32%), health literacy (28%) and financial stability (24%). Less need was reported in the categories of food (11%), transportation (5%) and housing (4%). Fifty-seven percent of women reported at least one social need among the six categories screened.

CONCLUSION:

Upstream SDoH, most notably social support, health literacy and financial stability are identified to be present and likely contributing to health quality, outcomes, and disparities within this gynecologic oncology patient population. Overall, these findings support the idea that SDoH should be assessed for each unique patient population - and for each patient receiving care for gynecologic cancer. While social support was the most frequently reported SDoH, many patients already received adequate help at home; suggesting that meaningful efforts should next be directed at improving health literacy in the population. Appreciation and assessment of SDoH potential to impact care and management should be used to design a routine screening tool for the study population and organize resources to address or mitigate the identified needs.

Qualitative Investigation of Factors Associated with Dietary Intervention Adherence as Perceived by Support Persons of Individuals with Multiple Sclerosis

Samantha Parks[1], Jacob Tinker[1], Tyler J Titcomb[1], Mary Ehlinger[1], Sandra Daack-Hirsch[2], Terry L Wahls[1]

[1]University of Iowa Carver College of Medicine
[2]University of Iowa College of Nursing

Introduction. Specialized diets have demonstrated promise in reducing symptoms of multiple sclerosis (MS) in preliminary trials. While it is widely accepted that family support is key to successful implementation of dietary interventions among people with multiple sclerosis (pwMS), this idea has never been formally evaluated.

Objective. This study aimed to identify barriers and facilitators to diet adherence perceived by the support persons of the pwMS enrolled in the dietary intervention study, and to investigate feelings of burden perceived by support persons of pwMS enrolled in dietary intervention studies.

Method. Study participants were asked to identify an individual who was key in supporting them while enrolled in the dietary intervention study. This support person was interviewed about their perceptions regarding the pwMS in adopting the study diet and asked to complete the Zarit Caregiver Burden Interview (ZCBI). 11 support persons were interviewed (9 male spouses, 1 female spouse, and 1 adult child). Interviews were recorded, transcribed, and coded using MAXQDA software. Responses were coded independently, verified, and discrepancies were resolved by a third investigator. Coded responses were then grouped into major themes that prevented or facilitated diet adherence.

Results. Barriers identified by support persons include time constraints, lack of motivation, lack of support, diet components, and recommended food inaccessibility. The most common facilitators identified by support persons were positive mindset/motivation, social support, structure/routine, and food enjoyment. On average, support persons rated study participant adherence to the diet as 8.4 ± 1.4, while they rated their own personal adherence as 5.1 ± 2.9 on a 1-10 scale (1 = minimal adherence, 10 = complete adherence). The support persons' hope for the future (1 = no hope, 10 = very hopeful) did not change from 6.5 ± 2.2 prior to the study intervention to 7.4 ± 2.5 ($P = 0.28$) after the study intervention. Based on preliminary results from ZCBI responses, support persons who perceived greater burden (ZCBI score > 21) more frequently referenced no change in participant MS symptoms and a personal lack of desire to follow the diet in support of the participant as barriers. However, regardless of burden, positive mindset/motivation was the top facilitator.

Conclusion. These findings indicate several common facilitators and barriers that can be targeted to facilitate successful implementation of dietary interventions. To achieve higher levels of adherence to dietary interventions among pwMS, future studies should explore methods to screen for high levels of personal motivation, enhance caregiver support, adapt dietary strategies to food preferences, and address physical abilities and food accessibility limitations while minimizing time commitment.

Abstract

Abstract Title: Effects of Chondromalacia with Recurrent Patellar Dislocations on Post-Operative Outcome Scores

Author Names and Titles: Pooja H Patel, B.S., Robert W Westermann, M.D., Natalie A Glass, PhD, Kyle R Duchman, M.D., Brian R Wolf, M.D., Matthew J Bollier, M.D., John P Albright, M.D.

Background: Recurrent patellar dislocations dispose patients to pain, instability, and chondral defects, often requiring a Fulkerson tibial tubercle medialization for realignment and/or medial patellofemoral ligament (MPFL) reconstruction for stabilization. Post-operatively, there is considerable variability in functional outcome scores. Consequently, it is paramount to determine the possible underpinnings of this functional discrepancy. It was hypothesized that the presence of chondromalacia intraoperatively worsens post-operative functional outcomes, and that the presence of anatomic, radiographic, or physical examination abnormalities are correlated with the presence of chondromalacia.

Methods: 86 patients, who underwent a Fulkerson procedure and/or MPFL reconstruction, were retrospectively examined for intraoperative presence of articular cartilage lesions and risk factors. The Outerbridge system was used to separate patients into two groups: no/minimal chondromalacia (grades 0-1) and severe chondromalacia (grades 2-4). Pre- and 2-year postoperative functional outcome scores, including KOOS, MARX, and SF 36, were compared between the groups. Separately, patients were also grouped by surgery type: Fulkerson osteotomy or MPFL reconstruction. To evaluate the correlation between various examination features and the presence of chondromalacia, patient charts were reviewed for patellar height, trochlear depth, patellar tilt, trochlear bump, and crepitus.

Results: 57/86 (66%) of patients had chondromalacia. They displayed significantly better KOOS-Activities of Daily Living (ADL) and KOOS-Pain scores than the control group (p = 0.0320 and p = 0.0171, respectively). Compared to Fulkerson patients, MPFL patients reported better pain and sport outcomes via KOOS-Pain and KOOS-Sports scores (p = 0.0288 and p = 0.0038, respectively). MPFL patients also had better pre- and post-operative MARX scores than Fulkerson patients (p = 0.0267 and p = 0.001, respectively), suggesting higher levels of activity. This coincided with a decreased mean patient age in MPFL patients compared to Fulkerson patients (19.3 years vs. 29.2 years respectively, p < 0.0001). Compared to the control group, the chondromalacia group only displayed a significant change in the patellar tilt at the time of surgery (p = 0.0343).

Conclusion: Patients with chondromalacia exhibited better post-operative outcomes for KOOS-ADL and Pain. Patients who underwent MPFL reconstruction reported better post-operative KOOS-Pain, KOOS-Sports, and MARX outcome scores than Fulkerson patients. Additionally, patellar tilt was correlated with the presence of chondromalacia.

Dr. Thomas Nickl-Jockschat
Dr. Rachel Sharkey
Milosch Pavic

Parcellation of Brain By Gene Expression

Key

*Kmeans 10-100-parcellation
*Cluster-individual clusters inside the kmeans
* Stable Cluster-areas of overlap that include all 12 of the kmeans

Background

Psychiatric and neurological illnesses are often complex and multifactorial, with many genes being implicated in their pathophysiology. Although there is an understanding of some of the specific genes involved in complex diseases such as schizophrenia, it is not known where these genes are being expressed in the cortex. Currently there are brain atlases that describe the brain in terms of functional or anatomic terms, such as Brodman's atlas. However, no map has divided the brain in terms of gene expression. A transcriptomic atlas of the brain would reveal the spatial organization of gene expression across the cortex. Genes of interest that are known to be implicated in disease could be investigated in terms of where they are being expressed.

Purpose

The purpose of this study is to build a brain atlas that maps the cortex on the basis of differences in gene expression. This will provide a link between genetics and imaging on the basis of gene expression. This allows us to understand gene expression across brains and to see where gene expression is conserved across brains and connect gene expression to imaging findings. Such an atlas can help guide future research.

Methods

mRNA data was obtained from the Allen Brain Institute based on mRNA extracted from sites across the cortex of left hemispheres from 6 donors. Spectral clustering was then performed by the Baek Lab on the gene expression data to parcellate the brain on the basis of regional gene expression. Multiple parcellations with differing numbers of clusters were generated and tested for stability. The stability deteriorated after 101 clusters so only the data from the first 10 parcellations was used. We then described the areas defined by the gene expression data within each parcellation and identified those which were anatomically or functionally interpretable. Interpretable clusters were overlaid on each other using the fslmaths toolbox to indicate how many clusters across the parcellations covered each particular area. We found twelve conserved areas of expression that overlap completely across each of the parcellations regardless of the parcellation breakdown, indicating that they are highly stable. These stable clusters corresponded more closely to functional regions than to anatomical or cytoarchitectonic areas. We then compared the expected function based on region to fMRI functional decoding of the stable clusters, which identifies regional functions based on a large functional MRI database. This confirmed our results are functionally relevant and also identified functions that were less obvious on observation.

Results

Our findings indicate that there are areas of gene expression that are conserved across human brains. These highly conserved areas relate more closely to function than to anatomy or cytoarchitecture and tend to relate to higher cognitive processes.

Conclusion

We have successfully parcellated the brain on the basis of gene expression. The resulting transcriptomic atlas could help guide future research and clinical practice. The atlas can be used to link relevant genes with structural and functional changes. Next we, plan to use the transcriptomic atlas to identify genes expressed in regions known to be atrophied in schizophrenia. We predict that this will identify genes previously implicated in schizophrenia in other, strictly genetic studies.

Student: Rebecca Peoples
Mentor: Craig Syrop

Title: Are predictors of arthritis following ACL reconstruction present at time of surgery?

Background: Post-traumatic osteoarthritis (PTOA) is a subtype of osteoarthritis that develops following a known injury to the joint (1). The ankle and knee joints are most vulnerable to the development of PTOA, and at least 50% of patients that have had an ACL injury develop PTOA (2). Unlike other forms of osteoarthritis, post-traumatic osteoarthritis has a single predisposing incident, meaning the development of PTOA is an endpoint to pathological processes that may be initiated as early as the initial trauma (1).

Purpose: The aim of this study is to analyze the metabolites present in synovial fluid extracted at the time of ACL surgery with respect to MRI data collected before surgery and the change in KOOS pain outcome scores to determine predictors of arthritis at six years follow-up.

Methods: Synovial fluid samples were taken from the knee joints of 92 patients undergoing ACL reconstruction between February 2014 and January 2015. 54 of these patients were included in the ACL registry, and information is available on their MRI findings and KOOS pain outcome scores. The metabolites that were analyzed represent amino acid metabolism, carbohydrate metabolism, mitochondrial oxidation, lipid metabolism, and nucleotide synthesis. These are to be analyzed with respect to MRI and KOOS data when all of the MRI data has been read by a radiologist.

Preliminary Results: At 2 years follow-up, patients without either a partial meniscectomy or meniscus repair at the time of ACL reconstruction improved their KOOS pain score on average 8.2 points more than those without meniscus involvement. Meniscus damage alone does not have a clinically meaningful difference in change in KOOS score from pre-op.

Discussion: 6-year outcome data will become increasingly more available as the year progresses, and more patients reach 6 years post-op. MRI readings will be completed shortly, and formal statistics can then be run to analyze the metabolites for correlation with future arthritis.

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Title: Epidemiology of Suicide in an Iowa Cohort
Student: Jane Persons, M4
Mentor: Marco Hefti, MD, Department of Pathology

Objectives:

Suicide is an ongoing public health problem in the US. The purpose of this epidemiologic investigation was to characterize and identify populations at risk of suicide, which in turn may lead to targeted intervention and improvements in suicide prevention.

Study Design:

This is a descriptive analysis of 657 suicide decedents autopsied by the University of Iowa Hospitals and Clinics between 7/1/2003 and 6/30/2018 (180 months, 15 years).

Methods:

Data were obtained via autopsy report abstraction. Chi-square tests were used for categorical variables and Wilcoxon Rank-Sum tests were used for continuous variables. Statistical analyses were conducted using SAS 9.3.

Results:

Decedents were primarily white (88.2%) and male (75.7%). Average age was 43 years. Suicides were more likely to occur at a residence (69.3%), in the earlier weekdays, and in the late night to early morning hours. Suicides were most likely to occur in spring and least likely to occur in winter. The most common method was a firearm (44.6%), most often a handgun (61.3% of firearm suicides). Less than one-half (42.8%) of decedents communicated intent to end their life. Approximately one-quarter (22.1%) of suicides were without a known identified life stressor or a known inciting event, a phenomenon that was markedly more common among men.

Conclusions:

More than one-half of decedents left no communication of intent to commit suicide, and one-quarter - more commonly men - had no known life stressor or other specifically identified motivating factor. While women were more likely to have a known mental health condition, prior contact with mental healthcare, or prior suicidal behavior, we found that, statistically speaking, the typical profile of a completed suicide is a white male who used a firearm in his place of residence. Future studies should seek to further elucidate factors leading to suicide in this at-risk population.

Abstract

Feasibility of Using Audiometric Mobile Application in Remote Memory Care
By: Katy Pham, MA; Carrie Nieman, MD, MPH; Esther Oh, MD, PhD

Background: Hearing loss is highly prevalent in older adults with cognitive impairment; however, it is often left unaddressed. Screening for and treating hearing loss in this vulnerable population may be highly beneficial because it may result in a decrease in dementia-related behavioral symptoms and improve quality of life. Due to the COVID-19 pandemic, there was a rapid switch to telehealth services. This prompted the need to seek remote and easy-to-administer methods to screen for hearing loss in cognitively impaired older adults.

Purpose of the study: To evaluate the feasibility of using a commercially available mobile hearing test application via telehealth to screen for hearing loss in older adults with cognitive impairment.

Methods: The study was conducted among the patients at the Johns Hopkins Memory and Alzheimer's Treatment Center, an outpatient memory clinic. During the study, older adult patients (mean age 74; n = 10) underwent a hearing screening via telehealth using Mimi Hearing Test, a commercially available iOS-based audiometric testing application. Montreal Cognitive Assessment-Blind (MoCA-B) or Telephone Mini-Mental State Exam (T-MMSE) were performed remotely to assess participants' cognitive function.

Results: Hearing screening was conducted in a total of 10 participants via Zoom. Five out of 8 participants (63%) received reliable results upon completion of their screening. It took an average of 34 minutes for a participant to finish the screening. The longest test duration was 75 minutes. Patients who had reliable results had higher MMSE scores. However, even patients with lower MMSE scores were able to successfully complete the screening test if they had a prepared and involved caregiver.

Conclusion:

Our study demonstrated that it is feasible to use a mobile app to screen for hearing loss among older patients with cognitive impairment. However, there were also challenges including less reliable test results with worse cognitive function, highlighting the association between cognitive function and ability to successfully complete hearing screening remotely. We also found that caregiver plays an important role in remote telehealth assessments, as some of the more cognitively impaired patients were able to successfully complete the assessment if they had an involved caregiver. Future research efforts may include creating commercially available audiometric testing applications that tailor to the unique needs of older adults with cognitive impairment.

A Meta-analysis of Endoscopic Endonasal versus Supraorbital Craniotomy Approaches for Anterior Skull Base Meningiomas

Anthony Piscopo B.S.[1]*, Scott C. Seaman M.D.[2]*, Marc A. Beer B.S.[3], Jeremy D.W. Greenlee M.D.[2]

Introduction

Anterior skull base meningiomas of the olfactory Groove (OG) and planum sphenoidale/tuberculum sellae (PS/TS) regions present challenging targets for surgical resection. Common minimally invasive approaches to these tumors include endoscopic endonasal approach (EEA) and supraorbital craniotomy (SOC). Few reports directly compare these minimally invasive corridors. Thus, we reviewed the available literature and compared relevant clinical, patient-oriented outcomes between these approaches.

Patients/Methods

Due to the lack of available comparative studies, PUBMED and Web of Science were queried for single-arm observational and/or case series for anterior skull base meningioma outcomes using either SOC or EEA. A total of 321 articles were identified for screening, 42 of which ultimately satisfied inclusion criteria according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A meta-analysis of was then performed using a logit transformation of the data to analyze the probability of a given occurrence for each variable. Analyses were performed across all locations and stratified by OG or PS/TS.

Results

In the 42 studies satisfying inclusion criteria, 427 patients underwent surgery via SOC approach and 524 via EEA. SOC resulted in a significantly higher gross-total resection (GTR) rate in comparison with EEA (84.5% vs 73.3%, $p = 0.0006$) across all locations, with significantly higher GTR for OG (90.5% vs 65.9%, $p < 0.0001$) and a strong trend in GTR for PS/TS (81.9% vs 74.3%, $p = 0.0542$). Across all locations, CSF leak rate was significantly higher with EEA than SOC (18.5% vs 7.2%, $p < 0.0001$), findings that persisted in OG (30.9% vs 10.9%, $p = 0.0003$) and PS/TS (15.3% vs 6.2%, $p = 0.0020$). Better visual outcomes were observed for the EEA cohort over SOC in both pooled and subgroup analyses, but this was not statistically significant. No difference in rates of stroke, seizure or recurrence existed between approaches.

Conclusions

SOC demonstrated a more favorable tumor resection and CSF leak rate compared with the EEA approach, with no difference in vision, seizure, stroke, or recurrence outcomes. In cases without a visual deficit, our data suggests SOC to be the superior approach. However, in cases with a visual deficit, the data suggests a slightly more favorable outcome with EEA, although this was not a statistically significant advantage. In these cases of clinical equipoise, considerations of surgeon preference, anatomical and radiographic factors, and patient preference need to be carefully considered.

Development of an active mouse model of Bullous pemphigoid (BP)
Student: Mia Poleksic
Mentor: Kelly Messingham, PhD

Background
Bullous pemphigoid (BP) is an autoimmune blistering disease of the elderly mediated by autoantibodies specific for Collagen XVII/BP180, a protein involved in adhesion of the epidermis to the dermis. Because the mechanisms of disease are not well understood, standard of care involves global immunosuppression, which leads to significant morbidity. Most untreated BP patients have elevated circulating IgE, and both IgG and IgE antibodies target the NC16A domain of BP180. BP is one of the only autoimmune diseases for which the autoantibody specificity and pathogenicity in humans has been demonstrated; however, the events leading to generation of these IgE antibodies are not understood. Furthermore, current mouse models of BP rely on passive antibody transfer and/or focus solely on IgG class autoantibodies. Thus, an active mouse model leading to both IgG and IgE autoantibodies is needed to understand the basic mechanisms of disease. We hypothesized that the route of antigen exposure was critical for the induction of a BP180-specific IgE autoantibody response in an active mouse model of BP.

Methods
A preliminary experiment was performed to explore how differential routes of immunization condition the immune response of mice. 10-12 week old C3H/B6 mice were immunized intranasally or via skin abrasion with either mBP180-aluminum sulfate (n=3 per immunization route) or sterile PBS (n=1) a total of three times in 3-4 week intervals. Mice were euthanized 11-12 weeks post initial immunization, and serum was screened via ELISA for total IgE antibody response. Skin samples were flash frozen and immunofluorescence staining was performed for examination of serum IgE and IgG antibodies.

A more expansive experiment using female SJL/J mice is ongoing. Mice were immunized with two doses of mBP180-aluminum sulfate or sterile PBS via three routes of antigen exposure: intradermal, intranasal, and skin abrasion (n=13 high dose, n=12 low dose, and n=5 control per immunization route). Serum was screened for total IgE and IgG antibody response via ELISA 15 days post immunization. Immunization boosts will be performed 3 times in 3-4 week intervals. Mice will be euthanized 14 weeks post initial immunization, and blood and skin will be collected for subsequent examination. Additionally, mouse skin will be visually examined for evidence of lesions every week throughout the study.

Results
The preliminary study showed some evidence for an increase in total serum IgE antibody response at 11-12 weeks post initial immunization of C3H/BL6 mice. Immunofluorescence staining for serum IgE and IgG on control mouse skin suggests deposition of antibodies along the epidermal basement membrane zone in mice immunized via skin abrasion, but further investigation is necessary. Differences in total serum IgG and IgE in SJL/J mice were not detected at 14 days post immunization.

Conclusions
These preliminary findings suggest that skin abrasion may produce immune responses in mice that are characteristic of human bullous pemphigoid disease. These results will be built upon in the ongoing experiment to further test different routes and doses of antigen exposure with the goal of inducing a BP180-specific antibody response in an active mouse model of BP.

Sleep Behaviors May Be a Risk Factor for the Development of Painful Diabetic Neuropathy in Medical Patients

Nikitha Pothireddy BS[1], Courtney Brennaman MS[2], and Beth L. Dinoff PhD[3]

[1]Carver College of Medicine, University of Iowa
[2]Counseling Psychology Doctoral Program, Department of Education, University of Iowa
[3]Departments of Anesthesia and Psychiatry, Carver College of Medicine, University of Iowa

Background: The pathogenesis of painful diabetic neuropathy (pDN) may begin earlier on the continuum from healthy patients to patients with type 2 diabetes mellitus (T2DM) than previously thought. Ecological momentary assessment (EMA) captured with wearable devices will serve as an objective measure of physiological data related to the behavior of sleep, including sleep duration and continuity. These data may help us understand which sleep-related health behaviors could lead patients to experience pDN. Previous literature demonstrates that sleep quality disruption may impair glycemic control, potentially impacting the trajectory from obesity to T2DM. There may also be a link between sleep and pDN through sympathetic nervous system (SNS) dysfunction. In healthy individuals, SNS activity has been found to have analgesic effects. In patients with pathophysiological changes, such as being overweight or having T2DM, the SNS may actually amplify pain perception. Sleep quality disruption may increase this dysfunctional SNS activity, contributing to spinal facilitation of pain. The relationship between sleep-mediated SNS changes and altered pain awareness may lead to improved understanding about the development of the pDN phenotype of diabetic neuropathies.

Objective: This study uses longitudinal EMA data to investigate the role that the SNS may have in the natural history of pDN. We will use sleep quality as a proxy variable for SNS arousal. Our aim is to explore the relationships between sleep behaviors and pain changes that occur along the continuum from healthy people to people with pDN.

Design and Methods: Participants for this study will be part of a larger study conducted at the University of Iowa Hospitals and Clinics. To better understand factors related to the progressive development of pDN, we will collect longitudinal data from 100 participants over the course of 2 weeks using the Fitbit Inspire. This wearable device will measure participant sleep quality as well as activity level throughout the day. Baseline disruptions in sleep quality, such as duration and continuity, will be measured using the Pittsburgh Sleep Quality Index (PSQI). The PSQI evaluates subjective sleep quality over the previous month using a 19-item questionnaire. Responses are weighed equally from 0-3 and contribute to 7 component scores, totaling in a global score ranging from 0-21. PSQI global scores greater than 5 indicate poor sleep quality. The longitudinal data collected from the Fitbit will be used in conjunction with global scores collected from the PSQI to evaluate the sleep quality of participants. Participants will receive 4 daily prompts or pings to submit ratings for both stress and pain on a 0 - 10 scale over the course of their 2-week participation in the study. The EMA data from the Fitbit will be linked to the ping-collected data via time matching in order to examine the impact of sleep-related behaviors on pain outcomes. Elevated SNS activity will be measured via proxy variables, including heart rate and stress ping responses. We will also have data from other self-report inventories (e.g., Brief Pain Inventory, PROMIS Neuropathic Pain Quality, Perceived Stress Scale-10, etc.) to evaluate the participants' subjective pain ratings. Important next steps of this study will include data collection from the ecological momentary assessment devices as well as extraction of patient health information from electronic health records.

Results: Data analyses will be conducted using the generalized linear mixed modeling (GLMM) framework. The model will include laboratory values, demographic information, questionnaire results, and EMA data. Pain ratings are expected to be positively correlated with sleep quality disruption; therefore, as sleep quality disruption increases we predict that pain ratings will also increase.

Discussion: By using ecological momentary assessment (EMA) to investigate the role of sleep in the progression of pDN, we will explore behavioral factors that may lead to the painful phenotype of diabetic neuropathy. We hope sleep quality disruption can be used in the future as a potential risk factor for pDN. Understanding pDN risk factors may ultimately improve early detection as well as lead to the development of prevention strategies. This research could provide some insight into determining how sleep, as a lifestyle intervention, might lead to better outcomes for people with pDN.

Comparison of Outcomes in Extremely Premature Babies with Respiratory Distress Syndrome through Administration of Curosurf and Survanta

Greg Power, Nichole Nidey, Sarah Tierney, John Klein, Kelli Ryckman, John Dagle

Background/Introduction: Babies born prematurely can have underdeveloped lungs from both a structural and functional standpoint, and a lack of surfactant can lead to neonatal respiratory distress syndrome. Artificial surfactants are administered to treat these patients. Research in the past has shown that for patients born 24 to 29 weeks of gestation, Curosurf may offer benefits over Survanta. However, for extremely premature infants, it is unknown whether one surfactant is more efficacious.

Purpose of study: In the University of Iowa NICU, three different surfactants (Infasurf, Curosurf and Survanta) are administered to premature babies with neonatal respiratory distress (RDS). Our initial research showed that Curosurf was not an inferior option to Survanta, and was potentially superior. Following our study, the UIHC protocol was updated to encourage the use of Curosurf. We now seek to determine whether the benefits of Curosurf exist when it is used more widely and in sicker, smaller premature infants.

Method: This was a follow up to our initial retrospective chart review study. We examined the patients born at the University of Iowa with a birth weight under 750 grams who received a surfactant dose during the period of September 2018 until March 2020 – a population of 54 patients. We looked at the primary outcomes of average time between first and second dose, the number of doses given, and patient mortality. Secondary outcomes included air leak disorders, and pulmonary hemorrhage. We divided the patients based on whether the first surfactant given was Survanta or Curosurf and stratified the patients by birth weight: 600 grams and under (34 patients) and 601 grams to 750 grams (20 patients). We compared the infants in the second group following the protocol change to the infants in the first group before the protocol change to determine the effects of the protocol change. Continuous variables were calculated as mean and compared using the Student's t-test. Categorical variables were calculated as a rate (percentage) and compared with Fisher's exact test. All tests were two-tailed, and the threshold for statistical significance was defined as p value < 0.05

Results: Compared to the initial group studied, the second group of infants showed no significant change in mortality or airleak disorders. Infants in the second group received fewer doses of surfactant on average (2.52 vs. 3.69 doses, p=0.0011) and had an increased time between first and second dose of surfactant (188.8 vs. 60.3 hours, p=<0.0001). When stratifying by birthweight, infants born 600 grams or under in the second group received fewer doses (2.71 vs. 4.62 doses, p=0.0003) and had an increased time between first and second dose of surfactant (166.5 vs. 57.3 hours, p=0.0009). Infants born 600 to 750 grams in the second group had an increased time between first and second dose of surfactant (240.8 vs. 63.8 hours, p=0.0024).

Conclusion/Discussion: This study aimed to compare the efficacy of Curosurf and Survanta when administered to extremely premature infants with a birthweight less than 750 grams. Our main findings were: (1) A decreased mortality rate in patients who first received Curosurf compared to those who received Survanta. (2) An increased percentage of patients who first received Curosurf only required one dose of surfactant. (3) For patients who required multiple doses, on average, those who first received Curosurf had a greater elapsed time before receiving their second dose. (4) There was no increase in airleaks in patients who first received Curosurf compared to those who received Survanta.

Early Results of a Novel Porous Metal Augment for Tibial Bone Loss in Revision Total Knee Arthroplasty

Dayton Rand, Christopher Carender MD, Nicholas Bedard MD, Jesse Otero MD PhD, Timothy Brown MD

Introduction:
Bone loss is common during revision total knee arthroplasty, and extensively porous metal augments have emerged as the most common method for filling proximal bony defects of the tibia. As evidence to support their use has gotten stronger and the technology to manufacture the implants has improved, new augments have become available and are in clinical use with minimal clinical data. We aim to report the early outcomes of one design tibial cone augment.

Patients & Methods:
After IRB approval, all revision total knee arthroplasties from August 2017 – August 2019 at our institution were reviewed. Records were reviewed to identify patients that had implantation of a Triathlon tibial cone (Stryker, Mahwah, NJ, USA) We found 117 patients met criteria. Mean age of the patient at time of surgery was 65.6 years, 50% were female, and mean BMI was 43 kg/m^2. Indication for revision knee arthroplasty was aseptic loosening in 68 (58%), periprosthetic joint infection in 26 (22%), instability in 13 (11%), periprosthetic fracture in 8 (7%), extensor mechanism disruption 1 (1%), and osteolysis 1 (1%). The majority of the cones were used in conjunction with a Stryker Triathlon revision knee system (100, 85%), with the remainder being used with a hinged implant. All implants were used in hybrid fashion with a cemented tibial stem.

Results:
Survivorship free from aseptic loosening was 100%. There were 2 intraoperative fractures (1.7%) complicating the implantation of the cones. There were 3 DAIR reoperations related to infection. 4 patients (3.4%) underwent manipulation under anesthesia for postoperative stiffness.

Conclusions:
At short-term follow up this novel porous titanium cone functions as a successful augment to tibial bone loss and provides adequate substrate for osseous integration at one-year radiographs. Longer follow up of this cohort will be necessary to demonstrate continued success from an aseptic loosening perspective.

Introductory findings: A therapeutic trial for safety and preliminary efficacy of the combination of axitinib and selenium in the chemical composition of selenomethionine (SLM) for adult patients with advanced metastatic clear cell renal cell carcinoma (CCRCC)

Student: Ryan J. Reis, M2
Carver College of Medicine
Mentor: Yousef Zakharia, M.D.
Clinical Associate Professor of Internal Medicine - Hematology,
Oncology and Blood and Marrow Transplantation, University of Iowa
Hospitals and Clinics

Abstract: Kidney cancer is a growing problem in the United States and around the world with more than 65,000 new cases and 14,000 attributable deaths in the United States alone in 2018. Further, clear cell renal cell carcinoma (ccRCC) is the most prevalent type of kidney cancer. Several distinct molecular and histological characteristics help identify ccRCC, but they also contribute to the behavior of this cancer. Notably, ccRCC is very chemo/radiotherapy resistant yet has a high dependence on an adequate blood supply. Due to this, the landscape of treatment options primarily consists of anti-angiogenic targeted therapies, mammalian target of rapamycin (mTOR) inhibitors, and immune checkpoint inhibitors. Such options have led to significant improvements to patient outcomes. With that being said, there is still a largely unmet need to provide robust and durable treatment options for ccRCC patients.

In order to address the this unmet need, a laboratory-based phase 1/2 clinical trial is underway as a means to investigate if the addition of selenium in the form of seleno-L-methionine (SLM) to the previously-approved anti-angiogenic therapy axitinib may increase patient responsiveness to therapy while having little to beneficial effects on the known safety profile of axitinib. Introductory findings of the first 19 trial recruitments suggest that the SLM/axitinib therapy may, in fact, provide a more robust and sustained response in advanced ccRCC patients who have failed at least one previous therapy, and importantly, such combination therapy appears to provide a safe treatment alternative for these and other similar patients. While the population used in these introductory findings is very limited, the data suggests appreciable benefits of SLM in combination with axitinib to both safety and efficacy when compared to previous research highlighting the anti-angiogenic axitinib, specifically the AXIS trial. If such success continues, this trial may truly serve as a new paradigm in the treatment of ccRCC, other SLM-target-expressing cancers, and other cancers, as a whole. The addition of a relatively cheap, orally bioavailable, and non-toxic trace element to existing and proven anti-cancer therapies provides significant opportunity for patients and researchers alike.

Characteristics and Retention of Emergency Department Patients that Left Without Being Seen (LWBS)

Nathan Roby, BS; Hayden Smith, PhD, MPH; Jonathan Hurdelbrink, PhD; Steve Craig, MD; Clint Hawthorne, MD, FACEP; Sam DuMontier, DO; Nick Kluesner MD, FACEP*

Corresponding Author. E-mail: nicholas.kluesner@unitypoint.org

ABSTRACT

BACKGROUND: Some patients, after presenting to the Emergency Department (ED), but before being evaluated by a qualified provider, choose to leave without being seen (LWBS). Minimizing LWBS is often a targeted outcome in ED process improvements, as high rates may pose patient safety and financial concerns. Acountable Care Organizations and the Affordable Care Act have introduced novel influences on healthcare utilization and reimbursement that could change how organizations approach LWBS. Previous studies have looked at the characteristics of patients that LWBS and why they chose to do so, but the overall impact of LWBS on future healthcare utilization has not been well studied.

STUDY OBJECTIVE: Characterize the post-ED care utilization of patients who LWBS to determine whether they were retained in the local healthcare system and examine the characteristics of those patients with or without subsequent care. Additionally, observe the frequency in which these subsequent visit address a concern related to the patient's index ED encounter.

METHODS: A retrospective observational study was conducted involving the review of electronic medical record data for patients 18 years or older who presented to an urban Midwestern ED between February 1, 2019 and January 31, 2020. Patients were classified as LWBS based on their documented ED disposition. Healthcare system records were reviewed for any subsequent utilization within 3-weeks related to their presenting ED chief complaint.

RESULTS: During the study period there were 45,456 ED encounters with 2,269 (5.0%) patients having a disposition of LWBS**.** The mean documented time until departure for LWBS patients was 128 minutes. Of the LWBS patients, 920 (40.5%) had an associated subsequent visit while 337 (14.9%) had a non-associated visit within the following 3-weeks. Included within the 920 subsequent encounters were returns to the ED (67.5%), family medicine or urgent care clinic visits (27.5%), and other outpatient visits (5.0%). Of note, 78.1% of patients that returned to the ED were considered 'bounce-back visits', meaning their return was within 72 hours of their original index ED visit. Patients not having a subsequent follow-up encounter tended to be younger, female, non-white, and presented with lower-acuity chief complaints.

CONCLUSIONS: A significant portion of patients that left the study ED without being seen received care within the study healthcare system during the 3-weeks following their index encounter. As a result, many of these patients were able to have their concerns evaluated by a provider within the healthcare system. This may be valuable new knowledge as healthcare systems explore the implications of new reimbursement and quality initiatives like Accountable Care Organizations. Most patients that returned to the ED did so within a 72-hour period, representing a population where that same emergency concern persisted, and hence highlights the need to better capture and provide services to these patients during their index encounter. Further research is still needed to fully understand the clinical impact of LWBS on patients seeking subsequent care.

Activation of Retinal Microglia and Astrocytes Across Murine Models of Traumatic Brain Injury

Ariel Roghair, Lucy Evans, William Castonguay, Nicole Hehr, Anne-Sophie Wattiez, Brittany Todd, Polly Ferguson, Elizabeth Newell, Levi Sowers, Matt Harper, Alexander Bassuk
University of Iowa Carver College of Medicine, Iowa City, IA

Introduction: Traumatic brain injury (TBI) causes about 30% of all injury-related deaths in the United States. Those that survive suffer from permanent deficits including a range of visual impairment. After the initial injury, ongoing inflammation, excitotoxicity, oxidative stress, and energy failure causes tissue damage in the brain. The retina and brain are CNS tissues with a shared embryological origin and are both considered immunoprivileged sites with protection from systemic inflammation via the blood-retina barrier and blood-brain barrier, respectively. Due to these similarities, the role of inflammation following TBI in the retina may indicate its role in the brain, as the tissues may have analogous responses to TBI. As morphological changes for inflammatory mediators are indicative of activation, we utilized retinal immunolabelling as an evaluator of immune cell activation, which can lead to continued secondary inflammation and visual deficits after TBI. Further, as different models of TBI can display varied pathological and inflammatory responses, our objective was to compare the retinal inflammatory response in mice across three models of mild TBI: blast-mediated (bTBI) injury, weight drop (WD), and fluid percussion injury (FPI).

Hypothesis: We hypothesized that the activation levels of inflammatory mediators following TBI will be similar in blast, WD, and FPI mice.

Method: Anesthetized 8-24 week old wild-type C57BL/6J male mice were exposed to three cycles of either bTBI, WD, or FPI. Control mice were handled in the same way without exposure to a blast wave, WD, or FPI. Following injury, blast experimental and control eyes were collected to conduct a time course monitoring inflammatory cytokine expression in retinal tissue via qPCR. After observing increased levels of inflammation along with heightened retinal microglia and astrocyte activation in blast mice, we further compared inflammatory mediator activation in FPI and WD mice. At seven days post-injury, blast, WD, FPI, and the corresponding sham eyes were collected for identification of the location of retinal microglia and astrocytes by IBA-1 and GFAP immunohistochemistry staining, respectively.

Results: Blast retinal tissue displayed significantly increased pro-inflammatory cytokine levels (IL-1α, IL-1β, IL-6, TNFα) four hours post-injury compared to sham. At one-week post-injury, we observed morphological changes in microglia with significant increases in their level of activation in response to bTBI, WD, and FPI compared to sham. Additionally, astrocyte activation was seen throughout the retinal layers in injured mice following bTBI or WD.

Discussion: Mild bTBI models result in increased retinal inflammation that includes heightened astrocyte and microglial activation following three different injury mechanisms. This increased inflammatory response may explain the visual deficits due to retinal structure and function observed in blast models. On-going experiments targeting the IL-1R inflammatory pathway indicate that inflammatory blockade may preserve retinal structure and function following blast injury. Our observation that retinal inflammatory biomarkers may be present across different forms of TBI suggests that retinal inflammation can be utilized as a surrogate measurement for cerebral cortex injury following TBI. When considered with our on-going IL-1R blockade discoveries, this further indicates that the pharmacological blockade of inflammatory pathways may be beneficial and improve visual outcomes and quality of life following various forms of mild TBI.

International Standards Guiding the Use of Simulated Patients in Medical Education: A Qualitative Research Study

Emily Ruba BS, Cathy Smith PhD, Henrike Hölzer PhD MME, Beate Brem MME, Jane Lindsay Miller PhD

BACKGROUND: In 2017, the Association of Standardized Patient Educators (ASPE) published their Standards of Best Practice (SOBP), a set of practical guidelines developed by international experts in medical education guiding the use of simulated patients (SPs) in the training and evaluation of medical trainees. These guidelines were developed to be flexible in order to accommodate their application across many cultures or healthcare systems. However, since these standards were developed in the United States by primarily North American experts, some practitioners have raised questions regarding their applicability to contexts outside of the United States. Data do not yet exist to illustrate how precisely the SOBP are being implemented by medical educators and to what extent, both within and outside of the United States.

PURPOSE: We hypothesize that cultural factors (such as perceptions about standardization, the role of simulation in medical education, etc.) impact the interpretation, adoption, and implementation of the ASPE SOBP outside of North America. To explore this hypothesis, we aim to 1) identify current applications of the ASPE SOBP across diverse settings in medical education, 2) obtain perspectives from international medical educators on the relevance of the components of the ASPE SOBP to their current SP methodology, and 3) elucidate cultural assumptions in the ASPE SOBP that may be limiting their current use, as well as possible avenues for future improvement in the SOBP and their implementation.

METHOD: We conducted 12 semi-structured qualitative interviews with medical education experts associated with ASPE who work with and train simulated patients, 10 of which have been included in this preliminary analysis. These interviewees were selected through purposeful sampling to capture participants from Asia, Europe, South America, North America, Africa, and Australia. Interviews were approximately 60 minutes each and conducted via Zoom. With participant consent, the interviews were recorded, transcribed using transcription software, and anonymized. A preliminary content analysis by five investigators identified themes present across the interviews. The qualitative research software NVIVO has been used to manage interview data and perform data analysis.

RESULTS: Our preliminary analysis reveals that international medical educators generally find the ASPE Standards of Best Practice to be flexible and applicable across cultural contexts, while also allowing for adaptations to be made when necessitated by specific institutional, economic, and professional factors. Interviewees used words like "liberating" and "validating" to describe the function the SOBP played in establishing and justifying program guidelines, especially with regards to regulations promoting sufficient training and safety of SPs. One interviewee depicted a common sentiment about the SOBP enabling creativity, saying, "It's like the standards have set the destination, but the route is up to every individual institution." Additionally, most interviewees mentioned the impact of the COVID-19 pandemic on their program and offered suggestions as to the role that ASPE might play in guiding the use of remote learning technologies in SP methodology.

DISCUSSION: The use of a standardized yet flexible set of guidelines to direct the international use of SPs has immense value in delivering high-quality educational experiences while paying regard to cultural differences in physician-patient interactions across a multitude of settings. Our preliminary analysis suggests that despite context-specific challenges, international medical educators are able to adapt the ASPE Standards of Best Practice and apply them to support their SP programs. Better understanding these practical applications and limitations of the SOBPs has broad significance in strengthening international medical education as well as international communities of medical educators.

Morphological Characterization of Cerebral Fusiform Aneurysms

Student: Ryan Sabotin M2
Mentor: Edgar A. Samaniego, MD
Collaborators: Jorge A. Roa MD, Alberto Varon MD, Ashrita Raghuram BS, Daizo Ishii MD, David M. Hasan MD

Introduction & Purpose

Unruptured intracranial aneurysms (UIAs) can be classified as saccular or fusiform in morphology. Fusiform aneurysms are described as a vessel wall dilation outside of major bifurcations, where the entirety of the aneurysm is formed as a result of diseased vessel. While fusiform aneurysms account for a small percent of UIAs, they are more prone to rupture and become symptomatic more often than saccular aneurysms. The etiology of fusiform aneurysms is not yet completely understood, but possible causes such as dissection, atherosclerosis, and collagen disease represent an underlying pathophysiology.

Additionally, current treatment options are limited and pose substantial risks. Therefore, there is a need to better characterize these vascular lesions. High-resolution vessel wall imaging (HR-VWI) has emerged as an effective tool in determining the angio-architecture of brain aneurysms and characteristics of the vessel walls. The aim of this study is to use advanced imaging and computational techniques to characterize cerebral fusiform aneurysms and better understand their unique pathophysiology.

Methods

Patients with UIAs were prospectively imaged from March 2018 to June 2020, undergoing 3T and 7T HR-VWI protocols with intravenous injection of 0.1mmol/kg gadolinium-based contrast agent. Fusiform aneurysms were defined as vessel wall dilation outside of major bifurcations with no discernable aneurysm neck. Aneurysmal wall enhancement was objectively quantified using signal intensity values adjusted for the pituitary stalk on T1 post-contrast. This was used to create a contrast ratio (CR) with a threshold of ≥ 0.60 to determine "enhancement". Additionally, another vessel within the circle of Willis (reference vessel) was analyzed for each patient with a fusiform aneurysm .

Several morphological features of each aneurysm were analyzed through segmentation: volume, height, width, and aneurysm boundaries. The presence of microbleed within the aneurysm wall was analyzed with quantitative susceptibility mapping imaging sequences. Computational fluid dynamics and finite element analysis of three patients with fusiform aneurysms was performed in collaboration with the department of biomedical engineering. Morphological parameters were analyzed with two-tailed Student's t tests and Pearson chi-squared tests.

Results

A total of 130 patients with 160 aneurysms underwent HR-VWI. 136 aneurysms had a saccular morphology and 24 were fusiform. Fusiform aneurysms had a significantly higher CR and diameter when compared to saccular aneurysms, with a multivariable logistic regression demonstrating that diameter was the only independent factor associated with UIA enhancement. Enhancing fusiform aneurysms had significantly larger volumes, diameters, and higher enhancement in a reference vessel compared to non-enhancing fusiform aneurysms Additionally, fusiform aneurysms with microbleeds had a significantly higher enhancement, volume, diameter, and proportion of aneurysms that enhanced when compared to fusiform aneurysms negative for microbleed.

Conclusion

This study demonstrates significant differences between fusiform and saccular aneurysms, while highlighting morphological characteristics that are unique to fusiform aneurysms. Fusiform aneurysms showed higher rates of enhancement on HR-VWI compared to saccular aneurysms. Similarly, fusiform aneurysms that enhanced had larger diameter and volume measurements compared to non-enhancing fusiform aneurysms. This suggests that aneurysm size is the primary determinant of contrast enhancement in both saccular and fusiform UIAs. However, reference vessels in patients with enhancing fusiform aneurysms displayed a higher degree of enhancement than those with non-enhancing fusiform aneurysms, suggesting a more prominent underlying cerebral vasculopathy in patients with enhancing fusiform aneurysms.

Title: Helping to control pulmonary hypertension in a Trisomy 21 infant with a Fenestrated Atrial Septal Defect device

Student: Stephanie Saey, BA, M2

Mentors: Dan McLennan, MBBS, DCH, FRACP, Kurt Bjorkman, MD, FAAP, and Jennifer Maldonado, BS-RTR

Introduction/Background: Transcatheter closure of an atrial septal defect (ASD) has become a standard treatment for patients when anatomically appropriate. This procedure typically results in complete closure of the defect with limited risks. However, in patients with ASD and coexisting pulmonary hypertension (PH), it is sometimes advantageous to keep a residual shunt as a decompression mechanism to maintain cardiac output in the setting of acute increases in pulmonary vascular resistance. We report the use of an Occlutech® fenestrated ASD (FASD) device in a patient less than 1 year of age.

Case Summary: An 11-month-old female with Trisomy 21 was diagnosed with ostium secundum ASD, left atrial hypertension secondary to left ventricular diastolic dysfunction and PH. Diagnostic cardiac catheterization confirmed PH and elevated right heart pressures. Partial closure of the defect with an FASD was considered given evidence of right heart dilation and right ventricular hypertrophy by echocardiogram, with concern for increased shunt possibly contributing to worsening PH and lung disease. IRB and FDA approvals were obtained, and the patient was scheduled for potential fenestrated closure of the ASD. On day of interventional catheterization, a 10mm Occlutech® FASD occluder was chosen and deployed via catheterization following standard ASD closure guidelines. Transesophageal echocardiography confirmed adequate positioning with no interference of the adjacent structures. The patient tolerated the procedure well and was discharged home one day after. Echocardiogram 3 weeks post-procedure revealed normalization of the right heart size and cardiac function, with the device well-seated and an expected left to right shunt through the fenestration. The patient was clinically improved.

Conclusion: The Occlutech® fenestrated ASD occluder is a safe device when implanted in small children requiring ASD closure with residual atrial communication -- reducing pulmonary over-circulation and associated symptoms while allowing for possible right-to-left shunting during times of high pulmonary arterial pressure.

Note: During the SRF time period, I authored the case report detailed above. Additionally, I wrote a protocol for testing mechanical properties of Lifetech© Iron-based Bioresorbable Scaffold (IBS®) stents for use in pediatric cardiac catheterization procedures. LifeTech© was unable to manufacture the stents in time, but we are expecting their arrival sometime this fall. I will briefly outline this protocol at the end of my presentation.

Recreational Off-Highway Vehicle Exposure, Safety Behaviors and Crash Experiences of Adolescents

Sienna Schaeffer

Mentor: Charles Jennissen, MD, Departments of Pediatrics and Emergency Medicine

Background: Recreational off-highway vehicles (ROVs), often called utility task vehicles (UTVs), have become increasingly popular since their introduction nearly two decades ago. ROV sales surpassed those of all-terrain vehicles (ATVs) in 2015 in the United States and across the world. With the increasing sales of these vehicles, there have been an increasing number of deaths and injuries associated with them, and they represent an emerging public health concern. All ROVs travel at least 30 mph and most can reach highway speeds. They are designed to be driven by those 16 years and older, and manufacturers generally do not recommend passengers on ROVs less than 12 years of age. However, many parents are not following these warnings. Despite their increasing prevalence, there have been very few studies published regarding the epidemiology of their use and the risk factors associated with ROV-related injuries and deaths.

Purpose: Our objective in this study was to determine the exposure of adolescents to ROVs, their use of restraint devices while riding them, and the ROV-related crashes they have experienced.

Method: The Iowa Off-Road Vehicle Safety Task Force presented a school-based program they developed called Safety Tips for ATV Riders (STARs) to adolescents. During the program, participants were surveyed using Turning Point, an audience response system. The survey included ROV-related questions which was initially just one question, but later increased to four. Data was collected anonymously from Spring 2011-Spring 2018. After compiling and cleaning the data, frequency and chi square analyses were performed using SAS software, V.9.4.

Results: A total of 4,023 students from 18 school districts participated. Participants ranged from 9-18 years of age with nearly three-quarters (74.4%) being 11-14 years old. There were equal proportions of males and females, and one-fifth (20.0%) lived on a farm, one-quarter (25.3%) lived in the country, but not on a farm, and over one-half (54.6%) were from town. Overall, 68.4% reported having ridden an ROV (n = 4,023). Youth ≤ 11 years of age had greater proportions that reported never riding an ROV (36.2%), and those ≥16 years had higher percentages riding ROVs at least weekly (31.6%). Males had higher percentages riding ROVs (70.1% vs. 66.7%, p=0.039) and of riding at least weekly (26.7% vs 19.5%, p<0.0001). The proportions having ridden an ROV by where one lived was: farm (84.7%) > country/not farm (73.1%) > town (60.0%), p<0.0001. Of those that were asked additional ROV questions (n=2,152), over one-quarter (26.2%) reported riding an ROV at least weekly and about two-fifths (39.7%) rode at least monthly in the previous 12 months. Of those riding an ROV in the past year, 28.5% had at least one crash (rollover, collision or ejection). Having had a crash was associated with riding frequency, p<0.0001. Males had a higher percentage with crashes in the past year compared to females (22.6% vs 17.0%, p=0.004). Those living on farms also had greater proportions with a crash as compared to those living elsewhere (31.0% vs 16.6%) p<0.0001. Nearly two-fifths (37.7%) always or almost always wore seatbelts when riding an ROV while a similar percentage (38.8%) never or almost never did. Wearing a seatbelt was strongly associated with age with progressively older youth having lower percentages always or almost always using their seat belt and greater percentages never or almost never wearing them, p<0.001. Females had higher percentages reporting always or almost always using a seat belt (42.4% vs 35.6%) and lower percentages of never or almost never wearing them (32.2% vs 42.5%), p=0.0015. Seat belt use was also related to where one lived: always or almost always--farm (24.2%) < country/not farm (39.%) < town (44.4%); never or almost never--farm (47.5%) > country/not farm (38.2%) > town (32.2%), p=0.0005. More frequent riders had greater proportions that never or almost never wore their seatbelt in an ROV: daily riders (53.1%) > weekly (40.6%) > monthly or less (33.1%), p<0.0001. Those in a crash had much higher percentages reporting never or almost never wearing their seat belt (51.9% vs. 31.6%) and much lower percentages always or almost always wearing their seat belt (25.9% vs 44.8%), p<0.0001.

Conclusion: Iowa adolescents are commonly exposed to ROVs. Many ride them frequently and often without a seatbelt which puts them at greater risk for serious injury or death should they be ejected or have a rollover. Almost 30% of riders had an ROV-related crash in the past year. Legislative measures and increased education of the public is needed regarding proper safety measures while operating and riding ROVs. In our study, we identified a number of risk factors which could be targeted in injury prevention efforts.

The Rotational Positioning of the Bones in the Medial Column of the Foot: A Weightbearing CT Analysis
Presenter: Eli Schmidt
Mentor: Dr. Cesar de Cesar Netto, MD, PhD
Collaborators:
Thiago Alexandre Silva, MD, Shuyuan Li, MD, PhD, Daniel Baumfeld, MD, Elijah Auch, BS, Victoria Vivtcharenko, BA, Kevin Dibbern, PhD, Nacime Mansur, MD

Introduction: Instability of the medial column (navicular, medial cuneiform, first metatarsal, and the proximal phalanx of the first toe) plays an important role in the development of various malformations of the foot. This includes adult acquired flatfoot and hallux valgus deformities as examples. Despite this significance, the typical rotational pattern of each bone of the medial column is not yet fully understood. The objective of this study was to evaluate the rotational position of these bones using three-dimensional weight-bearing CT (WBCT) images in order to serve as a reference for future studies.

Methods: A retrospective review was conducted for 95 patient (110 feet) who underwent WBCT assessment of various foot disorders. WBCT scans were performed used a cone-beam CT extremity scanner (PedCAT CurveBeam) and evaluated using dedicated software (CubeVue, CurveBeam). To measure the rotational profile, the angle of each bone was assessed in relation to the floor in the coronal plane (Figure 1-A). As standard, we defined supination as negative values and pronation as positive values.

Results: All bones of the medial column were found to have an average rotational alignment in pronation (internal rotation) (Figure 1-B). The mean value and 95% Confidence Interval (CI) for the rotational positioning of each bone was: navicular, 43.2º (CI, 41.1 to 45.3); medial cuneiform, 6.1º (CI, 4.0 to 8.3º); proximal first metatarsal, 33.9º (CI, 31.8 to 36.0º); distal first metatarsal, 18.5º (CI, 16.4 to 20.6º); and proximal phalanx of the first toe, 21.6º (CI, 19.5 to 23.7º) (Figure 1-B).

Conclusion: To the best of the author's knowledge, this is the first study that attempts to quantify the rotational profile of the bones of the medial column of the foot. We found that all bones of the medial column demonstrate some degree of pronation. The pronation is most pronounced in the navicular bone and is minimal in the medial cuneiform. Interestingly, the first metatarsal demonstrated an intrinsic relative supination, from proximal to distal, of about 15º. Our data can serve as reference values for future comparative, controlled and prospective studies.

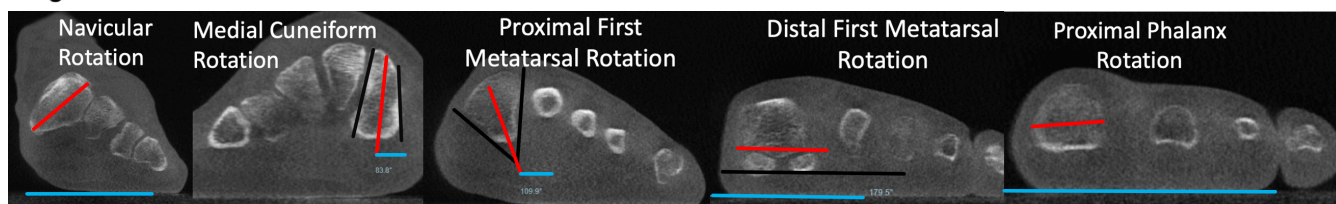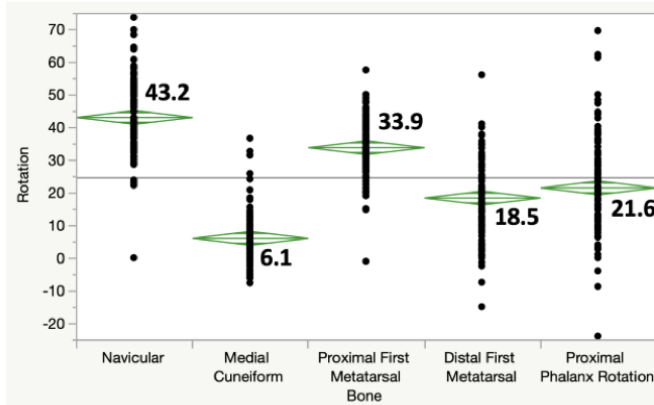The rotational positioning of the bones in the medial column of the foot: a weightbearing CT analysis

Understanding the Role of Interferons in Ebola Virus Infection of Keratinocytes
M1 Student: Kristina Sevcik
Mentor: Wendy Maury, Ph.D., Professor, Department of Microbiology and Immunology and Graduate Program in Immunology

It is well known that a variety of pathogenic viruses target the skin as a point of entry or egress from their host. However, few studies have been done to examine the interactions of RNA viruses with skin cells. Recently, the Maury lab has investigated Ebola virus (EBOV) infection of skin and has identified that EBOV traffics to skin at late points during infection, primarily infecting dermal fibroblasts and epidermal keratinocytes. With evidence of the skin's involvement late during infection, and the spread of EBOV via direct contact with those infected, it is thought that EBOV uses infection of these skin cells as a route of transmission to leave the body and progress to infect new hosts. Consequently, the effects of the innate immune system on fibroblasts and keratinocytes should serve as a final barrier before EBOV becomes transmissible. By exploring the function and interactions at this final barrier, we hope to open up possibilities for use of prophylactics in controlling outbreaks of EBOV.

Preliminary studies in the Maury lab found that a human keratinocyte line was responsive to type I (IFN-β) and type II (IFNγ) interferons and evaluated their effect against a BSL2 level model virus of EBOV, rVSV/EBOV GP. To extend our understanding of interferons on virus replication in keratinocytes, we investigated the ability of a broader range of interferons to block rVSV/EBOV GP as well as a BSL3 EBOV model virus, EBOV ΔVP30. Type I (IFNα A/D and IFN-β), type II (IFNγ), and type III (IFNλ_3) interferons were tested. We hypothesized that each of these interferons would enhance the ability of keratinocytes to block EBOV infection of keratinocytes.

Additionally, RNA was isolated from keratinocytes at two time points post-IFN-treatment with each of the four interferons and an untreated control and RNA seq was performed. We are currently analyzing the results to identify interferon-stimulated genes (ISGs) that are regulated in response to each interferon within keratinocytes. We will then utilize this information to investigate the roles of particular ISGs on EBOV infection.

Results and Conclusions:
Treatment of keratinocytes by each of the four interferons under investigation strongly blocked infection by the rVSV/EBOV GP model in a dose dependent manner, supporting our hypothesis as well as previous data. The protective effects by interferon treatment on EBOV VP30 were more modest, potentially due to the production of IFN antagonistic proteins by EBOV. To further investigate this, additional methods of detecting EBOV VP30 infection are currently ongoing. These studies suggest that EBOV may effectively target ISGs and/or pathways that elicit ISGs through mechanisms not currently appreciated. To evaluate this, we will analyze the RNA seq data, identify the overlapping subset of ISGs that are expressed following different IFN treatments, assess the direct impact of selected ISGs on virus infection and determine if EBOV VP30 infection suppresses the expression of those ISGs. Through these studies, we can understand the specific pathways and ISGs that are targeted by innate immune antagonistic proteins of EBOV.

Title: Evaluation of Educational Intervention in Addressing Culturally-Sensitive Care for the Transfeminine Patient
Student: Pombie Silverman, M2
Mentor: Amy Pearlman, M.D.
Other Collaborators: Paige De Rosa, M.D.

Background:
Transgender patients face serious healthcare barriers including a shortage of providers knowledgeable in transgender health. Fortunately, there are an increasing number of urology fellowship programs that offer training in gender-affirming genitourinary reconstructive surgery. While these sub-specialty training programs suggest advancements in transgender care, less emphasis has been placed on training medical staff to care for these patients pre- and post-operatively.

Purpose:
The purpose of our study was to assess the efficacy of a brief educational intervention on providing culturally competent care for transfemme and non-binary patients undergoing zero- and full-depth vaginoplasty.

Methods:
A 20-minute educational video designed by the authors was presented to nursing and medical support staff in the urology department of a tertiary academic medical center. The following topics were covered: transgender identity, health disparities, asking for and using gender neutral pronouns, surgical transition, pre- and post-operative care, and addressing transgender-related bias. Pre- and post-intervention survey data measuring participants' acceptability and knowledge of the material was measured on a 5-point Likert scale. Comparison of ratings was completed using the Wilcoxon signed rank test.

Results:
Thirteen health care providers (registered nurses and medical support staff) participated in the study. Following the brief educational intervention, participants reported improved confidence in understanding transgender health, transphobia, gender neutral pronouns, options for gender-affirming surgeries, sex versus gender, and social versus medical transition ($p < 0.05$). Participants reported the greatest understanding in the following topics: types of gender-affirming genitourinary surgeries, addressing transgender-specific biases, and entering transgender-specific health information on the electronic medical record.

Conclusions:
Our study suggests that a brief educational intervention can improve confidence and knowledge in providing transgender-related care. We believe that similar interventions should be considered part of the standard education for health care staff, especially at centers where gender-affirming genital surgery is routinely performed.

Title: Molecular Mechanisms of Skeletal Muscle Atrophy

Student: Zach Skopec, M2
Mentor: Chris Adams, MD, PhD, Professor of Internal Medicine

Background: Skeletal muscle atrophy diminishes the health and quality of life of tens of millions of people. Causes of muscle atrophy include aging, muscle disuse, malnutrition, critical illness, certain medications and a wide range of chronic illnesses including cancer, heart failure, COPD, diabetes, renal failure, cirrhosis, rheumatoid arthritis, and HIV/AIDS. Effects of muscle atrophy include weakness, impaired activity, falls, prolonged hospitalization, delayed rehabilitation, loss of independent living, and increased mortality. Despite its broad clinical impact, skeletal muscle atrophy lacks a specific and effective pharmacologic therapy and remains poorly understood at the molecular level. In preliminary studies, we identified p21 as a skeletal muscle fiber protein that is necessary and sufficient for skeletal muscle atrophy. We then used an unbiased biochemical approach to isolate and identify 13 proteins that specifically interact with p21 in mouse skeletal muscle fibers. The 13 proteins isolated included 4 different Cyclins (cyclins A2, B1, D1, and D3), 5 Cyclin-Dependent Kinases (CDKs 1, 2, 4, 5, and 6), proliferating cell nuclear antigen (PCNA), importin alpha3 (KPNA4), Arginase 1 (ARG1), and Histidine Ammonia Lyase (HAL). However, the exact mechanism by which p21 promotes muscle atrophy is not yet known.

Purpose: To investigate the roles of the 13 identified p21-interacting proteins in skeletal muscle atrophy using a reliable assay for screening of multiple candidate proteins.

Methods: To accomplish the project, RNAi was chosen as a method to alter expression of the proteins of interest due to a number of advantages it provides for screening purposes. To generate and validate RNAi constructs, we used a well-established strategy we previously used to knockdown ATF4, Gadd45a, and other proteins. Briefly, oligonucleotide duplexes of know sequences targeting the mRNAs of interest were purchased and ligated into the pcDNA6.2GW/EmGFP miR plasmid (Invitrogen), which contains a CMV promoter driving co-cistronic expression of engineered RNAi constructs and emGFP. For each targeted mRNA, we developed two different RNAi constructs targeting two different regions of the mRNA that encodes the specific isoform(s) of the protein found to interact with p21. Both RNAi constructs were tested for specific and significant knock down of expression of the targeted mRNA in skeletal muscle, as assessed by qPCR measurements of the targeted mRNA and control transcripts, and by immunoblot analysis when validated antibodies were available. Once validated, plasmids were then transfected into mouse TA muscle fibers by electroporation. The TA muscles were harvested 7 days post-transfection and were assessed for muscle fiber size.

Results: RNAi constructs and overexpression plasmids for 4 of the identified p21 interacting proteins (PCNA, Cyclin A2, Cyclin B1, and Cyclin D1) were successfully generated and validated by qPCR and immunoblot analysis. We've begun to transfect mouse TA muscles with the validated constructs to asses for any effect on muscle fiber size in the absence of p21 overexpression. The project will be continued, and more results will be gained throughout school year with the collaboration of a full-time graduate student in the lab. Subsequent experiments will involve altering the expression of the proteins of interest in a p21-overexpressed model of muscle atrophy and assessing for any change in p21's effect on muscle fiber size.

Determining the Differences Between 10 Hz Repetitive Transcranial Magnetic Stimulation (rTMS) and Intermittent Theta Burst Stimulation (iTBS) in Treating Major Depressive Disorder

Nathen Spitz BA, Patrick Ten Eyck Ph.D. Krystal Nizar MD, Ph.D, Nicholas Trapp MD

Introduction:

Repetitive transcranial magnetic stimulation (rTMS) is an increasingly researched, FDA-approved, non-invasive therapy for major depressive disorder. Transcranial magnetic stimulation works by generating pulsed magnetic fields that travel through the scalp to induce electrical currents that increase activity and excitability in regions of the brain, like the left dorsolateral prefrontal cortex (DLPFC), that are hypoactive in people with depression. The standard of care rTMS protocol includes 3,000 pulses of 10 Hz stimulation to the left DLPFC over a 37.5-minute treatment session. Intermittent theta burst stimulation (iTBS) is a newly FDA-approved treatment modality that more rapidly modulates brain activity by delivering 600 in just over three minutes, as compared to the 37.5-minute session of 10 Hz rTMS.

Purpose of the Study:

Existing literature suggests that when targeted at the left DLPFC, 10 Hz rTMS and iTBS therapy for major depressive disorder are non-inferior; however, few studies currently exist that directly compare the standard 10 Hz rTMS to iTBS across an array of treatment outcomes. We aim to further examine if there are any potential differences between 10 Hz rTMS and iTBS in treating major depressive disorder.

Methods:

This retrospective cohort study consisted of 105 participants who received between 20 to 36 open-label 10 Hz rTMS treatments to the left DLPFC or left sided iTBS treatments between December 2017 and February 2020. Participants included patients (age ≥ 18) with a diagnosis of major depressive disorder that were recruited and evaluated by psychiatrists or neurologists with expertise in rTMS while patients were receiving psychiatric treatment at the University of Iowa Hospitals and Clinics. Exclusion criteria included having an age less than 18 years; patients with epilepsy or seizure disorder; or patients with implanted ferromagnetic equipment in their face or skull near the stimulation target. Demographic information, as well as outcome measures consisting of depression rating scales that included the Patient Health Questionnaire 9 (PHQ-9), were stored in a password secure online REDCap database. Data analyses were performed using IBM SPSS Statistics (Version 26).

Results:

The final patient population in the analyses were comprised of 105 adults (59% female, mean age 52.08 ± 16.25) with a diagnosis of major depressive disorder. In this study, to compare 10 Hz rTMS and iTBS therapy for the treatment of depression, we used the PHQ-9 as our primary outcome measure, and the scores reported were used to evaluate efficacy of the treatment through previously validated response criteria. Using Chi-Square statistical analyses to compare differences in categorical outcomes of treatment efficacy amongst participants that received 10 Hz rTMS or iTBS, we found no significant differences in response to treatment, defined as a > 50% improvement from baseline, X^2 (1, N = 105) = 0.064, p = 0.800; for those who had achieved remission, defined as a score less than 5, X^2 (1, N = 105) = 0.744, p = 0.389; and for those who had achieved a minimum clinically important difference (MCID), defined as a change from baseline of more than 5 points, X^2 (1, N = 105) = 0.364, p = 0.546. To investigate differences between the two treatment options in continuous outcomes of treatment efficacy, we used Independent Sample t-Tests, and found that the overall score change of the PHQ-9 from baseline to end of treatment in 10 Hz rTMS (M = -7.38, SD = 6.778) and iTBS (M = -7.89, SD = 7.098) was non-significant, t(103) = 0.362, p = 0.718, and we found that the percent change in the PHQ-9 from baseline to end of treatment in 10 Hz rTMS (M = -41.94, SD = 36.15) and iTBS (M = -39.00, SD = 38.55) was non-significant, t(103) = -0.270, p = 0.788.

Conclusion:

Our study determined that there were no discernable differences between 10 Hz rTMS and iTBS therapy when delivered to the left DLPFC in treating patients with major depressive disorder. As no significant differences were found, expanding the option of using the more time efficient iTBS treatment modality could greatly increase capacity to treat people with major depressive disorder, as well as reduce the time burden for future patients.

Cystic Fibrosis Pig Model to Study the Pathogenesis of Meconium Ileus

Hannah Steenblock; Yunxia O'Malley Ph.D.; Aliye Uc M.D.
University of Iowa Carver College of Medicine, Stead Family Department of Pediatrics

Background: Cystic fibrosis (CF) is an autosomal recessive disorder caused by mutations in the gene that encodes the cystic fibrosis transmembrane conductance regulator (CFTR). CFTR is expressed on the apical membrane of epithelial cells, including intestinal epithelial cells, where it modulates chloride and bicarbonate secretion. Fifteen-twenty % of babies with CF are born with meconium ileus, requiring surgery to relieve the obstruction. In contrast to humans, meconium ileus is 100% penetrant in pigs with CF. The pathogenesis of meconium ileus in CF remains uncertain, but it is largely explained by the loss of CFTR, leading to acidic secretions, mucus accumulation and obstruction of intestine with mucofeculant material.

Purpose: Using the porcine model of cystic fibrosis, the purpose of this study was to identify the differences between the non-CF ((CFTR +/+) and (CFTR +/-)) and CF (CFTR -/-) intestine. Specifically, we first aimed to query the presence of various differentiation, proliferation and signaling markers, and anion channels in newborn pig intestine and assess whether there were differences between the two phenotypes and along the length of the intestine.

Methods: Newborn pig intestine was obtained from CF and non-CF pigs following euthanasia (n=3). The intestines were excised and lumen was flushed with ice water to clean meconium. Segments of intestine were identified as duodenum (1), jejunum (2), ileum (3), proximal spiral colon (4), and distal spiral colon/rectum (5). Sections from each intestinal segment were obtained, and lumens were dissolved in Trizol, followed by RNA extraction and RT-PCR (n=1 for each segment). The following primers were selected: e-cadherin (epithelial cell marker and housekeeping gene), SGLT1 (sodium glucose co-transporter, enterocyte marker), MUC2 (Mucin 2, goblet cell marker), Lgr5 (Leucine-rich repeat-containing G-protein coupled receptor 5, intestinal stem cell marker), NKCC1 (The Na-K-2Cl cotransporter isoform 1, anion channel), CFTR (anion transporter), PCNA (proliferating cell nuclear antigen, proliferation marker), and Wnt3a (Wingless Type 3a, involved in intestinal proliferation, differentiation and development signaling). Results were visualized using gel electrophoresis with ethidium bromide. Images were processed on ImageJ.

Results: Compared to non-CF pigs, CF pig intestines showed meconium-filled loops with obstruction observed at mid-jejunum to ileum. There was a clear size discrepancy at the site of obstruction with dilatation proximally and smaller caliber intestine and microcolon distally. SGLT1, NKCC1, PCNA and Wnt3a were expressed in CF and non-CF intestines at all segments. Mucin2 was expressed in all intestinal segments of non-CF pigs; it was expressed at all segments except duodenum in CF pigs. Lgr5 signal was faint, but present in all samples. CFTR was expressed at all levels of the intestine in non-CF pigs, absent in CF pigs.

Summary and Conclusions: As expected, the gross anatomical findings were consistent with meconium ileus in CF pigs. In this preliminary study, we have confirmed that various differentiation, proliferation and signaling markers, and anion channels were expressed in newborn pig intestine. Using RT-PCR, we have not found major qualitative differences between CF and non-CF except CFTR expression. Future steps will include qRT-PCR and immunostaining for comparison of various markers between CF and non-CF, and organoid cultures for functional studies.

Prevalence of COVID-19 in the delivering pregnant population at the University of Iowa Hospitals and Clinics and associated demographic characteristics

Haley A. Steffen, BA, Samantha R. Swartz, BS, J. Brooks Jackson, MD, MBA, Kimberly A. Kenne, MD, MCR, Abbey Merryman, MD, Patrick Ten Eyck, MS, PhD, and Mary Rysavy, MD

Background: Novel coronavirus (COVID-19) is a respiratory virus that first appeared in China in late 2019 and spread to the United States by early spring 2020. As the virus moved across the United States, it quickly became apparent that demographic factors were affecting who was most at risk of infection. Many interventions meant to slow the spread of the virus only exacerbated previously existing health care disparities for patients of racial and ethnic minorities or low socioeconomic status. Early studies of COVID-19 have shown Black patients to be at a heightened risk of infection by SARS-CoV-2. However, this observation has not yet been studied in pregnant women.

Objectives: This study aimed to determine the seroprevalence of SARS-CoV-2 IgG antibodies within the population of delivering mothers at the University of Iowa Hospitals and Clinics (UIHC) and to assess demographic characteristics and clinical factors associated with COVID-19 infection.

Methods: Excess plasma from previously collected type-and-screen samples was collected on all delivering pregnant women at UIHC between May 1 and August 2, 2020. Plasma samples were used to determine the seroprevalence of SARS-CoV-2 IgG antibodies within this population. Samples were run on both the LIAISON® SARS-CoV-2 S1/S2 IgG test (DiaSorin) and Elecsys® Anti-SARS-CoV-2 (Roche) assays. Discrepancies were reconciled with a third antibody assay, the EUROIMMUN SARS-COV-2 ELISA (IgG). 103 plasma samples that had been collected from the UIHC patient population prior to the COVID-19 outbreak were run on the DiaSorin to serve as the study control. Demographic, historical and clinical data were obtained on all patients from the EPIC electronic medical record system and entered into a REDCap database. Double entry of all data took place to ensure accuracy. The SAS System was used for statistical analysis.

Results: Of the 613 women who delivered during this time frame, 5.06% (31) tested positive for SARS-CoV-2 IgG antibodies. The majority of these women did not appear to have COVID-19 symptoms during delivery. 50% of the COVID-Ab positive patients self-reported a preferred language other than English. These languages included: Spanish, French, Arabic, Portuguese, Lingala, and Other. 70% of COVID-Ab positive women were Black or Latinx. Other race/ethnicities indicated were White, Asian, Multiracial, and American Indian/Alaska Native. The mean body mass index of patients at delivery was 33.40 ± 8.20, and 33.30 ± 6.90 lbs for COVID-19 positive patients specifically. 51.6% of the 613 study patients were covered by private insurance, 44.2% Medicaid/Medicare, 0.33% Other, and 3.9% did not have insurance. 99.8% of all delivering mothers had access to at least some prenatal care. 34.2% of deliveries during this period were cesarean, 6.4% of women experienced preterm labor, 17.9% had a postpartum hemorrhage of greater than one liter, 1.28% resulted in neonatal death, and the mean total blood loss for these 613 consecutive delivery hospitalizations was 467.0 ± 360.7 mL.

Conclusions: These data indicate that the number of COVID-19 infections within 613 consecutive births at UIHC were disproportionately greater among racial/ethnic minorities. While only 0.1% of the studied patients were non-English speaking and 22.2% of Black or Latinx ethnicity, they accounted for 50.0% and 70.0% of COVID-Ab positive cases, respectfully. These results support previous studies suggesting that patients of ethnic minorities and/or facing language barriers during the COVID-19 pandemic are at a heightened risk of becoming infected by the SARS-CoV-2 virus. In this study population, no significant correlations were identified between COVID-19 infection rate and patient BMI at delivery admission. UIHC's cesarean delivery rate for the study period (34.22%) is slightly above the 2018 national average of 31.9%.

Prevalence of COVID-19 Among Delivering Women at the University of Iowa Hospitals and Clinics and Associated Maternal and Neonatal Outcomes

Samantha R Swartz, BS, Haley A Steffen, BA, J Brooks Jackson, MD, MBA, Kimberly Kenne, MD, MCR, Abbey Merryman, MD, Matthew D Krasowski, MD, Patrick Ten Eyck, MS, PhD, Mary Rysavy, MD

Background: COVID-19 is a novel coronavirus that causes respiratory infection as well as a myriad of other symptoms. Pregnancy puts the body into an immunosuppressive state, making pregnant women especially susceptible to infection, but early observations have not suggested that pregnant women are more susceptible to COVID-19 than the general population. Studies of other coronaviruses, SARS and MERS, have shown adverse outcomes for infected pregnant women and their neonates, and research to date suggests that pregnant women hospitalized with COVID-19 may have higher rates of pre-eclampsia, preterm birth, cesarean section, and perinatal death of the neonate. However, information about how COVID-19 affects pregnancy is still very limited.

Objectives: The aim of this study was to determine the seroprevalence of COVID-19 antibodies in women who delivered at the University of Iowa Hospitals and Clinics (UIHC) and observe associations between COVID-19 antibody seroprevalence and adverse maternal and neonatal outcomes.

Methods: Leftover plasma was collected from type and screen specimens from every woman who delivered at UIHC between May 1, 2020 and August 2, 2020 to reach a sample size of 613 women. Each plasma sample was run in the LIAISON® SARS-CoV-2 S1/S2 IgG test (DiaSorin) and the Elecsys® Anti-SARS-CoV-2 (Roche) assay for seroprevalence of SARS-CoV-2 (COVID-19) antibodies. Discrepant results were resolved using the Euroimmune assay at the Iowa State Hygenics Laboratory. One hundred plasma samples collected prior to the COVID-19 pandemic were also run on the DiaSorin to serve as a control group. Clinical data, including COVID-19 viral prevalence, demographic information, and maternal and neonatal outcomes, were collected from the institution's electronic medical record system and entered it into a REDCap database. All data were double entered to ensure accuracy and analyzed using standard statistical methods.

Results: Of the 613 women from whom plasma samples were collected, 31 (5.1%) had COVID-19 antibodies. 12 of these women also tested virus-positive at some point during their pregnancy. 2 women in the study tested positive for COVID-19 on delivery admission but tested antibody-negative. None of the women who tested viral- or antibody-positive received any treatment for COVID-19. No significant associations were seen between having COVID-19 antibodies and maternal blood loss, postpartum hemorrhage, hypertensive disease, ICU admission, placental abruption, chorioamnionitis, maternal sepsis, non-reassuring fetal status, preterm labor, premature rupture of membranes, or unscheduled cesarean section. There were no significant associations between a mother's COVID-antibody positivity and any of the following neonatal outcomes: hypoglycemia, sepsis, Apgar scores, hypoxic ischemic encephalopathy, or neonatal death. 2 of 35 (5.7%) babies born to mothers with COVID-19 antibodies and 8 of 594 (1.3%) of babies born to mothers with COVID-19 antibodies were stillborn.

Conclusion: 5.1% of delivering mothers at UIHC between May 1, 2020 and Aug 2, 2020 were found to have COVID-19 antibodies. That number is likely to be higher in the general population, as pregnant women were advised to maintain social distancing during pregnancy. Women with COVID-19 antibodies do not appear to be at a greater risk of maternal or neonatal complications than women who have not had COVID-19. However, our sample size is relatively small, including only 31 women with COVID-19 antibodies. COVID-19 is still prevalent in the UIHC community, and the project will continue to collect more data and further assess whether associations exist between COVID-19 and maternal or fetal outcomes.

Analysis of *Campylobacter jejuni* infection in 9-month-old infants in relation to zoonotic exposures in low-income peri-urban settlements of Kisumu, Kenya

Student: Zainab Tanveer, M2
Mentor: Kelly Baker, Ph.D., Assistant Professor of Occupational and Environmental Health

Background: The bacteria *Campylobacter jejuni* is a common cause of gastrointestinal infection around the world. While infection via the fecal-oral route stemming from animal exposure is well-known, the intricate pathways of transmission of this bacterium to humans is still inconclusive. This study aids in the understanding of *C. jejuni* infection pathways.

Methods: A conceptual model was created *a priori* to propose transmission pathways and the interacting variables that mediate *C. jejuni* infection from zoonotic exposure. Data obtained from the Safe Start Trial conducted in Kisumu, Kenya on enteric pathogen infections in infants was analyzed using SAS software. Multi-variable logistical regression model was applied to estimate the association between household living conditions that could transmit *C. jejuni*, and then determine the influence of animal presence in the household on these pathways.

Results: Of the 704 infants analyzed, 14.29% were positive for *C. jejuni* infection and 13.76% of individuals with *C. jejuni* infection indicated self-reported diarrhea. 11.26% of non-infected individuals kept domestic animals inside the house. Chickens and cats were among the most common animals kept inside the home. Vinyl flooring (odds ratio of 0.383, 95% CI of 0.186-0.789) and finished flooring (OR 0.539, CI 0.295-0.985) was a protective factor against *C. jejuni* infection compared to dirt flooring. Presence of both soap and water, when analyzed in relation to *C. jejuni* infection, was a protective factor (OR 0.664, CI 0.456-0.967). Furthermore, eating fruit one day prior was determined to be a shielding factor as well (OR 0.414, CI 0.187-0.919). After adjusting for zoonotic exposure, there was not a strong association between each mediating pathway to infection and the presence of animals in the home.

Conclusion: The low odds ratio values suggest that vinyl/finished flooring, the observed presence of soap and water in the home, and consumption of fruit one day prior decreases the likelihood of *C. jejuni* infection in infants. Animal presence inside the home did not contribute to these pathways of infection.

Using Human Vitreous Biopsies to Understand Exudative Age-Related Macular Degeneration

Presenter: Marcus A. Toral

Mentors: Alexander G. Bassuk, Vinit B. Mahajan

Collaborators: Benjamin Ng, Gabriel Velez, Jing Yang, Stephen H. Tsang

Background: Exudative age-related macular degeneration (eAMD) is a highly-prevalent, chronic inflammatory disease of the eye which affects the retina and underlying vascular tissue. In many cases, eAMD can lead to severe vision loss. To treat eAMD, patients receive therapy which inhibits the protein vascular endothelial growth factor (VEGF) in the eye. However, despite anti-VEGF therapy, eAMD patients experience persistent fibrosis, cellular atrophy, retinal degeneration, and edema. These features may be the result of molecules active in the disease other than VEGF.

Purpose: The purpose of this study was to identify molecular pathways which persist in eAMD despite anti-VEGF treatment in order to identify new molecular targets for improved treatment options.

Methods: We used a multiplex antibody array to quantify 1,000 human proteins in vitreous biopsies from eight eAMD and six control patients. Differentially expressed proteins were identified using one-way ANOVA, enrichment of gene and protein functional pathways were measured using the online WebGestalt bioinformatic toolkit, and available pharmacological treatments were identified for potential drug repositioning.

Results: We observed marked differential expression of interleukin-21 receptor (IL-21R), sialic acid binding Ig like lectin-7 (SIGLEC-7), cytotoxic T lymphocyte associated protein 4 (CTLA4), phosphoenolpyruvate carboxykinase 1 (PCK1), sphingosine kinase 1 (SPHK1), ST3 Beta-Galactosidease Alpha-2,3-Sialytransferase 1 (ST3GAL1), Cadherin-6 (CDH6), and Sulfotransferase Family 2A Member 1 (SULT2A1). Additionally, we observed enrichment of gene ontology categories and protein pathways consistent with cytotoxic lymphocyte activity, neuronal damage, and angiogenesis. Five available drugs were identified which target key differentially expressed proteins found in our analysis.

Conclusions: This study is the first large-scale antibody-based proteomic analysis of vitreous biopsies from eAMD patients following anti-VEGF treatment. Our analysis implicates cytotoxic lymphocyte signaling pathways as a potential new area for development of eAMD therapies.

Evaluation of a screening tool for the identification of neurological disorders in rural Uganda
Student: **Andy Tran**
Mentor:

Background: Neurological disorders likely contribute significantly to morbidity and mortality in sub-Saharan African, but accurate neuroepidemiologic data are lacking from the region. A screening tool to capture the prevalence of neurological disease at the community level could provide these data. In this study, we assess the feasibility and validity of one such tool in a rural Ugandan cohort with high HIV prevalence.

Methods: The screening tool, developed in Tanzania and previously validated in Tanzania and Ethiopia, was comprised of questionnaire and examination components. Participants were recruited from the Rakai Neurology Study in Rakai District, Uganda. A research nurse was trained to administer the tool and a sociodemographic survey to participants. 100 participants (75 who screened positive and 25 who screened negative) returned for validation examinations by a neurologist (validation cohort). The diagnostic utility and validity of the instrument was calculated and demographic characteristics of those with and without neurological disorders were compared.

Results: The tool was administered to 392 participants who were 48% female, 33% people with HIV (PWH), and had an average age of 35.1 ± 8.5 years. 33% screened positive in the study cohort. These participants were older [mean (SD): 38.3 (9.7) vs. 33.5 (7.1) years, $p < 0.001$], had a lower Karnofsky score [89.8 (8.4) vs. 93.9 (7.5), $p < 0.001$] and a lower body mass index (BMI) [21.8 (3.3) vs. 22.8 (3.7), p=0.007] than those who screened negative. Amongst the validation cohort, 54% had a neurological abnormality of which 46% were symptomatic. The tool had a sensitivity of 57.4% and a specificity of 73.9% for the detection of any neurological abnormality and was 80% sensitive and 69.3% specific for detecting symptomatic abnormalities. The accuracy of the instrument for classifying participants with or without neurological disease was 66% for any neurological abnormality and 71% for any symptomatic abnormalities. ***Conclusions***: Our study found a lower sensitivity and similar specificity for the screening tool than the two previous studies. The lower validity of the tool in this study was likely at least partially due to the high percentage of asymptomatic neurological abnormalities detected and also exemplifies the cultural specificity of screening instruments As such, the screening tool will require further refinement and cultural contextualization before it can be widely implemented across new populations.

INFLAMMATORY MEMORY IN HUMAN AIRWAY EPITHELIA

Rosarie A. Tudas[3], Alejandro A. Pezzulo[1,2]

Internal Medicine[1], Pappajohn Biomedical Institute[2], Carver College of Medicine[3]
University of Iowa

Abstract: Asthma is composed of multiple endotypes, with 50% of individuals with asthma having Th2-high endotype driven by IL4/IL13 signaling. Th1 cytokine IFNγ and Th17 cytokines IL17 and TNFα, among others may drive airway inflammation in Th2-low asthma endotype. While patients with Th2-high asthma respond to treatments such as IL13-receptor antibody therapy, success in treating patients with Th2-low asthma remains limited. Understanding the mechanisms that underly the development of inflammatory pattern responses is critical in developing therapies. In preliminary experiments, we measured periostin, a biomarker of Th2 eosinophilic response, in the basolateral media of human airway epithelial (HAE) cells. We found that HAE cells previously exposed to IL13 showed an earlier increase in periostin secretion upon re-exposure to IL13. Based on these findings, we hypothesized that exposures to inflammatory triggers induces airway epithelial inflammatory memory that enables the airway cells to respond to triggers promptly upon re-exposure. Furthermore, we also hypothesized that epigenetic changes ensue as a result of exposure history. Thus, memory to inflammatory triggers are retained by basal cells, which act as airway stem cells, and not only a result of a change of cell composition in the epithelia. To test this hypothesis, we took HAE grown at air-liquid interface and exposed them to IL13 or IL17+TNFα to establish Th2 and Th1/17 inflammatory response patterns, respectively. The cells were then trypsinized and seeded on plastic to promote de-differentiation and expand the basal cells. The basal cells were then treated with different inflammatory triggers such as Ascaris extract, LPS, and heat-killed *Staphyloccocus aeurus* (HKS). To assess Th2 and Th1/17 response patterns, we measured periostin and G-CSF, respectively, in the media. We found that cells with history of IL-13 exposure had: 1) increased periostin production at baseline, 2) suppressed G-CSF secretion in response to LPS, and 3) increased G-CSF secretion in response to HKS. Our data suggests that epithelial (likely epigenetic) memory modulates the basal cell response to inflammatory stimuli; we will investigate the mechanisms involved in these responses.

Medical Student: Ashley Vaughan | Mentor: Dr. Amy Pearlman, MD | Collaborator: Dr. Emily Wentzell, BA, MA, PhD

Title: Patient and partner expectations before and satisfaction after inflatable penile implant surgery: a mixed-methods analysis

Introduction: Erectile dysfunction (ED) is among the most common sexual disorders affecting males. A variety of non-surgical and pharmacological therapy options are available and often serve as a first line of treatment for ED. If the aforementioned options are unsuccessful, poorly tolerated, and/or contraindicated, surgical therapies may be considered. Surgeons who commonly perform penile implant surgery report high satisfaction rates for both patients and partners, though the various questionnaires used to "objectively" measure degree of satisfaction among these patients are not particularly applicable to the surgical patient, and data are lacking when it comes to assessing partner satisfaction. Understanding paient and partner expectations prior to penile implant surgery and variables impacting satisfaction of both following surgery will help providers counsel patients and partners appropriately prior to surgical intervention.

Objective: The purpose of this study is to qualitatively and quantitatively investigate patient and partner expectations prior to penile implant surgery and satisfaction after surgery at various intervals.

Method: Eligible subjects consist of adult males between the ages of 18-99 undergoing penile implant surgery for erectile dysfunction by a single urologist at an academic institution. Patients and partners who agree to participate will participate in a series of interviews led by a trained medical student interviewer. Between enrollment and surgery, preoperative interviews will take place individually, either in person or via telephone. The preoperative interview will last approximately 30 minutes. Prior to surgery, patients will complete the following questionnaires: the International Index of Erectile Function (IIEF), the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS), and the Sexual Encounter Profile (SEP3). Partners will complete the version of the EDITS questionnaire designed specifically for partners and the Female Sexual Function Index (FSFI). The postoperative interview will occur about 4.5 months and 1 year following penile implant surgery. Patients will complete the IIEF questionnaire, the EDITS questionnaire, and the Quality of Life and Sexuality with Penile Prosthesis Questionnaire (QoLSPP), and the SEP3. Partners will complete the version of the EDITS questionnaire designed specifically for partners, as well as the FSFI. Grounded theory approach will be used to analyze transcribed interviews. This method develops common themes through the analysis of individual cases, developing codes to apply to successive interviews.

Results: Involvement in this study will last from the time of surgery scheduling to 1-year after penile implant surgery for erectile dysfunction. Due to the duration of this study, data collection is still underway and results are not available.

Conclusion: Data collection is still underway and conclusions have not yet been formulated.

Comparison Between Cotton Test and Tap Test For The Assessment of Coronal Syndesmotic Instability: A Cadaveric Study

Presenter: Victoria Y. Vivtcharenko, BA

Mentor: Cesar de Cesar Netto, MD, PhD

Collaborators: Ivan Giarola, MD; Shuyuan Li, MD, PhD; Fernando S. Martins; Eli L. Schmidt; Alexandre Leme Godoy-Santos, MD, PhD

Introduction:
Detection of subtle syndesmotic instability (SI) is challenging and the dynamic nature of the widely used Cotton test presents inconsistencies in the distraction force magnitude and direction when pulling the fibula away from the tibia while maintaining correct radiographic positioning. The novel Tap test advances a cortical tap through a drilled hole in the fibula with a stable, unidirectional distraction force applied to the tibia. The objective of this cadaveric study was to compare the DTFS widening when using the Cotton and Tap tests as diagnostic tools for coronal plane syndesmotic instability. We hypothesized that the Tap test would perform equally or better than the Cotton test.

Methods:
Tibiofibular Clear Space (TFCS) of 10 cadaveric specimens was measured for: intact, non-stressed; intact, stressed (Tap and Cotton tests); injured, non-stressed; and injured, stressed (Tap and Cotton tests). TFCS values were compared by paired Wilcoxon. Diagnostic performance was assessed using a relative increase of TFCS>2mm when comparing intact stressed and injured conditions. P-values <0.05 were considered significant.

Results:
The intraclass correlation coefficient (ICC) for intraobserver and interobserver reliability was respectively, 0.96 and 0.78, both considering potential bias and interactions. TFCS measurements were similar in intact non-stressed, intact stressed (Cotton and Tap tests) and injured non-stressed conditions, with mean values and 95% Confidence Intervals of: intact non-stressed, 3.5mm (CI, 3.0 - 3.9mm); intact stressed, 3.6mm (3.1 - 4.1mm) (Cotton test) and 4.0mm (3.5 - 4.5mm) (Tap test); injured non-stressed, 3.8mm (3.3 - 4.3mm). TFCS was significantly increased (p<0.0001) in injured and stressed ankles for Cotton and Tap tests, with values of respectively, 6.2mm (.8 - 6.7mm) and 6.1mm (5.7 - 6.6mm). A graphical plot comparing all mean values is presented in Figure 1. Example fluoroscopic Mortise images are presented in Figure 2. The Cotton test had 73.3% sensitivity, 100% specificity, and 86.7% diagnostic accuracy. The Tap test had 70% sensitivity, 90% specificity, and 80% diagnostic accuracy.

Conclusion:
Our cadaveric study demonstrated that the Tap test is comparable to the Cotton test regarding diagnostic accuracy of coronal syndesmotic instability (SI). In our experience of the Cotton test, it is difficult to apply a steady distraction force while maintaining a perfect Mortise view and the test is frequently not reproducible. We recommend the Tap test as a more stable, controlled, and reproducible intraoperative diagnostic test for coronal plane syndesmotic instability.

Figure 1 – Tibiofibular Clear Space (TFCS) Measurements By Ankle Conditions (Intact Non-Stressed, Intact Stressed, Injured Non-Stressed and Injured Stressed)
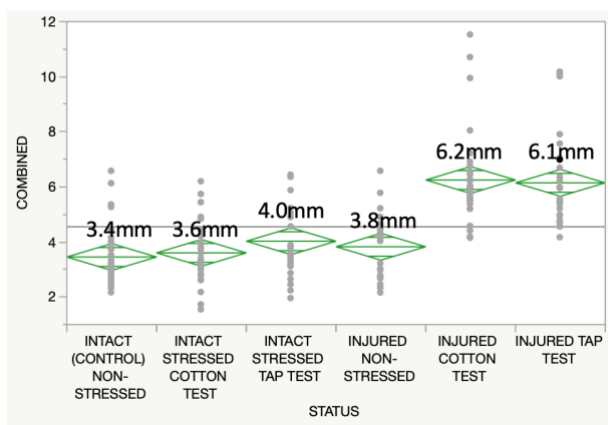

Figure 2 – Example of Sequential Fluoroscopic Mortise Images: (A) Intact Non-Stressed; (B) Intact Stressed Tap Test; (C) Intact Stressed Cotton Test; (D) Injured Non-Stressed; (E) Injured Stressed Tap Test; (F) Injured Stressed Cotton Test

Choriocapillaris Gene Expression Changes in Age and Age-Related Macular Degeneration

Andrew P Voigt, Kelly Mulfaul, Nathaniel K Mullin, Edwin M Stone, Budd A Tucker, Todd E Scheetz, Robert F Mullins

The human choroid is a complex tissue that provides crucial support to the retina. In particular, the choroid contains a rich vascular network that supplies approximately 85% of the oxygen to retinal photoreceptors. Disease affecting this supportive tissue can result in loss of photoreceptor support and subsequent retinal degeneration, such as in the disease age-related macular degeneration. In this study, single-cell RNA sequencing was performed on CD31-expressing endothelial cells isolated from the choroid from 8 human donor eyes. We identified gene expression signatures along the choroidal vascular tree, classifying the transcriptome of human choriocapillaris, arterial, and venous endothelial cells. We found that the choriocapillaris highly and specifically expresses the regulator of cell cycle gene (*RGCC*), a gene that responds to complement activation and induces apoptosis in endothelial cells. In addition, *RGCC* was the most upregulated choriocapillaris gene in a donor diagnosed with AMD. Differentially expressed genes were also identified between infant (<1 year) and adult (>60 year) human donors. The gene encoding the surface gene product *CD34* was elevated in infant choriocapillaris endothelial cells while the adhesion protein *ICAM1* was enriched in adults. These findings were validated with immunohistochemical studies. Collectively, these results provide a characterization of the human choriocapillaris transcriptome, offering potential insight into the mechanisms of choriocapillaris dysfunction with age and in age-related macular degeneration.

Title: Omacetaxine targets Inhibitor of DNA binding proteins in pediatric sarcoma
Presenter: Ellen Voigt
Mentor: David Gordon

Abstract:

The Inhibitor of DNA binding family of proteins (ID1-4) are upregulated in many cancers and not only control cell fate of cancer, but also promote a more aggressive phenotype —increasing metastasis, chemoresistance, and vascularization. The ID proteins work by binding basic helix-loop-helix (bHLH) transcription factors, blocking their binding to DNA and preventing bHLH-directed transcription, resulting in dedifferentiation. Over two decades of studies have shown ID proteins are potential therapeutic targets in cancers, including in sarcomas. Yet efforts to develop a small-molecule drug to target have not resulted in a viable pharmaceutical approach in the clinic. ID proteins have short half-lives of under one hour and are rapidly degraded by the proteasome, thus we hypothesized cancer cells rely on active protein synthesis to keep ID protein levels high. We found that homoharringtonine (HHT; omacetaxine) an FDA approved drug for the treatment of chronic myeloid leukemia (CML) that inhibits protein synthesis by binding to the A-site of the ribosome, reduces levels of ID1-3 protein in sarcoma cell lines. We then targeted the proteasome degradation pathway by treating with SJB3-019A (SJB), an inhibitor of the deubiquitylating enzyme USP1, which also decreases ID1-3 proteins. Here we will detail this promising combinatorial therapeutic approach to target ID proteins *in vivo.*

Postoperative narcotic use in elective colorectal surgery patients does not correlate with preoperative psychiatric medication use

Joyce Wahba, Peige Zhou, Irena Gribovskaja-Rupp

Background

The opioid epidemic has led to an increase in scrutiny of today's prescribing practices, as well as the need to individualize care to minimize risks of addiction. According to the CDC, 18.9% of adults in the United States struggled with mental illness in the past year, and the overlap between mental illness and addiction has long been documented. The effect of mental illness on patients' postoperative narcotic use is poorly understood.

Methods

This study was designed to examine the connection between preoperative psychiatric medication use and acute postoperative (days 0–3) narcotic use. This retrospective chart review examines opioid use after elective colorectal surgeries done at the University of Iowa Hospital and Clinics between 2015–2018. Indications for surgery included inflammatory bowel disease (Crohn's and Ulcerative Colitis), malignant neoplasms, and colorectal deformities. Out of the 592 patients studied, 54.2% were female, and the mean age was 57 ± 15 years old. Approximately 40% (n=236) of the patients had at least one psychiatric diagnosis, and 34% (n=203) were taking at least one psychiatric medication. While depression (22%), anxiety (19%), and history of substance use (14%) were the most common diagnoses, bipolar, somatoform disorders, and personality disorders were also documented. Most of these patients were prescribed either antidepressants or anxiolytics.

Results

Univariate analysis showed that there was an increase in opioid usage between postoperative days 0–3 in patients with more psychiatric diagnoses ($p<0.01$) as well as taking more psychiatric medications ($p<0.01$). However, the multivariate analysis, which controlled for age, sex, smoking status, pre-operative narcotic use, and abdominal pain, showed that the number of psychiatric medications was not in fact significant ($p=0.11$).

Conclusion

When controlled for confounding variables, acute postoperative narcotic use was not correlated with preoperative psychiatric medication use. Even multiple neuropsych medications did not lead to an increase in postoperative narcotic use.

Effect of Distance from and Time to Definitive Care on Traumatic Brain Injury Outcomes in the Setting of a Rural Trauma System

Student: Madi Wahlen, M2G

Mentor: Jim Torner, PhD, Department of Epidemiology

Background and Aims

Traumatic brain injury (TBI) is a major cause of morbidity and mortality in the United States, and the consequences of TBI are especially profound in rural regions, where TBI fatality rates are 23% higher than in metropolitan regions. The time-sensitive nature of the acute management of TBI may be further complicated in rural settings because of the long distances between the scene of injury and a high level trauma facility for many rural patients leading to increased time from injury to definitive care. Connecting trauma patients to high-level trauma care quickly to achieve improved patient outcomes is facilitated by the implementation of coordinated regional trauma systems. In Iowa, a statewide trauma system was implemented in 2001, with the University of Iowa Hospitals and Clinics (UIHC) serving as one of two Level 1 Trauma Centers (L1TCs) in the state. Here we identified risk factors associated with mortality and other outcomes after TBI, and examined the effect of distance to L1TC, time to definitive care, and transfer status on mortality and other outcomes after TBI.

Methods

The study population for this analysis was identified through the UIHC trauma registry and includes 5,911 patients with TBI treated at UIHC from 2008 to 2019. Analyses were stratified based on transfer status, mortality, TBI severity, and head injury pathology. Descriptive and comparative statistics were examined using chi-square and Wilcoxon rank-sum tests. A survival analysis was conducted using Kaplan-Meier survival curves and Cox proportional hazards model.

Results

Risk factors associated with mortality following TBI include age, gender, injury severity, etiology and mechanism of injury, comorbidities and complications, and decreased time to definitive care. Transfer status is associated with overall in-hospital mortality, however there is no difference in survival across time for transfer patients versus directly admitted patients. In-hospital mortality is not associated with distance to L1TC or isolated head injury.

Conclusions and Future Directions

Based on these findings, injury severity is one of the most important risk factors for mortality following TBI. Time to definitive care is more important than distance traveled as a predictor of outcome after TBI. Further research is needed to examine the relationship of transfer and head injury severity on outcome, and to examine the relationship between distance, time and head injury pathology on outcome.

Title: Viewpoints on Healthcare Delivery Science Education Among Practicing Physicians in a Rural State

Presenter: Kristin Weeks
Mentor: Mary Charlton (PhD) and Alan Reed (MD)

Authors: Kristin Weeks, Morgan Swanson, Amanda Manorot (MD), Gabriel Conley, Joseph Nellis (MD, MBA), Mary Charlton (PhD), Alan Reed (MD, MBA)

Introduction

Healthcare Delivery Science Education (HDSE) covers important aspects of the business of medicine, including, operations management, managerial accounting, entrepreneurship, finance, marketing, negotiations, e-health and policy/advocacy. HDSE has not historically been incorporated in formal medical training or continuing medical education (CME). Practicing physicians' viewpoints on HDSE are unknown and need to be elicited, especially in rural states where HDSE could be an important tool for access and management obstacles.

Purpose of the Study

We aim to provide a rich, contextualized understanding of the HDSE experiences and interests of physicians practicing in a rural state through the intensive study of particular cases.

Methods

We interviewed 18 practicing physicians from a rural, Midwestern state over the telephone about their viewpoints on past experiences obtaining HDSE, interest in HDSE, barriers to pursuing HDSE, and interest in an example HDSE certificate program over 4 months in 2019. Participants were recruited through purposive convenience sampling until saturation was achieved.

Results

Qualitative findings suggest physicians had not received didactic HDSE after residency. Some had received informal on-the-job training or attended single subject conferences/lectures. Physicians were interested in HDSE and potentially participating in a sample certificate program, but participant-barriers, such as time and cost, and systemic-barriers, including a lack of programs, had limited HDSE enrollment in the past.

Conclusion

HDSE opportunities are needed while physicians are in training and more HDSE opportunities are needed for practicing physicians that have low cost and time burdens and high specificity to their specialties. Physicians were dissatisfied with their limited HDSE and their lack of skills to advocate for a change in their practices or for their patient populations. The insights related to the culture experienced by this group of practicing physicians informs other researchers of potential cultures in their own study populations and informs generalizable quantitative studies of larger physician populations.

Title: An Unmet Need in Healthcare Leadership: A Survey of Practicing Physicians' Perspectives on Healthcare Delivery Science Education

Presenter: Kristin Weeks
Mentor: Mary Charlton (PhD) and Alan Reed (MD)

Authors: Kristin Weeks, Morgan Swanson, Hayley Hansen, Katherine Merritt (MS), Joseph Nellis (MD, MBA), Mary Charlton (PhD), Alan Reed (MD, MBA)

Introduction

Healthcare delivery science education (HDSE) is the interdisciplinary, integrated study of social science, public health, population health, bio-design thinking, business, law and medicine toward improving the effectiveness and proficiency of patient-centered care. HDSE is increasingly needed by physicians balancing clinical care, practice management, and leadership responsibilities in their daily lives. However, most practicing physicians have received little HDSE in undergraduate through residency training. This quantitative study builds upon a prior qualitative study by presenting numerical data and classifying physicians' viewpoints.

Purpose of the Study

The purpose of this study is to 1) quantify the perception of need for HDSE and interest in HDSE among a diverse sample of physicians, and 2) determine if perspectives on HDSE vary by specialty, rurality and years in practice.

Methods

Using a cross-sectional, single state, mailed questionnaire we surveyed 170 physicians about their perspectives on HDSE and interest in a HDSE program. Descriptive statistics and a multivariable logistic regression are presented.

Results

Among the 70.5% of responding eligible physicians, 75% of physicians had less HDSE than they would like and 90% were interested in obtaining more HDSE. 35% of physicians were interested in joining the described HDSE program. The most prevalent barriers to obtaining HDSE were a lack of time and existing programs. Physician perspectives were similar across specialties, years in practice and rurality.

Conclusion

There is a high unmet need for HDSE among practicing physicians. Diverse and innovative HDSE programming needs to be developed to meet this need. Programming should be developed not only for physicians, but also for undergraduate through residency training programs.

Lower Extremity Gunshot Wounds in a Rural Setting
Student: Kirk Welsh, M2
Mentor and Collaborator: Joseph Buckwalter V, MD, PhD; Ignacio Garcia-Fleury, MD

Introduction
Gunshot wounds (GSWs) put a significant strain on the healthcare system. Popularly portrayed as an urban problem, the per capita rate of GSWs in a primarily rural setting does not substantially differ from the national average. The specific character of these GSWs and related care is not well understood. We believe understanding how and why these injuries occur in a rural setting can provide information about how to reduce the occurrence of such injuries. We are particularly interested in understanding GSWs to the lower extremity and foot and will focus our efforts there.

Purpose
We developed a retrospective, epidemiological database of GSWs to the foot and lower extremity that occurred in a rural, Midwestern population. We hope to identify modifiable factors and trends that can be employed to prevent the occurrence of further GSWs.

Methods
Our population for this study included all adult patients treated at a large, Midwestern level 1 trauma center who suffered GSWs to the lower extremity over the ten-year period from November 2009 to December 2019. We used patient medical records to abstract information from history and physical examinations including mechanism, date, and precise location of injury. We used x-rays and other imaging used in the patient's care to further characterize and classify the injury. We collected data on demographics of the patients involved to include: sex, race, ethnicity, and age.

Results
Our sample size for this study included 71 participants with 2 fatalities (3%). The population suffering GSWs to the lower extremity was predominantly male (90%), white (56%), and had a mean/median age of 31/27 years of age. Substance use was a common factor including illicit drugs (41%) and alcohol (35%). The most common mechanisms of injury were assault (44%) and unintentional injury (41%). Fractures occurred in a large percentage of cases (62%), but complications requiring re-operation were rare (11%). Handguns were the most common weapon type involved in these injuries (38%) with shotguns (11%) and rifles (8%) also making up a portion. A large number of the GSWs that occurred due to assault had an unknown weapon type with an unknown firearm being involved in 42% of all injuries. Injuries occurred with a mild temporal association with the November hunting season with 34% of all cases occurring in the months of October-December.

Conclusions
Firearm injuries to the foot and lower extremity in a rural population are primarily due to assault or unintentional injury and are typically not fatal. Firearm injuries to the foot and lower extremity in a rural population demonstrate mild seasonal variation with the local hunting season. We believe this population could benefit from interventions aimed at improving firearm safety through education and training.

TITLE: Application of Mucous Fistula Stool Refeeding in Surgical Pediatric Patients following Bowel Resection

Medical Student: Cody West

Mentor: Dr. Riad Rahhal

Institution: The University of Iowa Roy J and Lucille A Carver College of Medicine, Iowa City, IA, USA

ABSTRACT

Background: Pediatric patients, especially neonates, can develop severe abdominal pathology that requires surgical resection with creation of a small bowel ostomy (enterostomy) and mucous fistula (MF). Refeeding of stool output from the small bowel ostomy into the distal MF may help recruit the distal remaining bowel, possibly assisting in improved intestinal absorption with advancement of enteral nutrition, reduced dependence of venous nutrition and reduced liver disease frequency and severity.

Objective: This study evaluated the impact of stool refeeding into the distal MF following bowel resection in children at a tertiary medical center.

Design/Methods: This was a retrospective cohort study of patients who had ostomy creation and takedown at the University of Iowa in those < 5 years of age at the time of initial surgery between January 2010 – February 2020.

Results: In total, 47 patients were identified including 29 patients in the stool refeeding group and 18 in the non-refeeding (control) group. There were no differences in baseline characteristics between groups (gestational age, birthweight, surgery indications, age and weight at ostomy creation, ostomy type) except for more patients in MF feeding group having the entire colon preserved (79% vs 50%, p=0.04).

Median time from stoma creation to start of enteral feeding and number of days of venous nutritional support were similar between groups. The control group had more patients without any enteral nutrition (0 vs 33%, p=0.002) and more deaths (3% vs 33%, p=0.009) during their hospital stay than the MF feeding group. All patients were admitted to an intensive care unit (ICU), neonatal or pediatric. When excluding patients that died, median ICU days and total hospital days were similar between groups. Difference in frequency of cholestasis (defined as direct bilirubin ≥ 1 mg/dL) was not statistically significant (56% in MF refeeding group vs 75% in control group, p=0.2). No complications were encountered that were related to MF refeeding.

Conclusion(s): MF refeeding is safe and shows potential to reduce the incidence of cholestasis and subsequent liver damage.

False Positive Electroretinograms from the RETeval Device

Student: Jennifer Wu; Mentors: Arlene Drack, MD—Director, Electrophysiology, Department of Ophthalmology and Visual Sciences; Wanda Pfeifer, O(C)C, COMT, Coordinator, Electrophysiology, Department of Ophthalmology and Visual Sciences

Background: Electroretinograms (ERGs) are the gold standard for diagnosis of congenital and juvenile retinal dystrophies, major causes of pediatric blindness. However, the ERG is challenging to perform in children. Although UIHC's Pediatric Ophthalmology staff have a pediatric-friendly method of getting awake ERGs with the Diagnosys, many institutions have adopted a new ERG device called the RETeval. While the Diagnosys requires a separate room and utilizes corneal fiber eye electrodes, the RETeval is easily portable and utilizes more comfortable skin electrodes. However, RETeval ERG waveforms have lower amplitudes. This complicates interpretation, particularly when diagnosing retinal dystrophies that present with flatter waveforms. An infant was recently referred to the UIHC based on RETeval results with a diagnosis of "blinding retinal degeneration", only to be a false positive.

Purpose: We predict that even some normal infants will have a non-recordable RETeval ERG, and that overall RETeval amplitudes will be lower than Diagnosys amplitudes. We want to explore differences between Diagnosys and RETeval ERGs, see if electrode type affects amplitudes, and determine potential causes of misinterpretation.

Methods: We conducted a retrospective chart review of 5 pediatric patients (4M, 1F) referred for possible retinal dystrophies who had both RETeval and Diagnosys ERGs. Patient age averaged 3 years and 9 months (range 3 months to 11 years and 9 months). We then collected RETeval and Diagnosys ERGs on 4 normal subjects (4F, ages 22 to 52) to find conversion factors for waveform amplitude and latency under the following conditions: 20 min dark adaptation (DA) dim flash (0.01 cd s m^{-2} [rod response]), 20 min DA bright flash (3.0 cd s m^{-2} [combined rod and cone response]), light adaption bright flash (3.0 cd s m^{-2} [primarily cone response]), and 30 Hz flicker test (pure cone response). We calculated conversion factors by dividing a- and b wave amplitudes and latency times obtained with Diagnosys by the values obtained with RETeval. To further explore causes of waveform differences, we collected Diagnosys ERGs on 5 normal subjects (female, ages 22 to 52) with both corneal and skin electrodes, and calculated additional conversion factors by dividing corneal electrode values by skin electrode values.

Results: *Diagnosys vs. RETeval*: Latency differences were insignificant. Amplitudes were significantly larger in Diagnosys than RETeval (P<0.05) in all conditions except DA 3.0 (a wave) (P=0.07). Mean amplitudes ± SE (μV) for each condition with Diagnosys data first and RETeval data second were: 310.6 ± 74.4 vs 45.7 ±7.6 (DA 0.01 b wave), 360.6 ± 68.1 vs 96.6 ± 7.2 (DA 3.0 b wave), -182.4 ± 54.8 vs -33.4 ± 2.9 (DA 3.0 a wave), 158.8 ± 28.3 vs 29.1 ±3.9 (LA 3.0 b wave), -33.9 ± 6.5 vs -5.8 ± 0.6 (LA 3.0 a wave), 119.8 ± 21.6 vs 23.0 ± 3.6 (Flicker peak). **The amplitude conversion factors for RETeval to Diagnosys range from 4.2 to 7.1.** *Corneal vs skin electrodes:* Latency differences were insignificant. Corneal electrode amplitudes were significantly larger. Mean amplitudes ± SE (μV) in each condition with corneal electrode data first and skin electrode data second were: 287.2 ± 62.2 vs 90.2 ± 11.6 (DA 0.01 b wave), 376.6 ± 59.3 vs 131.2 ± 31.7 (DA 3.0 b wave), -177.3 ± 42.8 vs -57.3 ± 7.0 (DA 3.0 a wave), 157.0 ± 23.0 vs 56.5 ±12.3 (LA 3.0 b wave), -32.4 ± 6.5 vs -12.0 ± 2.3 (LA 3.0 a wave), 115.9 ± 17.1 vs 46.1 ± 7.8 (Flicker peak). **The amplitude conversion factors for skin electrodes to corneal electrodes range from 2.7 to 3.3.** Of patients who had both RETeval and Diagnosys ERGs, two had retinal dystrophies, one had a chromosomal anomaly but normal retina, and two were normal children. Both patients with normal retinas had low RETeval amplitudes.

Conclusions: Amplitude data were lower in RETeval than Diagnosys ERGs by 4.2 to 7.1-fold. Of particular interest is the largest conversion factor of 7.1, obtained in DA dim flash. This waveform is the most difficult to obtain in both devices, often giving borderline low amplitudes even in normal children. We saw this in both normal retina cases. Clinicians should be wary of RETeval ERGs with supposedly non-recordable DA dim flash waveforms, but recordable waveforms in all other conditions. Due to lower amplitudes in RETeval, DA dim flash waveforms can appear to show abnormalities and increase false positives. Difficulty getting children to cooperate can lead to even flatter waveforms. The RETeval markets itself as ideal for obtaining child ERGs due to its use of skin electrodes. However, the 2.7 to 3.3-fold amplitude difference between skin and corneal electrode ERGs suggests that usage of skin electrodes contributes 46% (DA 0.01) to 78% (DA 3.0) of amplitude reduction for RETeval. Its main selling point- more comfortable electrodes- actually limits its usefulness. Values obtained with RETeval should be converted and compared with standard norms before making a diagnosis of retinal dystrophy in an infant.

Title:

Diagnostic Utility of Noncontrast Three-Dimensional Steady-State Free-Precession Magnetic Resonance Angiography compared to Conventional Contrast Magnetic Resonance Angiography in Pediatric and Adult Patients for Aortic and Pulmonary Artery Dimensions

Presenting Author:

Anthony Zhang

Presenting author's email address:

anthony-zhang@uiowa.edu

Co-authors:

Ravi Ashwath, Jennifer Maldonado, Bijoy Thattaliyath, Prashant Nagpal, Sarv Priya, Bridget Zimmerman Mahi Ashwath

Abstract:

Background: Contrast magnetic resonance angiography (cMRA) is an important diagnostic modality for aortic and pulmonary artery imaging in pediatric and adult patients. Currently, gadolinium-based contrast agents are widely used, but we have poor understanding of the long-term effects of gadolinium deposition in long term monitoring that requires serial imaging. We compare three-dimensional steady state free precession (3D–SSFP) with respiratory navigation and ECG-gating against gadolinium cMRA to evaluate its ability to accurately assess aortic and pulmonary artery dimensions as a potential alternative.

Methods: 156 patients were identified who had both 3D-SSFP and gadolinium cMRA scans as part of their routine cardiac MRI studies. Five physicians took aortic and pulmonary artery measurements at 5 locations for both types of scans. Accuracy of measurements from 3D-SSFP scans was examined, with cMRA as gold standard, using concordance correlation coefficient (CCC) to measure agreement with 95% tolerance limits. Bland-Altman plots were constructed to show the distribution of the measurement differences.

Results: Agreement was best in the aortic sinus of Valsalva and mid ascending aorta with CCC of 0.980 and 0.984, with difference between formats within 0.3 cm with 95% probability (Table 1). The main pulmonary artery had the largest difference, with 95% probability of a difference between (-0.503, 0.391) cm between sequences, likely due to non-standardized locations of measurement and limited image quality due to the contrast being timed for best visualization of the aorta.

Conclusions: 3D-SSFP MRA with ECG-gating and respiratory navigation should be considered in place of contrast MRA for patients requiring serial imaging. In 4 of the 5 measured locations we can confirm with 95% confidence that the measurements are equally represented. Additionally, 3D-SSFP offers several other benefits including removing any potential side effects from gadolinium exposure and IV placement, superior edge definition, and easier image acquisition without a breath hold.

Validation of 3D volume-based treated tumor response assessment over standard RECIST v1.1

Student: Robert Zhu, M1
Mentor: Yusung Kim, Ph.D., DABR

Non-small-cell lung cancer (NSCLC) approximates 80-85% of lung cancer diagnoses and is the most prevalent cause of cancer-related deaths throughout the world. As such, the goal of diagnostic and prognostic measures for not just NSCLC, but all types of cancer should have the highest possible accuracy and fidelity. Currently, one of the most widely used tools for tumor evaluation and response is the "Response Evaluation Criteria in Solid Tumors" (RECIST). We believe that while the standard RECIST v1.1 is a useful tool for tumor evaluation, it is limited by its unidimensional and bidimensional criteria. In our study, we propose the use of a highly accurate and interpretable framework based on the success of deep convolutional neural networks (CNN) for tumor segmentation which can provide accurate volumes of the tumor being examined as an alternative to standard RECIST v1.1. We collected 96 NSCLC patient data sets and performed a retrospective data analysis on standard RECIST v1.1 and 3-D volumetric measurements taken from PET/CT scans. For this data set, we determined the tumor response for each of the 96 cases. Using RECIST classification, tumors are categorized into one of four categories at first follow-up to treatment: Complete Response (CR), Partial Response (PR), Stable Disease (SD), and Progressive Disease (PD). Based on the literature, we grouped CR, PR, and SD together into a new category that we call Disease Control (DC). We assessed each patient based on their overall survival (OS) and used this information to generate Kaplan-Meier curves. Based on our results, we did not find a statistically significant improvement in predictive power when comparing our CNN volumetric analysis to standard RECIST v1.1. We believe that the reason for this is due to several potentially confounding variables including but not limited to staging at diagnosis, age at diagnosis, and presence of brain metastases at time of treatment. While the results of our Kaplan-Meier curves were not as expected, we believe that there is still immense potential for our research. Kaplan-Meier curves alone cannot account for other variables that would potentially influence overall survival. As a result, the next step that we are taking is to generate Cox regression models and use these models to derive ROC curves.