UTHealth
The University of Texas
Health Science Center at Houston

McGovern
Medical School

2019 SUMMER RESEARCH PROGRAM
STUDENT ABSTRACTS

This page left blank

Contents

This page left blank

Preface

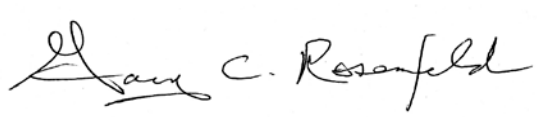
The University of Texas Medical School at Houston (UTMSH) Summer Research Program provides intensive, hands-on laboratory research training for MS-1 medical students and undergraduate college students under the direct supervision of experienced faculty researchers and educators. These faculty members' enthusiasm for scientific discovery and commitment to teaching is vital for a successful training program. It is these dedicated scientists who organize the research projects to be conducted by the students.

The trainee's role in the laboratory is to participate to the fullest extent of her/his ability in the research project being performed. This involves carrying out the technical aspects of experimental analysis, interpreting data and summarizing results. The results are presented as an abstract and are written in the trainees' own words that convey an impressive degree of understanding of the complex projects in which they were involved.

To date, more than 1,900 medical, college, and international medical students have gained research experience through the UTMSH Summer Research Program. Past trainees have advanced to pursue research careers in the biomedical sciences, as well as gain an appreciation of the relationship between basic and clinical research and clinical practice.

UTMSH student research training is supported by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and/or by financial support from the Dean and the departments and faculty of the medical school and School of Dentistry.

Biomedical science education remains a vital and integral part of our nation's interests. The UTMSH Summer Research Program, and the dedication of our faculty and administration exemplify the institution's commitment to training and educating the future leaders in our biomedical scientific communities.



Gary C. Rosenfeld, Ph.D.
Director, Summer Research Program
Associate Dean for Educational Programs

This page left blank

Acknowledgements

This publication marks the completion of the twenty-sixth year of The University of Texas Medical School at Houston's (UTMSH) Summer Research Program. The longevity and success of the program are rooted in the overwhelming support received from the deans, faculty, staff and students of the medical school.

Indicative of this support is the administrative assistance and financial support for the Program's college and medical students provided by UTMSH. Sincere appreciation is expressed to Dean Giuseppe Colasurdo M.D. and Patricia M. Butler, M.D., Vice Dean, Office of Educational Programs who continue to ensure the yearly success of the Summer Research Program.

Major financial assistance for medical students has also been provided through a short term research grant by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK; 5 T32 DK007676).

Negotiated cooperative agreements with several international medical schools have been set up to offer tailored research programs at UTMSH for selected foreign medical students who interact fully with the other students in the Summer Research Program.

The success of the Summer Research Program depends primarily on the faculty who volunteer to mentor the trainees. These dedicated educators organize and guide the research projects that includes for each student data analysis, preparation of an abstract and public presentation of results. Our sincere appreciation to all faculty mentors.

This page left blank

Lab Research Ownership

Publication and/or Disclosure

Each student participating in this program is required to read, agree to, and sign this disclosure form. The original signed copy is on file in the Summer Research Program office; the student and their faculty mentors are each furnished with a copy.

"In reference to the laboratory research you will perform this coming summer through The University of Texas Medical School at Houston's Summer Research Program, you are required to comply with the standard restrictions regarding participation in the Summer Research Program:

"All of your laboratory research is *CONFIDENTIAL* and although your abstract will be available through our website, you cannot independently disclose or publish any research findings or data in any form (including at meetings or conferences) without the express prior written approval of The University of Texas Medical School at Houston. If you wish to submit your abstract to any third party, you must first contact your faculty mentor no less than three (3) weeks prior to any deadlines in order to obtain the necessary written approvals.

"Because your research was generated from ideas and funds that originated with your faculty mentor and The University of Texas Medical School at Houston, ownership of any data generated by you during the Summer Research Program belongs to The University of Texas Medical School at Houston or the Principle Investigator (PI)."

This page left blank

UTHealth The University of Texas Health Science Center at Houston | McGovern Medical School

Medical Students

Last Name	First Name	Page #
Anderson	Brady	15
Anding	Caroline	16
Arani	Naszrin	18
Aziz	Moez	19
Bagott	Rickard	21
Banner	Katherine	22
Biaggi-Ondina	Andrea	23
Black	Christopher	24
Boyle	Mariaelena	25
Brown	Sydnee	27
Bundrant	Bethany	29
Bur	Delfina	30
Ceron	Santiago	32
Chatterjee	Treena	33
Chinea	Luis	34
Cigarroa	Natasha	35
Clynes	James	36
Dhanji	Sohail	38
Dhother	Karanvir	40
Drake	Madeline	42
Due	Bradley	43
Fallah	Kasra	44
Fan	James	46
Flores	Alan	47
Garcia	Victor	48
George	Timothy	49
Ghosh	Saurendro	50
Goodman	Colin	52
Harvey	Hannah	53
Hinojosa	Ezekiel	54
Holmes	Emma	55
Hunt	Charlotte	56
Immadi	Amrutha	57
Johnson	Nicholas	58

Last Name	First Name	Page #
Kamat	Pranali	60
Kennady	Emmett (Bard)	62
Khansari	Neik	64
Knight	Brandon	65
Li	Jesse	67
Luthra	Komal	68
Lynch	Morgan	69
Masson	Manon	71
Masterson	Wylie	73
Neela	Niharika	74
Ngo	Daniel	75
Noorbaksh	Ali	76
Ortiz	Hannah	78
Paladugu	Sreelekha	80
Phan	Luan	82
Polamraju	Vinathi	83
Posada	Luciano	85
Pothiawala	Azim	87
Rasool	Ayeshum	88
Rieger	William	89
Rojas	Ibis	90
Rondon	Alexis	91
Sen	Shayak	92
Shei	Jasperina	93
Taye	Telavive	94
Tejani	Mubeen	95
Vehawn	Jeffrey	96
Wang	Andrew	98
Wang	Jevons	99
Watson	Jacob	100
West	Julianna	102
Wilken	Lindsay	103
Willenbring	Taylor	104
Yan	Jun	105

UTHealth The University of Texas Health Science Center at Houston | McGovern Medical School

Undergraduate Students

Last Name	First Name	Page #

Last Name	First Name	Page #

UTHealth | McGovern Medical School
The University of Texas Health Science Center at Houston

International Medical Students

Last Name	First Name	Page #

UTHealth | McGovern Medical School
The University of Texas Health Science Center at Houston

Medical Students

ABSTRACT

Predicting Velopharyngeal Insufficiency in Patients with Cleft Palate

BRADY J. ANDERSON *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Matthew R. Greives, MD, FACS, Department of Pediatric Plastic Surgery
Supported by: Kasra N. Fallah, BSA; Joseph Moffitt, BS; Phuong Nguyen, MD; John F. Teichgraeber, MD; Kim-Loan Luu, SLP; Courtney Stout, SLP; Phuong D. Nguyen, MD; Matthew R. Greives, MD.
Key Words: Palatoplasty, Velopharyngeal Insufficiency, Risk Factors

Background: Velopharyngeal insufficiency (VPI) after primary palatoplasty has been associated with various patient and surgical factors, including cleft size, genetic conditions and fistula formation. Despite this information, a predictive risk stratification tool has not been developed for factors associated with VPI development. Although VPI affects the speech of up to 50% of patients undergoing primary palatoplasty, diagnosis requires long-term follow-up after speech development. We reviewed over 15 years of primary cleft repairs to examine predictive factors for VPI.

Methods: A retrospective review of patients who underwent primary palatoplasty from 1999 to 2014 was performed. Inclusion required follow-up past age 5 and speech production. Patient demographics, Veau class, medical history, surgical details, and follow-up information were collected. The primary outcome was VPI, defined as revision palatoplasty or recommendation for surgery by a speech-language pathologist. Genetic diagnosis was defined as positive genetic testing for a craniofacial syndrome. Univariate analysis was performed, and variables with a $p<0.20$ were included in a multivariate regression analysis.

Results: Of 274 patients included, 158 (57%) were male. Median age at primary repair was 1 year (0.9, 1.1) with a median age of 8.1 at last follow-up. One hundred and four (38%) patients developed VPI at a median age of 4.9 years (3.8, 6.5). 11% of Black non-Hispanic patients developed VPI, compared to 39% of Hispanic patients and 45% of white non-Hispanic patients ($p<0.05$). VPI was 65% in patients who developed posterior fistulae (Pittsburgh 1-4) compared to 13% in those without ($p<0.01$). VPI was lower following Furlow (7%, n=14) than straight-line repairs (40%, n=260; $p<0.05$). VPI in patients with Pierre-Robin was higher (55%, n=38) than those without (35%, n=236; $p<0.05$). Following a bidirectional stepwise selection for a linear model, factors remaining associated with VPI were African-American race (OR 0.18, 0.04-0.66), posterior fistula (OR 12.2, 6.6-23.6) and genetic diagnoses (OR 3.2, 1.2-9.3). There were no differences associated with demographic factors, birth complications, or cardiac issues.

Conclusions: VPI following palatoplasty is a known complication. Development of a posterior palatal fistula was associated with increased odds of revision surgery, likely due to persistent nasal regurgitation refractory to speech therapy. While limited in number, lower rates of VPI among patients receiving Furlow palatoplasty are promising for improved outcomes, warranting further investigation into follow-up and implementation rates. Lower rates of VPI in African-American patients and higher rates in patients with a genetic diagnosis may suggest a genetic component.

ABSTRACT

Preoperative Opioids Associated with Increased Postoperative Opioid Use in Pediatric Appendicitis

CAROLINE ANDING *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Mary T. Austin, MD, MPH, Department of Pediatric Surgery
Supported by: Mary T. Austin, MD, MPH, Department of Pediatric Surgery; McGovern Medical School Office of the Death
Key Words: Postoperative, Opioids, Pediatric, Appendicitis

Introduction: Despite an increasing awareness of the opioid epidemic, there are currently no guidelines for optimizing perioperative pain management while minimizing opioid use in pediatric appendicitis. We aimed to evaluate factors that predict postoperative opioid requirement in pediatric appendicitis patients.

Methods: We performed a retrospective review of all pediatric (age<18) patients who underwent laparoscopic appendectomy for acute appendicitis between January 1, 2018 and April 30, 2019 at a single center. Patients who underwent open or interval appendectomy were excluded. To differentiate opioids prescribed by anesthesiology versus surgery, intraoperative medications were defined as any medication administered between 1 hour before incision and 2 hours after surgery stop time. Regional blocks were performed before or after surgery and were not included in case duration. The primary outcome was postoperative opioid use measured in morphine milliequivalents per kilogram (MME/kg) within 2-24 hours after surgery. Factors thought to influence postoperative opioid use were chosen a priori based on prior literature and clinical knowledge and included patient age, weight, diagnosis (simple vs complicated appendicitis), preoperative opioids and non-opioids, regional block, local anesthetic, and intraoperative opioids and non-opioids. Multiple variable linear regression was performed to evaluate factors independently associated with postoperative opioid use.

Results: Of 546 patients, 28% received postoperative opioids (n=153). Patients who did and did not receive postoperative opioids were similar by age, gender, weight, race/ethnicity, and insurance status. Patients who received postoperative opioids had a longer median symptom duration prior to admission (48 vs 24 hours, p<0.001), were more likely to have complicated appendicitis (55% vs 21%, p<0.001), and had a longer mean case duration (47 vs 40 minutes, p<0.001). Patients who received postoperative opioids were more likely to have received preoperative morphine (53% vs 31%, p<0.001) and acetaminophen (58% vs 38%, p<0.001). Regional and/or local anesthesia utilization was similar between groups. Nearly all patients (99%) received intraoperative opioids (n=541). On multiple variable linear regression, every 1 MME/kg a patient received preoperatively was independently associated with receiving 0.3 additional MME/kg postoperatively (95% CI 0.12-0.45).

Conclusion: Preoperative opioid administration was independently associated with increased postoperative opioid use in pediatric appendicitis. Further research is needed to determine

whether this association is due to increased pain acuity in specific patients or if opioid utilization is self-perpetuating.

ABSTRACT

Anti-Wolbachia Surface Protein IgG as an early marker for cancer-related lymphedema

NASZRIN ARANI *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Melissa B. Aldrich, MBA, PhD, Center for Molecular Imagine, The Brown Institute for Molecular Medicine
Supported by: NIH R01CA203487
Key Words: Lymphedema, cancer, autoimmunity, Wolbachia

Background: According to the Lymphatic Education and Research Network, up to 10 million Americans suffer from lymphedema (LE), a disease characterized by limb and/or trunk swelling, extremity pain, skin fibrosis, cellulitis, and depression. Mutations in genes coding for components of the lymphatic system account for a small portion of this population; interestingly, most U.S. LE patients encounter the disease after cancer treatment. While the etiology of LE was previously unknown, recent literature has suggested that the pathogenesis of LE has autoimmune characteristics. In particular, a surface protein originating from bacterium *Wolbachia pipentis*—a common resident in arthropods that is widely implicated in lymphatic filariasis—has been linked to LE pathogenesis, with serum antibodies against Wolbachia Surface Protein (WSP) spiking in concentration shortly before LE onset. It is theorized that molecular mimicry between WSP and lymphatic tissue, and type II hypersensitivity induced by cancer treatment, is responsible for LE.

Methods: Breast cancer patients at M.D. Anderson Cancer Center were imaged before axillary lymph node dissection, after dissection but before radiation treatment, and at 6, 12, and 24 months after radiation treatment using near-infrared fluorescence lymphatic imaging (NIRFLI). Serum samples from these patients were tested for anti-Wolbachia SP antibodies using enzyme-linked immunofluorescence assay (ELISA) and positive samples were further analyzed using a Western blot.

Results: NIRFLI shows an exudative leakage from lymphatic vessels in LE patients, which is consistent with an inflammatory disease state. On Western blot, all patients diagnosed with LE showed cross-reactivity with WSP.

Conclusions: LE patients exhibited increased levels of anti-WSP IgG during disease onset compared to the control, suggesting that LE may have autoimmune characteristics. This study is limited by the fact that almost all 50 patients enrolled in the study thus far have developed LE; this required normal human serum from a patient without breast cancer to be used as a negative control. Future study will include a larger sample size and more negative controls, yielding more statistical power.

ABSTRACT

Stent Healing in Cancer Patients with Cardiovascular Comorbidities

MOEZ K. AZIZ *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Donald A. Molony, MD, Internal Medicine at UTHealth McGovern Medical School and Cezar A. Iliescu, MD, FACC, FSCAI, Cardiology at MD Anderson Cancer Center
Supported by: Donald A. Molony, MD, and Cezar A. Iliescu, MD, FACC, FSCAI
Key Words: Oncocardiology, cardiac stent placement, cancer patients, heart disease

Background: The growing patient population with cancer and cardiovascular comorbidities has generally been excluded from large cardiovascular randomized clinical trials and is therefore understudied. A minimum of 6 months of dual anti-platelet therapy (DAPT) (aspirin plus a P2Y12 inhibitor) is recommended post stent placement in acute coronary syndrome (ACS) patients; however, cancer patients often require earlier DAPT discontinuation to undergo cancer treatment. Early DAPT interruption increases risk of stent thrombosis, while prolonged DAPT risks delay of cancer care based on perceived increased bleeding risk. Optical coherence tomography (OCT) is an intracoronary imaging method that can help assess stent healing to help determine when DAPT may be safely discontinued in cancer patients. Safe and early DAPT discontinuation can expedite cancer care without theoretically increasing cardiovascular morbidity and mortality, thereby potentially improving overall survivorship.
Hypothesis: Delayed stent healing based on OCT is present in cancer patients who undergo PCI with modern DES and reflects lower survivorship in this population.
Experimental Design: Cancer patients who underwent PCI with stent placement and subsequent OCT at The University of Texas MD Anderson Cancer Center between 11/2009 and 11/2018 were retrospectively studied with baseline characteristics obtained from chart review. Unknown stent brand, poor imaging quality, undocumented stent placement date, and multiple stent brands were criteria for exclusion. Eight outcomes validated by existing literature were used to quantify stent healing: 2 major adverse cardiovascular events (MACE) (death and ACS), 3 stent parameters (neointimal hyperplasia heterogeneity, in-stent restenosis, and stent thrombosis), and 3 strut parameters (strut coverage, apposition, and expansion). Statistical analysis included Kaplan-Meier survival curves, Cox regression, and exact binomial tests to compare to literature values of stent healing in non-cancer patients stratified by stent brands.
Results: A total of 122 cancer patients underwent PCI with stent placement and subsequent OCT; 37 patients were excluded. The 86 patients remaining had 127 stents and 21,000 struts analyzed. While this population had higher MACE driven by cancer-related death when compared to literature values for patients with purely cardiovascular pathologies for Xience-brand stents (n = 30) (23.81%/year vs. 4.9%/year incidence, $p < 0.001$), stent and strut parameters did not reflect this survivorship difference and were generally similar to literature values regardless of stent brand. Cancer stage was the only baseline characteristic associated with overall survival with a hazard ratio of 3.187 (95% confidence interval: (1.211, 8.385)).
Conclusion: Stent healing is not delayed in the studied cancer population with contemporary DES. Shorter courses of DAPT can be offered to cancer patients requiring oncologic therapies,

as cancer mortality is driving the decreased survival rather than stent healing. Recent cardiovascular revascularization or active DAPT should not delay timely cancer therapies.

ABSTRACT

Meniscal Transplant Post-Surgical Imaging and Follow-Up

RICKARD BAGOTT *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Pritish Bawa, MD, Department of Diagnostic and Interventional Imaging
Supported by: Pritish Bawa, MD, Department of Diagnostic and interventional Imaging
Key Words: Knee, Meniscus, Meniscal Transplant

Meniscal tears are the most common type of knee injury with an incidence of 61 per 100,000 people.[1] The gold standard treatment of meniscal injuries has long been meniscectomy, the long-term outcomes of which is well-documented and demonstrate a high incidence of osteoarthritic degeneration and decline in function.[2] Meniscal allograft transplantation is an increasingly popular procedure to reduce symptoms and improve function in young, active patients who have previously undergone meniscectomy. Due to its relatively recent use as a standard therapy, limited research has been performed on patient outcomes. In this study, the efficacy of meniscal allograft transplantation was assessed using patient self-reported outcomes in knee symptomatology and functionality pre- and post-transplantation. Fifty-two patients who underwent meniscal allograft transplantation at Memorial Hermann Hospital were examined via the Allscripts electronic medical record and Picture Archiving and Communications System (PACS). Symptoms and functionality were reported via a standardized survey and averaged into a symptom (S) score and function (F) score, both ranging from 1-10 (higher number correlating with greater severity of symptoms and dysfunction). Paired t-test was used to evaluate pre- and post-transplant scores. Comparison of score change between two subgroups was evaluated by two-sample t-test. Statistically significant decreases in both S score and F score were observed between pre-transplant and post-transplant patient populations, indicating improved symptoms and functionality ($p<0.001$ and $p=0.031$, respectively). A statistically significant difference in F score change (pre − post) was found when comparing patients who received a meniscal transplant within three years of meniscectomy versus those who waited longer ($p=0.042$). No statistically significant differences in S and F score changes were observed in regard to patient sex, medial versus lateral transplant, associated ACL tear, associated adjacent meniscus tear, or type of meniscectomy performed. Meniscal allograft transplantation appears to improve subjective patient assessments of knee symptoms and functionality. This improvement seems to be independent of patient sex, presence of ACL tear or adjacent meniscus tear at time of injury, or medial versus lateral transplantation.

REFERENCES

1. Elattar M, Dhollander A, Verdonk R,Almqvist AF, Verdonk P. Twenty-Six Years of Meniscal Allograft Transplantation: Is It Still Experimental? A Meta-Analysis of 44 Trials. Knee Surgery, Sports Traumatology, Arthroscopy 2010;19(2):147–157.
2. Roos, H, Lauren M, Adalberth T, Roos EM, Jonsson K, Lohmander LS. Knee Osteoarthritis after Meniscectomy: Prevalence of Radiographic Changes after Twenty-One Years, Compared with Matched Controls. Arthritis & Rheumatism 1998;41(4):687–693.

ABSTRACT

Effects of Frequently Prescribed Diabetes Drugs on Normoglycemic Osteoblast Growth and Survival

KATHERINE A. BANNER *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Catherine G. Ambrose, PhD, Department of Orthopaedic Surgery
Supported by: Catherine G. Ambrose, PhD, Department of Orthopaedic Surgery
Key Words: In-Vitro; Diabetes; Osteogenesis; Osteoblast; Pharmacotherapy

Purpose: Previous studies have suggested differing effects regarding frequently prescribed diabetes drugs and osteogenesis. Any detrimental effects caused by commonly prescribed treatments could exacerbate the consequences already resulting from poor bone quality in T2DM. SGLT-2 inhibitors, like canagliflozin, have been shown to negatively affect osteogenesis, while pioglitazone (TZD) has been shown to dose-dependently increase cell viability in normoglycemic cells. Metformin, the first-line pharmacotherapy for T2DM, and glimepiride (sulfonylurea), may also promote osteogenesis. Here we aimed to investigate the *in-vitro* effects of pioglitazone, canagliflozin, glimepiride and metformin, alone and in combination, on normoglycemic osteoblasts cultured in normal and high glucose conditions.
Methods: Primary osteoblasts were cultured through the trabecular bone explant model using discarded bone samples collected from primary total hip arthroplasties performed on three patients, through an IRB-approved protocol. Subjects were chosen randomly, and investigators were blinded to patient demographics with the exception of sex, age, and HbA1C. Osteoblasts were exposed to canagliflozin, pioglitazone, glimepiride, metformin, or each of the first three drugs in combination with metformin for 48h in either normal or high glucose conditions. Cell viability was tested via a resazurin assay, and alkaline phosphatase (ALP) and total protein levels were measured.
Results: In normal glucose conditions, canagliflozin decreased osteoblast viability as the concentration increased, but none of the changes were significant. However, combination with metformin significantly increased viability ($p=0.003$). The effect of pioglitazone significantly increased osteoblast viability ($p=0.002$) at the 2 μM concentration. 8 μM metformin significantly increased osteoblast viability ($p=0.042$) as well. There was no significant data on the effect of glimepiride alone on cell viability, but combination with metformin increased cell viability ($p<0.001$). With the exclusion of canagliflozin, culturing in high glucose media resulted in a significant decrease in cell viability compared to the normal glucose media ($p<0.001$).
Conclusions: This project provides *in-vitro* data regarding the effects of frequently prescribed diabetes drugs on osteoblasts, as well as *in-vitro* data regarding the effects of some of these drugs in combination with metformin. These results suggest that commonly prescribed T2DM drugs have significant effects on osteoblast viability. The data suggests that pioglitazone or metformin, or metformin in combination with canagliflozin or glimepiride, may limit the detrimental effect that T2DM has on bone.

ABSTRACT

Antibiotic usage in gunshot wounds to the face

ANDREA BIAGGI-ONDINA *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: David J. Wainwright, MD, Department of Plastic Surgery
Supported by: David J. Wainwright, MD, Paul J. Deramo, MD, Department of Plastic Surgery
Key Words: GSW, infection, antibiotic

Purpose: Gunshot wounds (GSW) to the face are at particular risk of infection due to contamination from the projectile, the degree and extent of tissue injury, and the often-observed violation of oral and sinus cavities. Because of this increased risk, most studies reporting the management of gunshot injuries to the face recommend broad-spectrum antibiotics; however, there are no detailed reports on clinical experience with specific antibiotics, their timing or duration. The use of postoperative antibiotics is currently determined by the surgeon and is not supported by evidence. This study aims to characterize antibiotic usage in the setting of a gunshot wound to the face.

Methods: A retrospective chart review of GSW to the face from January 1, 2014–Decemebr 31, 2016 was performed using the UT Health at Houston Trauma Database. Inclusion criteria were patients who had a gunshot injury to the face, survived more than 48 hours post admission and received care at Memorial Hermann Hospital. Factors including age at injury, sex, ethnicity, type of weapon used, structures injured, length of time on antibiotics, type of antibiotic, occurrence of infection of the head and neck, and type of organism in cultures were recorded.

Results: 101 patients qualified for the study. 80.2% of qualified subjects were males who mostly identified as white (34.7%) or black (33.7%). The average age of the population was 31.0 years. 12.9% of patients developed an infection of the head and neck. Of those, 84.6% received antibiotics on admission in comparison to the 84.1% of patients who did not develop an infection. The infection rates classified by type of weapon used were highest in the shotgun group (40.0%). Involvement of specific structures also showed infection rates higher than that of the entire study sample in patients with mandibular (14.0%), sinus (15.7%), and oral cavity (16.4%) violation. The antibiotic most frequently prescribed on admission was Clindamycin. After confirmation of an infection, the average length of a treatment course of antibiotics was 4.6 days. 76.9% of head and neck infections were culture positive, with the most common organism type being gram-negative rods. *Prevotella* was the most common organism and was present in 36.4% of cultures.

Conclusions: Antibiotic usage on admission had no significant impact on infection rates, as demonstrated by the similar percentages of subjects receiving antibiotics on admission in the group that developed infections and in the group that did not. The use of shotguns and the involvement of the mandible, sinuses, or oral cavity were associated with higher infection rates compared to the overall study sample.

ABSTRACT

Which Normalizer? An important question in RT-qPCR

CHRISTOPHER BLACK *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Heinrich Taegtmeyer, MD, DPhil, Cardiovascular Medicine
Supported by: Axes of Oncometabolism in the Heart (5R01HL061483-16)
Key Words: Reference Gene RT-qPCR Validity

Scientific rigor requires precision, accuracy, and reproducibility in the measurement of biological material. A conclusion is only as valid as the observations on which it has been based. Case in point, the quantitative reverse transcription polymerase chain reaction (RT-qPCR) is a powerful tool in the analysis of gene expression when appropriate normalization methods are utilized. Unfortunately, assumptions regarding these normalization methods often compromise the accuracy and reproducibility of RT-qPCR. These assumptions stem from overconfidence in 'gold standard' genes believed to serve as universal reference genes. Due to considerable inter- and intramodel variation in expression of these genes, independently validating reference genes is necessary for each model to obtain reproducible data. A validated reference gene displays stable expression across all genotypes and tissues sampled under both control and experimental conditions. This allows researchers to accurately quantify a gene of interest relative to the reference gene while also ensuring that any variation will relate to the object of research and control to the same extent. With these considerations in mind, we tested a panel of 30 candidate reference genes in the tuberin (TSC2) conditional knock out and Cre control animals, in both heart tissue and isolated adult mouse ventricular cardiomyocytes (AMVC). Because the conditional knockout of TSC2 is restricted to the heart muscle, the reference gene panel was restricted to heart tissue and AMVC. The CFX Maestro reference gene selection algorithm was used to evaluate and rank the expression stability (M value) of these candidate genes. 14 genes were validated, showing stable expression across all 4 conditions. 5 of these validated genes were subsequently excluded from consideration as reference genes due to their involvement in metabolic pathways. 4 reference genes were chosen: ribosomal protein L30, non-POU-domain-containing, octamer binding protein, heat shock protein 90 alpha (cytosolic), class B member 1, and TATA box binding protein. With validated reference genes for this specific model, reproducible RT-qPCR can be performed; however, if additional tissues from the model require RT-qPCR analysis, reference genes must be revalidated. Although scientists may view this validation process as additional work, the process ultimately ensures accuracy and reproducibility in RT-qPCR and cannot be neglected.

ABSTRACT

Transplanted Human Intestinal Organoids (HIOs) Demonstrate Enhanced Tight Junctions Compared to *in vitro* HIOs

MARIAELENA BOYLE *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Allison L Speer, MD, Department of Pediatric Surgery
Supported by: Allison L Speer, MD, Department of Pediatric Surgery
Key Words: Tight junction, human intestinal organoid (HIO), intestinal barrier function

Introduction
Short bowel syndrome (SBS) is a clinically significant problem and current therapies are inadequate. Tissue-engineered intestine is a potential therapeutic solution. One of the remaining challenges precluding the use of tissue-engineered intestine as therapy for SBS is confirmation of proper function. The intestine has three functions: propulsive peristalsis, nutrient absorption, and barrier maintenance. Intestinal epithelial tight junctions preserve the barrier against luminal pathogens while allowing selective absorption of nutrients. Human intestinal organoids (HIOs) are a novel model used to generate tissue-engineered small intestine by transplanting HIOs into immunocompromised mice (tHIOs). Prior tHIO studies have shown the presence of tight junction protein-1 (*TJP1* or *ZO-1*), junctional adhesion molecule 1 (*F11R* or *JAM-1*), and metadherin (*MTDH*). However, there has not been investigation of two major tight junction proteins: claudins and occludin. We hypothesized that claudins 3 and 15, occludin, and zonula occludens-1 (ZO-1) would be present in HIOs and tHIOs, but with higher expression levels in tHIOs due to the fetal-like transcriptome previously described in HIOs.

Methods
HIOs were generated *in vitro* from hESCs. After 28 days, HIOs were collected for analysis or transplanted into the kidney capsule of immunocompromised mice. tHIOs were harvested at 4 or 8 weeks. RT-qPCR and immunofluorescent (IF) staining were performed.

Results
8-week old tHIOs demonstrated significantly ($p<0.05$) higher expression levels of *CLDN3* (12x), *CLDN15* (6x), *OCLN* (400x), and *ZO-1* (4x) normalized to *GAPDH* versus HIOs. 4-week old tHIOs demonstrated significantly ($p<0.01$) higher levels of *CLDN3* (8x), *OCLN* (510x), and *ZO-1* (5x) versus HIOs. There was no significant difference in expression of these tight junction genes between 4 and 8-week old tHIOs. IF staining revealed the presence of claudin 3, claudin 15, and ZO-1 in both HIOs and tHIOs; however, occludin was only present in tHIOs. Overall, tHIO tight junction morphology was better developed.

Conclusion
tHIOs and HIOs contain several tight junction components necessary for intestinal barrier function; however, HIOs have lower levels of tight junction mRNA, absence of occludin protein, and appear morphologically immature. These results are consistent with prior studies

suggesting HIOs are more fetal-like than tHIOs. Future studies confirming adequate tHIO tight junction function will be crucial prior to the therapeutic application of tissue-engineered intestine in humans with SBS.

ABSTRACT

Investigation of Endothelial Cell Differentiation in Induced Pluripotent Stem Cell Derived from Women with Turner Syndrome

SYDNEE BROWN *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Siddharth K. Prakash MD, PhD.
Internal Medicine; Genetics
Supported by: Siddharth K. Prakash
Key Words: BAV, Turner Syndrome, EMT

SPECIFIC AIM: Differentiate ips cells derived from turner syndrome patients into endothelial cells to create an in vitro model system for aortic valve development in Turner syndrome (TS) that characterizes EMT based on gene expression, proliferation and invasion into hydrogels.
BACKGROUND AND SIGNIFICANCE: Bicuspid aortic valve (BAV) is conditions where the aortic valve has two leaflets instead of three. BAV is the most common congenital cardiovascular defect effecting 0.5-1.2% of the population and is associated with many other pathological conditions of the outflow tract of the heart and vasculature (4). TS is a genetic condition where an individual only contains one copy of the X chromosome, this can be in the form of complete (XO) or partial monosomy (XXq). One third to one half of women with this condition also have BAV or coarctation of the aorta (1). The increased prevalence of BAV in turner syndrome patients is thought to be associated with dosage reduction in the X chromosome. dosage compensation studies show that haploinsufficiency of genes located the X p arm that regulate EMT may be involved in BAV in TS (6). A human cell in vitro model would allow for investigation of paracrine signaling, migration, arrangement of ECM proteins, and even genetic influence on EMT. Development of the aortic valves begins when endothelial cells overlying the early endocardial cushions invade the cushion matrix in a process known as epithelial- to-mesenchymal-transition (EMT), resulting in relatively large and cellularized endocardial cushions (4). BAV is associated with defects in EMT and histological studies show distinct disorganization of ECM protein. Using photo-polymerizable polyethylene glycol diacrylate (PEG-DA) hydrogel as biomimetic model for the endocardial cushions, endothelial cell migration, transcriptional regulation of EMT, and ECM defects can be analyzed.
METHODS AND RESULTS: PBMC were collected from patients with turner syndrome and transformed into induced pluripotent stem cells using sendai virus reprogramming. The ips cells were then separated based on the following karyotypes; 45 XO, 46XX, XXq. One ips cell line for each karyotype were differentiated into endothelial cells over the course of 8 days. First mesodermal induction was induced on days 0-2 using BMP-4, CHIR99021, and FGF-2. Vascular induction was done on days 2-8 using VEGF and SB431542. RNA was collected on days 2,4, and 8 of differentiation for q-PCR analysis. Q-PCR data showed a decrease in pluripotency marker expression and a significant increase in the expression of endothelial cell markers VECAD, CD34, and CD31 for all three cell lines. Magnetic cell separation (MACS) using CD144 (VECAD) magnetic beads was used to purify the endothelial cells. The positive fraction was collected and plated for later immunofluorescent (IF) imaging studies using CD31 antibodies. IF imaging showed an enriched population of CD31 positive staining cell in the XO cell line.

Once IF demonstrates an enriched population of CD31+ staining cells in the other cell lines, the ips-EC well be seeded onto hydrogels where EMT will be induced using TGF-B.

ABSTRACT

Targeted Therapeutic Strategies for the Treatment of DIPGs

BETHANY BUNDRANT *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Dr. Leomar Y. Ballester, MD, PhD, Pathology Department
Supported by: Dr. Leomar Y. Ballester
Key Words: Diffuse Intrinsic Pontine Gliomas; DIPG; MGMT; TERT; ACVR1

Diffuse intrinsic pontine glioma (DIPG) is a devastating pediatric solid tumor arising in the brainstem. The tumor's critical anatomic location combined with the absence of effective chemotherapeutic regimens results in 100% fatality in DIPG patients in 1-2 years. Importantly, no therapeutic progress has been made in the treatment of DIPGs in the past few decades. However, the growing body of information regarding the genetic alterations in DIPGs has opened up new opportunities for the development of novel targeted therapeutic approaches. Alterations in the expression or activity of activin receptor-like kinase 2 (ALK2), telomerase (TERT), and O-6-methylguanine-DNA methyltransferase (MGMT) are some of the genetic alterations found in DIPGs that have been identified as potential therapeutic targets. Mutations in the *ACVR1* gene, which encodes ALK2, have been observed in a subset of DIPGs and are associated with increased proliferation via the SMAD signaling cascade. Additionally, DIPG expression of MGMT may contribute to DIPG resistance to treatment with temozolomide, an oral DNA alkylating agent. Finally, upregulation of telomerase is a major mechanism through which tumor cells obtain replicative immortality, and elevated expression of TERT has been observed in the majority of DIPG cells, identifying telomerase as a potential therapeutic target. The aim of this study was to investigate the therapeutic potential of inhibition of ALK2, MGMT, and TERT against DIPG tumors. To accomplish this, the sensitivity of *ACVR1* mutant (DIPG4) and *ACVR1* wild type (DIPG24 and DIPG33) cell lines was tested against newly-developed ACVR1 inhibitors as well as previously-characterized MGMT and TERT inhibitors. The CSLP-31 ACVR1 inhibitor compound revealed selective activity against *ACVR1* mutant DIPG4 cell line compared to WT. The UH15-6, -15, -22, and -26 ACVR1 inhibitor compounds demonstrated ACVR1 independent- and caspase-dependent cytotoxicity against DIPG cells. Gene and protein analysis of MGMT revealed the absence of promoter methylation and expression of MGMT protein in DIPG cells. Furthermore, treating DIPG4 and DIPG33 cells with the MGMT inhibitors O6-Benzylguanine and Lomeguatrib increased sensitivity of cells to temozolomide treatment. Finally, DIPG4, DIPG24, and DIPG33 cells all exhibited dose-dependent decreases in cell viability in response to treatment with the TERT inhibitors: Costunolide, BIBR1532, and RHPS4. In conclusion, these initial screening results suggest a promising role for targeted therapeutic strategies for the future management of this otherwise incurable disease; however, further *in vivo* and clinical studies are required.

ABSTRACT

Whole blood or component therapy: differences in outcome and resource utilization among pediatric trauma patients presenting in extremis

DELFINA BUR *McGovern Medical School at UTHealth* *Class of 20*

Sponsored by: Bryan A. Cotton, M.D., M.P.H., F.A.C.S., Department of Surgery
Supported by: CeTIR
Key Words: Trauma, Blood Transfusions

Background and Significance:
Trauma is a leading cause of death in people under 45 years old with severe hemorrhage being a common cause of death, especially within the first 24 hours of the incident. Currently component therapy- RBC and or plasma (COMP groups) is used for blood transfusion. However, our institute previously demonstrated that low-titer group O whole blood (LTO-WB) had a superior hemostatic profile (less blood products required) to that of reconstituted whole blood (1:1:1 of plasma:platelets:RBC). We set out to evaluate the differences in outcome and resource utilization among pediatric trauma patients presenting in extremis.

Specific Aim: Evaluate the differences in outcomes in pediatric patients presenting in extremis receiving LTO-WB versus COMP at Memorial Hermann Hospital.

Design and Methods: Retrospective study, examining coagulation panels, development of clinically identifiable transfusion complications, necessity of transfusion products and 30-day survival outcomes. Trauma patients at Memorial Hermann receiving transfusions of uncrossed, emergency release blood products under the age of 19 admitted between 11/01/2017 and 07/01/2019 were included in the study.

Results: 85 pediatric patients were included; 27 received LTO-WB (31.8%)and 58 received COMP therapy (68.2%). There was no significant difference in organ-specific AIS scores between groups. However, the overall ISS was higher in LTO-WB receiving patients (p=0.016). LTO-WB patients presented with lower systolic blood pressures on initial evaluation in the ED (p=0.018). LTO-WB patients also presented with higher lactate (p=0.048). There was no significant difference between the rTEG values on arrival**.** The number of transfused products in the ED were similar between groups in exception of LTO-WB patients receiving more WB than COMP patients. LTO-WB patients demonstrated a 70% reduction in post ED transfusions (p=0.09). The primary outcome was the degree of post-transfusion complications between patients receiving LTO-WB versus COMP; these included acute renal failure, VTE, pneumonia, sepsis, UTI, hospital acquired infections, ARDS, and SIRS. We found no difference in any of these complications between the two groups. With respect to 30-day survival, there was no difference between LTO-WB and COMP groups.

Conclusion: Our results indicate that emergency transfusion of cold-stored LTO-WB is safe in pediatric trauma patients as there is no difference in post-transfusion complications or mortality in these patients when compared to pediatric patients receiving COMP therapy. Furthermore, pediatric patients receiving LTO-WB demonstrated a 70% reduction in necessary post ED transfusions when compared to those who received component therapy.

ABSTRACT

Opioid Prescribing Practices and Attitudes Among Pediatric Surgical Providers

SANTIAGO CERON *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Dr. KuoJen Tsao, MD, Pediatric Surgery
Supported by: Dr. KuoJen Tsao, MD; McGovern Medical School at UTHealth – Office of the Dean
Key Words: Opioid prescriptions, pediatric surgery

Introduction: The opioid epidemic has been declared a public health emergency, with opioid prescriptions identified as an area for possible intervention. Guidelines for postoperative opioid prescriptions have been developed for adults, but none currently exist for children. We aimed to determine baseline opioid-related knowledge and attitudes and describe current prescribing practices amongst attending physicians who manage pediatric surgical patients.

Methods: A cross-sectional survey (May-July 2019) of attending physicians who manage pediatric (<18 years) surgical patients at a single center was conducted. The survey was emailed to all pediatric hospitalists and surgeons, representing general surgery, urology, neurosurgery, cardiothoracic surgery, plastic/craniofacial surgery, otorhinolaryngology, and orthopedic surgery. Questions assessed providers' opioid-related knowledge, attitudes toward the opioid epidemic, and clinical practices–including opioid prescribing, patient education, and pain assessment–over the preceding 12 months. Descriptive statistics and univariate analyses were utilized.

Results: Of 46 physicians surveyed, 42 responded (91%). Twenty-four respondents were surgeons (57%), 15 were non-surgeons (36%), and 3 did not specify (7%). Fifty-four percent of physicians typically prescribed a combination of 3 different agents at discharge. Single-agent opioids were the most commonly prescribed agent overall (70%), followed by non-steroidal anti-inflammatory agents (67%), acetaminophen (65%), and combination opioid/non-opioid (19%). Although less than half (40%) of respondents believe that the opioid epidemic is an issue in their pediatric population, 52% believe that their own prescribing practices play a significant role; however, surgeons reported less concern than non-surgeons. In response to the opioid crisis, 64% have changed or are currently changing their pain management practices. The majority (67%) of physicians had registered on the state prescription monitoring website, but only 39% of those registered had ever looked up a pediatric patient. Responses also demonstrated a knowledge gap in opioid disposal techniques, with only 17% of respondents correctly answering that it is safe to dispose of unused oxycodone by flushing it down the toilet.

Conclusion: Physicians who care for pediatric surgical patients show variability in opioid-related attitudes and a deficit in opioid-related knowledge. Non-surgeons were more likely than surgeons to recognize or suspect an opioid problem in their patient population. Formal physician education and the development of opioid prescription guidelines for pediatric surgical patients are needed to address opioid-related concerns in this population.

ABSTRACT

Characterization of GPR56-targeting antibodies and drug-conjugates for the treatment of colorectal cancer

TREENA CHATTERJEE *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Dr. Kendra Carmon, Ph.D., Brown Foundation Institute of Molecular Medicine
Supported by: Welch Foundation Endowment Fund Award (L-AU-0002-19940421)
Key Words: Antibody-drug conjugates, GPR56, colorectal cancer

GPR56 an adhesion G-protein coupled receptor (GPCR) has been shown to be highly upregulated in colorectal tumors and is abundantly expressed in nearly all colon cancer cell lines, but little is known of the function and mechanism of GPR56 in colorectal cancer (CRC). We recently showed that knockdown of cancer stem cell receptor LGR5 in colon cancer cells induced GPR56 expression and enhanced drug resistance to irinotecan chemotherapy. GPR56 knockdown decreased drug resistance in multiple CRC cell lines and suppressed tumor growth in vivo. Furthermore, GPR56 was shown to regulate expression of multidrug resistance protein 1 (MDR1). These findings suggest targeting GPR56 using antibody-drug conjugates (ADCs) may provide a novel strategy for the treatment of CRC and overcoming drug resistance. ADCs can be used as cancer therapeutics which bind tumor cell surface antigens and are internalized for subsequent processing in the lysosome and release of cytotoxic drugs.

In the present study, we evaluated GPR56-targeted monoclonal antibodies (mAbs) and ADCs, which were previously conjugated with the potent cytotoxin and DNA alkylating agent duocarmycin, for therapeutic efficacy amongst several CRC cell lines including SW-403, HT-29, DLD-1, RKO, and LoVo. GPR56 expression was measured by western blot for all cell lines. Immunocytochemistry was performed to assess internalization of anti-GPR56 mAbs to the lysosomes of SW-403 cells, using antibodies against LAMP1. Dose-dependent cytotoxicity assays (CellTiter-Glo) were performed on cell lines treated with either GPR56-targeted mAb or ADCs. ADCs were also tested against GPR56 knockdown and overexpressing DLD-1 cells to compare efficacy amongst various states of transfected and endogenous GPR56 expression. IC50 values were determined using GraphPad Prism.

Western blot analysis confirmed high GPR56 expression in HT-29, SW-403, and DLD-1 cells, which was consistent with GPR56 mRNA expression data from the Cancer Cell Line Encyclopedia (CCLE). Confocal microscopy showed co-localization of GPR56 with lysosome marker LAMP1 in the SW-403 cell line. Cytotoxicity assays showed ADC IC50 values as follows: SW-403 = 1.22 μg/ml, HT-29 = 2.38 μg/ml, DLD-1 = 10.98 μg/ml, RKO = 14.10 μg/ml, LoVo = 19.96 μg/ml. IC50 values reflected ADC efficacy corresponding to levels of GPR56 expression, with the exception of DLD-1 cells. Unconjugated mAb had no significant effect on cell viability. Western blot analysis showed high expression of MDR1 in DLD-1 cell lines, and MDR1 levels were further increased with GPR56 overexpression. Interestingly, cytotoxicity assays showed that GPR56 overexpression in DLD-1 cells did not make cells more sensitive to the ADC, potentially due to the simultaneous increase in MDR1 expression conferring increased resistance to duocarmycin. Overall, these findings demonstrate that GPR56-targeted ADCs may be a promising treatment for CRC.

ABSTRACT

Examination of Human Lactoferrin to Modulate Macrophage Cell Phenotypes during Development of Trehalose 6,6′-Dimycolate Induced Granulomas in Mice

LUIS CHINEA *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Jeffrey K. Actor, PhD, Department of Pathology
Supported by: Jeffrey K. Actor, PhD
Key Words: Lactoferrin, Macrophage Phenotype, Trehalose 6,6′-Dimycolate, Granuloma

Lactoferrin has significant immune-modulating properties, with specific effects on limiting inflammatory response during acute granulomatous responses. Preliminary data suggests that mice treated with lactoferrin had a markedly modified pathology upon intravenous treatment with mycobacterial TDM; granulomatous responses were less compact, and macrophages appeared to be in a higher state of activation. We show that lactoferrin attenuates macrophage expression of pro-inflammatory cytokines TNF-α, IL-1β and anti-inflammatory cytokines post administration of mycobacterial TDM. Relative to tuberculosis infection, lactoferrin treatment permits a granulomatous response that allows greater penetration of adaptive cells into regions of pathology. This coincides with a shift in presence of macrophages away from those that resemble the M1 phenotype, with reduction in number of responding cells expressing CD38 and CD86. Overall, the microenvironment orchestrated by lactoferrin may be more amenable to delivery of tuberculosis combating therapeutics due to subsequent changes in granulomatous structure.

ABSTRACT

Retrospective Analysis of Rapidly Progressive Hepatocellular Carcinoma

NATASHA CIGARROA *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Venkateswar R Surabhi MD Department of Radiology
Supported by: Venkateswar R Surabhi MD Department of Radiology, Dean's Matching Fund
Key Words: Hepatocellular carcinoma, texture analysis

Background: Hepatocellular carcinoma is the fifth most common tumor worldwide and incidence is increasing. A particularly aggressive lesion has been characterized as Rapidly Progressive Hepatocellular Carcinoma (RPHCC). While slow progression allows for moderated therapy, RPHCC follows an expedited growth course and requires aggressive therapy.
Purpose: The purpose of this study was to characterize CT/MRI findings of rapidly progressive hepatocellular carcinoma (RPHCC).
Methods In this retrospective study, baseline and follow up CT/MRI images were reviewed by an experienced radiologist to establish rapid progression. Baseline images were then analyzed for characteristic radiologic features.
Results Of the cases analyzed, 37.5% of RPHCC lesions displayed irregular margins compared to 0% in the control group ($p<0.005$). Notably, radiologic features including internal vascularity ($p=0.68$), pseudo-capsule formation ($p=0.3$), necrosis ($p=0.14$), washout ($p=1.0$), and tumor thrombus ($p=1.0$) did not exhibit significant differences between RPHCC and control groups. Similarly, patient AFP values were compared with no significant difference between groups ($p=0.68$).
Conclusion Patients with RPHCC have limited characteristic features on early CT/MRI scans that indicate risk of rapid progression. The definition of margins has some potential to estimate risk of rapid progression, however our results suggest that more research is required to flag patients at risk for developing rapid progression that could benefit from increased screening and early intervention.

Further analysis of CT/MRI baseline images will be done using texture analysis to characterize the heterogenous features of baseline RPHCC tumors against a control. Quantitative analysis of texture features creates a unique opportunity to objectively analyze CT images beyond human capacity. Tumors will be outlined manually on deidentified and blinded CT/MRI images then processed for second order texture feature extraction. We anticipate that RPHCC will express characteristic features that can distinguish it from normally progressing HCC at an early stage. Texture analysis has the potential to demonstrate features of CT/MRI scans that could be used as a diagnostic tool with the potential to improve early intervention and patient prognosis

ABSTRACT

Expression of Bile Regulated Proteins TRB3 and KRTDAP in Esophageal Biopsies From Patients With Gastroesophageal Reflux Disease

JAMES CLYNES *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Mamoun Younes, MD, Department of Pathology and Laboratory Medicine
Supported by: Mamoun Younes, MD, Department of Pathology and Laboratory Medicine
Key Words: Bile reflux, GERD, PPIs

Background: Gastroesophageal reflux disease (GERD) affects millions of people worldwide and can be caused by reflux of acid, bile, or both. Common treatments for GERD such as proton pump inhibitors (PPIs) may be ineffective in treating bile reflux, so it is important to be able to determine the type of reflux. Studies have shown that several proteins in the squamous cells lining the surface of the esophagus are regulated by bile. These include tribbles-homology-3 (TRB3) and keratinocyte differentiation-associated protein (KRTDAP). This study tests the hypothesis that expression of bile acid-regulated proteins in esophageal biopsies from patients with GERD could be used as a diagnostic tool for bile reflux.

Methodology: 88 esophageal biopsies were studied from 88 patients with clinical and histological diagnosis of GERD who had a follow up visit. The study cohort included 29 males and 59 females, with age ranging from 20 to 84 years (mean 54.6, median 54). Sections of the biopsies were cut and stained by immunohistochemistry (IHC) using antibodies to TRB3 and KRTDAP. The IHC slides were reviewed and the staining intensity was recorded as 0 (no stain), 1 (weak), 2 (moderate), or 3 (strong). The extent of staining was recorded as 0 (no stain), 1 (<10%), 2 (11-25%), 3 (26-50%), 4 (51-75%), or 5 (>75%). A protein Expression Score (ES) was determined by multiplying the intensity score by the extent score. TRB3 ES of 8 or greater was considered high, and KRTDAP ES of 4 or greater was considered high.

Results: 82 patients were treated with proton pump inhibitors (PPI). Follow up (first visit after biopsy) ranged from 2-60 months (mean 18.9 months, median 10 months). Nineteen patients had no change in reflux symptoms and 63 had either improvement or complete resolution of symptoms. High TRB3 ES was not associated with significant response to PPI treatment ($p = 0.2994$). However, all 19 patients who had no response to PPI treatment had lower TRB3 staining intensity (less than 3) in contrast to none of those with high (3) staining intensity ($p = 0.060$). High KRTDAP ES did not correlate with PPI treatment response ($p > 0.999$), and neither did high KRTDAP staining intensity ($p = 0.4271$). High TRB3 ES was associated with smoking history (18 of 45 or 40% vs 7 of 43 or 16%, $p = 0.018$), but not with history of alcohol use (42% vs 56%, $p = 0.288$) or Barrett's esophagus (18% vs 19%, $p > 0.999$). High KRTDAP ES was associated with Barrett's esophagus (11 of 38 or 29% vs 5 of 50 or 10%, $p = 0.0279$). Although high KRTDAP was more likely to be associated with history of smoking (37% vs 22%) and alcohol (61% vs 40%), these were not significant ($p = 0.155$ and $p = 0.0846$, respectively).

Conclusions: Our results show significant association between KRTDAP expression and Barrett's esophagus but not with response to PPI treatment. By contrast, increased expression of TRB3 may predict response to PPI treatment in patients with GERD, suggesting that weaker TRB3 expression may correlate with bile reflux and unresponsiveness to PPI treatment.

Additional larger studies are needed to confirm these findings. IHC analysis with DSG1 is still in progress.

ABSTRACT

Aortic Biomechanics and Outcomes in Thoracic Aortic Disease

SOHAIL DHANJI *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Dr. Siddharth Prakash M.D, PhD
Supported by: Dr. Prakash and $1000 Dean's Office Stipend
Key Words: Thoracic Aortic Disease, Exercise, Restrictions

In recent clinical practice guidelines, hypertension was identified as the most important risk factor for acute aortic dissections in patients with heritable thoracic aortic disease (HTAD). Additionally, it has also been found that acute physical activity can trigger hypertension and aortic dissections in HTAD patients. However, HTAD patients may be particularly vulnerable to the cardiovascular effects of a sedentary lifestyle, because that will worsen other cardiovascular risk factors such as obesity and hypertension. There has been little data examining the relationship between specific exercises and acute changes in blood pressure. Therefore, we attempted to identify rational limits based on blood pressure responses to exercise in order to develop individualized exercise prescriptions and to ameliorate patients' anxiety about experiencing potential cardiovascular events during exercise.

Experimental subjects were recruited if they had had a Thoracic Aortic Aneurysm and/or Dissection, but were excluded if they were not 18 years of age, had uncontrolled hypertension, or were unable to complete the exercises. They were also excluded if they had had a myocardial infarction, stroke, or aortic surgery within the last year. Consenting patients filled out a questionnaire covering their height, weight, and regular activity levels. Then, baseline blood pressure measurements were taken before the exercise protocol, which consisted of a series of isometric and dynamic exercises. Recovery measurements were taken ten minutes after the last exercise. All measurements were completed using a Space Labs On Trak Ambulatory Blood Pressure Monitor. We used two-tailed t-tests to compare our patient and control groups for each exercise regarding variables such as systolic blood pressure (SBP), diastolic blood pressure (DBP), change in SBP, change in DBP, and change in SBP during recovery. We then used linear regressions to determine whether any causative relationships existed between these variables and body mass index, moderate activity levels, or vigorous activity levels in our experimental subjects. We hypothesized that alterations in vascular reactivity during exercise may cause exaggerated systolic blood pressure responses in our HTAD cohort compared to our control cohort, which will limit the types of exercise that HTAD patients can safely perform.

We completed the exercise protocol with fifteen control subjects and twelve affected subjects over the summer. Our results showed a statistically significant increase in SBP values during wall sit and more limited recovery of blood pressure after exercise, when we compared our patients to controls. No significant differences in baseline DBP, change in SBP, or change in DBP were found between our two cohorts for any exercise. Additionally, we found a correlation between higher moderate activity levels and lower SBP and DBP values for almost all exercises among controls. We did not find this correlation between vigorous activity levels and SBP or DBP values in affected individuals. Therefore, we can conclude that HTAD

patients may safely perform most moderate intensity exercises, with the notable exception of isometric exercises that include abdominal straining.

Effects of the General Anesthetics Propofol and Isoflurane in the Development of Cognitive Impairments: A Review

Karanvir Dhother *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Marie-Francoise Doursout, PhD, Department of Anesthesiology
Supported by: Marie-Francoise Doursout, PhD, Department of Anesthesiology; The University of Texas at Houston Medical School-Office of the Dean
Key Words: Anesthesia, Propofol, Isoflurane, Neurodegeneration

There is growing concern that the use of both inhalational and intravenous general anesthetics may cause neurodegeneration, especially with intermediates involved in the pathogenesis of Alzheimer's Disease [1]. The purpose of this mini review is to discuss the current knowledge on this topic, as well as make recommendations for further study specifically focusing on isoflurane and propofol. Studies comparing isoflurane vs. propofol-mediated neurodegeneration have shown that there are age dependent effects. In one case that measured the effect of both anesthetics on neuron maturation in the dentate gyrus of the hippocampus in rats, isoflurane was noted to decrease the number of differentiating neurons in aged rats, while propofol decreased the number of differentiating neurons in young rats [2]; essentially suggesting possible age dependent cognitive impairment following anesthesia exposure. Additional studies have also compared the two drugs via their induction of S100β, a biomarker for anesthetic mediated neurodegeneration, as well as caspase-3, a biomarker for cell death via apoptosis. While isoflurane administration significantly increased levels of S100β in the brains of neonatal mice, propofol did not increase levels of S100β significantly. Additionally, both drugs were noted to increase the levels of caspase-3 in the brains of neonatal mice, with isoflurane producing a more potent increase [3]. However, in the same study, neither were noted to increase the levels of proinflammatory cytokines or have a significant effect on cognitive function measured via the Morris Water Maze. Further studies have also compared the effects of isoflurane and propofol on the accumulation of AB amyloid protein in vivo and in vitro; in both cases, propofol was shown to attenuate isoflurane induced caspase-3 activation in conditions of already elevated AB levels [4]. These findings all suggest that both isoflurane and propofol can have significant neurodegenerative effects. Further studies are needed to show the evidence of long term memory impairment and neuroinflammation, along with the proposed mechanisms of neurodegeneration caused by these drugs. This topic is being further explored in our laboratory, and we have proposed a study to characterize both the short- and long-term neurodegenerative effects of propofol and isoflurane in APP overexpressed mice; the experiment is ongoing and will assess the time course of Tau, B amyloid, brain derived neurotrophic factor, and alpha synuclein levels in the hippocampus of APP mice treated with and without isoflurane and propofol in the hopes of exploring long term effects and a potential mechanism of neuronal damage.

References:

1) Eckenhoff, Roderic G., et al. "Inhaled Anesthetic Enhancement of Amyloid-β Oligomerization and Cytotoxicity." *Anesthesiology*, vol. 101, no. 3, 2004, pp. 703–709., doi:10.1097/00000542-200409000-00019.
2) Erasso, Diana M., et al. "Effects of Isoflurane or Propofol on Postnatal Hippocampal Neurogenesis in Young and Aged Rats." *Brain Research*, vol. 1530, 24 July 2013, pp. 1–12., doi:10.1016/j.brainres.2013.07.035.
3) Yang, Bin, et al. "Comparison of Neurodegeneration and Cognitive Impairment in Neonatal Mice Exposed to Propofol or Isoflurane." *PLoS ONE*, vol. 9, no. 6, 16 June 2014, doi:10.1371/journal.pone.0099171.
4) Zhang, Yiying, et al. "Anesthetic Propofol Attenuates the Isoflurane-Induced Caspase-3 Activation and Aβ Oligomerization." *PLoS ONE*, vol. 6, no. 11, 1 Nov. 2011, doi:10.1371/journal.pone.0027019.

ABSTRACT

Exploring Molecular Links Between Fibroblasts and Macrophages in Pancreatic Tumorigenesis

MADELINE DRAKE *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Yanna Cao, MD and Tien C. Ko, MD, Department of Surgery
Supported by: Department of Surgery and Office of the Dean, The University of Texas Health Science Center at Houston McGovern Medical School
Key Words: Pancreatic ductal adenocarcinoma, chronic pancreatitis, macrophage, Gremlin1, macrophage migration inhibitory factor

Background: Pancreatic ductal adenocarcinoma (PDAC) is known for its desmoplastic microenvironment containing activated fibroblasts and macrophages. We reported that chronic pancreatitis leads to increased secretion of Gremlin1 (Grem1) by activated pancreatic fibroblasts. Grem1 is a key pro-fibrogenic cytokine and has been shown as an endogenous inhibitor of macrophage migration inhibitory factor (MIF) in atherosclerotic disease. MIF stimulates classical activation of macrophages (M1), which are tumor-inhibiting. In contrast, alternatively activated macrophages (M2) are tumor-promoting. We reported that M2 positively correlate with Grem1 in PDAC. We hypothesize that upregulation of Grem1 during PDAC development blocks MIF, promoting M2 activation and pancreatic tumorigenesis. In this study, we used human PDAC samples and mouse macrophages to test our hypothesis. **Methods:** For human study, a commercial human pancreatic tissue microarray containing 70 PDAC cases was acquired. Grem1 RNA *in situ* hybridization, and immunohistochemistry (IHC) staining of α-smooth muscle actin (activated fibroblasts), MIF, CD68 (total macrophages), and CD163 (M2 macrophages) were performed. The most densely stained area per case was imaged and quantified by two investigators blind to case identities. MIF/CD163 co-staining was further performed and quantified. Data analysis was performed to identify correlations. For *in vitro* study, mouse peritoneal macrophages were isolated and treated with vehicle control, MIF (125ng/ml), Grem1 (250ng/ml), and combination of MIF and Grem1. M1 activation was measured via immunofluorescence (IF) staining by CD86 and quantified. **Results:** In human study, MIF expression is observed mainly in tumor cells, and Grem1 expression is exclusively in activated fibroblasts. MIF is positively correlated with Grem1 in PDAC ($r=0.32$, $p<0.01$), but not correlated with CD68 (total macrophages). MIF/CD163 (M2 macrophages) co-staining revealed a negative correlation between MIF and CD163 ($r=-0.29$, $p<0.001$). In *in vitro* study, MIF alone increased the expression of M1 marker, CD86. Grem1 alone had no effect, however, Grem1 attenuates the effect of MIF (with fold changes of 1, 2.09, 0.84, 0.49 respectively to Control, MIF, Grem1, MIF+Grem1, $p<0.01$). **Conclusion:** MIF is positively correlated with Grem1 and negatively correlated with M2 macrophages in PDAC, which suggests regulation of MIF activity plays an important role in determining M2 phenotype. The *in vitro* study supports that Grem1 negatively regulates MIF activity. Furthermore, the interrelated Grem1 and MIF may mediate crosstalk between fibroblasts and macrophages during pancreatic tumorigenesis, thus become potential novel therapeutic targets for PDAC.

ABSTRACT

Measuring Blood Coagulation Parameters with a Novel Linear Thromboelastometry Device

BRADLEY H. DUE *McGovern Medical School at THealth* *Class of 2022*

Sponsored by: Brijesh Gill, MD, Department of Surgery, Charles S. Cox, JR. MD, Department of Pediatric Surgery
Supported by: Brijesh Gill, MD, Department of Surgery, Charles S. Cox, JR. MD, Department of Pediatric Surgery, The University of Texas at Houston Medical School – Office of the Dean
Key Words: TEG, Thromboelastography, Novel Device, Coagulation, Trauma

Introduction: Thromboelastography (TEG) is used in numerous surgical and non-surgical specialties to obtain detailed information about blood coagulation kinetics. We describe a novel linear thromboelastography device (LTD) driven by a microelectromechanical system (MEMS). The LTD device uses 80% less blood volume than current TEG technology (70uL vs 340uL) and offers the potential for downward scaling to a handheld, portable device for coagulation studies outside the hospital setting. We hypothesize the LTD will demonstrate significant correlation with TEG performance in both healthy and level 1 trauma patients.

Methods: Venous blood was collected from healthy adult and Level 1 trauma patient volunteers into citrated tubes. The blood was recalcified and mixed with either Rapid TEG reagent, Kaolin reagent, or no additional reagent. Blood with or without reagent was then injected into a 70 uL well mounted to a MEMS driven, linear translational stage. The unfixed end of a nickel-based cantilever probe was inserted into the blood filled well. As the blood coagulated, it formed a platelet-fibrin mesh which exerted an increasing amount of force on the cantilever probe, which caused deflection as the stage oscillated. The deflection of the probe was optically measured with a high-resolution camera. The coagulation parameters of the blood sample were measured as follows: time from start of the assay until the first evidence of probe deflection (R-Time), the maximum deflection of the probe (MA), and the maximum rate of change in probe deflection throughout the assay (Max Slope). To correlate the efficacy of the novel LTD device with existent TEG technology, the blood from 5 Level 1 trauma patients and 3 healthy volunteers were assayed with all 3 aforementioned reagents. All samples were run on TEG devices in parallel with the LTD assays. The parameter data generated from the LTD were then correlated with the data generated from TEG.

Results: Clinically relevant LTD generated parameters correlated with equivalent TEG data in both healthy and trauma patient populations. LTD R-Time correlated strongly with TEG R-Time ($R = 0.85$), LTD MA correlated strongly with TEG MA ($R = 0.80$), and LTD Max Slope correlated moderately with the tangent line of TEG angle ($R = 0.65$).

Conclusion: This study demonstrates a strong correlation of LTD performance with current TEG technology, despite LTD utilizing 80% less blood than TEG. This suggests the potential for future scaling of LTD to a portable device to generate clinically relevant data in the non-hospital setting.

ABSTRACT

Risk Factors Associated With Free Flap Reconstruction In The Pediatric Population Following Lower Extremity Trauma

KASRA N. FALLAH *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Matthew R. Greives, MD, FACS, Department of Pediatric Plastic Surgery
Supported by: Brady J. Anderson, BS; Jessica F. Rose, DO; Grigorios A. Lamaris, MD PhD; Phuong D. Nguyen, MD; Matthew R. Greives, MD
Key Words: Free Flap, Lower Extremity, Trauma, Pediatrics

Background:
Post-traumatic reconstruction of the lower extremity has continued to be challenging, even with abundant advances in the surgical field. Due to the larger volume of cases in adults compared to children, the majority of the medical literature has focused on adult lower extremity reconstruction. However, the procedures performed in adults are not always translatable to the growing pediatric population. Many surgeons have been uncertain about the efficacy of utilizing pediatric free flaps due to the lack of tissue availability, tendency of vessel vasospasm, and small vessel size. This study describes the risk factors associated with the need for free flap reconstruction in the pediatric population following lower extremity trauma.

Methods:
An IRB-approved retrospective chart analysis over a 5-year period (January 1, 2012 to December 31, 2017) was performed analyzing all pediatric patients (<18 years old) diagnosed with one or more lower extremity wounds at the Memorial Hermann Trauma Institute. Age, sex, median income, race, mechanism of injury, trauma type, trauma team activation, and injury severity score were reviewed. Statistical analysis consisted of univariate and multivariate regression models to compare the free flap and no free flap cohorts.

Results:
One thousand eight hundred twenty-one patients were identified who fit our search criteria. Out of these patients, free flap reconstruction was observed in forty-one (2.25%) cases, local flap reconstruction was observed in sixty-five (3.57%) cases, and skin graft reconstruction was observed in nineteen (1.04%) cases. Increased age (OR 1.134; P=0.002), all-terrain vehicle accidents (OR 6.698; P<0.001), and trauma team activation (OR 2.443; P=0.034) were associated with the need for free flap reconstruction following lower extremity trauma in the pediatric population.

Conclusion:
As pediatric patients age, they may be more likely to need free flap reconstruction to repair lower extremity wounds than their younger counterparts. The mechanism of injury and trauma team activation of lower extremity trauma may also increase the likelihood of needing free flap reconstruction. This information can be implemented to help develop a predictive model that defines the need for complex lower extremity reconstruction in the pediatric population.

Further analyses should include surgical-specific variables in addition to diagnosis, procedure, outcome, complication, and comorbidity data.

ABSTRACT

Real-World Analysis of EST Outcomes for Patients with Large Vessel Occlusions After Inter-Hospital Transfer

JAMES FAN *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Sunil A. Sheth, MD, Department of Neurology
Supported by: Sunil A. Sheth, MD, Department of Neurology, Dean's Office stipend
Key Words: Endovascular stroke therapy, Stroke, Large Vessel Occlusion

Introduction
Prior studies suggest that patients with large vessel occlusion (LVO) who undergo endovascular stroke therapy (EST) after inter-hospital transfer (IHT) have worse outcomes than those who present directly to EST centers. However, these studies were largely derived from clinical trials or registries and may not be representative of real-world clinical practice.

Methods
We performed a multicenter, observational cohort study on acute ischemic stroke (AIS) patients with LVO that presented to EST-capable centers directly (LVO-D) or after IHT (LVO-T) between Jan 2018 to Feb 2019. The study included 11 hospitals in the Houston area, of which 4 are EST-capable. Clinical data were collected using our cerebrovascular data registry. All transfers were from non-EST capable hospitals to EST-capable hospitals. Logistic regression adjusted for age, NIHSS, occlusion location and direct vs transfer arrival was used to assess the likelihood of good outcome, defined as discharge to home or rehabilitation. Results are given as median [IQR] and OR [95% CI].

Results
Among 4,313 patients with AIS, 772 (18%) patients had LVO. Among LVO patients, median age was 68 [59-79], 47% were female, 51% were white, 378 (49%) were LVO-D and 394 (51%) were LVO-T. Median IHT time was 152 min [114-198]. LVO-D patients arrived at EST-treating hospitals with superior ASPECTS compared to LVO-T (9 [7-10] vs 7 [6-9], p<0.0001), but comparable CTP RAPID infarct cores (5 mL [0-31] vs 7 mL [0-38], p=0.59). LVO-D and LVO-T patients were just as likely to have ICA occlusions (13% vs 12%; p=.64) and proceeded to have equivalent rates of EST (43% vs 47%, p=0.95). Among LVO patients who did not receive EST, good discharge outcomes were comparable (34% vs. 35%, p=0.66, LVO-D vs. LVO-T). Good discharge outcomes were also similar for those receiving EST (34% vs. 37%, p=0.57, LVO-D vs. LVO-T). In logistic regression adjusted for age, NIHSS, and occlusion location, likelihood of good discharge outcome was comparable between the two groups (OR 0.98 [0.71-1.36]).

Conclusion
In this real-world cohort of a multi-center stroke network, IHT was not associated with worse outcomes for patients with LVO, for both patients who did receive EST and those that did not.

ABSTRACT

Patient Experience and Outcomes Following Implementation of an Inpatient NPO Guideline for Enhanced Satiety Time (INGEST) Protocol

Alan Flores *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: George Williams, MD, Department of Anesthesiology
Supported by: George Williams, MD, Department of Anesthesiology
Key Words: Clear liquid diet, NPO, patient satisfaction

Purpose: Perioperative fasting guidelines have been historically used to prevent complications such as aspiration. New data suggests that clear liquid intake is not detrimental and may even be beneficial in preventing nausea and vomiting and may help improve patient satisfaction. The purpose of this study was to investigate the effects of an ASA guideline compliant preoperative clear liquid diet on patient pain and hunger levels, as well as on angiography contrast-induced nephropathy.

Methodology: Patients admitted to hospital with a known inpatient procedure were assessed at bedside at specific times the day of their procedure. The primary endpoints were pain and hunger levels, and the secondary endpoints were changes in angiography contrast-induced nephropathy.

Results: Self-reported hunger levels were reduced in the post intervention group ($P < 0.001$), while there were no significant changes in pain or creatinine levels.

Conclusion: Implementation of an ASA compliant preoperative clear liquid diet safely reduced hunger levels in hospital patients.

ABSTRACT

Relevance of Deep MCL Repair in ACL Trauma

VICTOR A. GARCIA *McGovern Medical School at THealth* *Class of 2022*

Sponsored by: Manickam Kumaravel, MD, Department of Diagnostic and Interventional Imaging
Supported by: Department of Diagnostic and Interventional Imaging; McGovern Medical School- Office of the Dean
Key Words: Deep MCL repair, ACL trauma, surgical outcomes

Background
The deep MCL (dMCL) plays an important functional anatomical role by acting as both a static and rotational stabilizer of the medial knee. ACL trauma is often accompanied by other ligamentous injuries, particularly the deep MCL, and the typical treatment for operative dMCL injury associated with ACL surgery is a non-operative option. Few studies have evaluated the effectiveness of dMCL repair in shortening the healing duration of ACL repair surgery.

Materials/Methods
The retrospective study compared the outcomes of non-repaired dMCL tears with repaired dMCL tears in patients who have undergone ACL surgery. Patient data was gathered from PACS and EMR. The repaired dMCL patients (n=20) and the non-repaired dMCL patients (n=29) were compared by evaluating activity level at two timepoints. Activity level was subdivided into "Light activity" (LA) and "Full activity" (RTP), and an univariate analysis was done to determine the percentage of patients in both cohorts who were able to perform light or full activity at 6 and 12 months post op.

Results
The repaired dMCL group had 89.4% LA clearance at 6 months, while the non-repaired group had 76.5% clearance. At 12 months, the repaired group had 88.5% RTP clearance, while the non-repaired group had 69.9% clearance.

Conclusions
Given the functionality of the dMCL and the results of the study, the operative fixation of the dMCL may provide patients with a prognostic benefit. There was an overall improvement in return to light activity (s/p 6 months) and full release (s/p 12 months) for patients who had a dMCL repair. Due to the study's low statistical power, however, a larger subject pool is needed to further compare the operative versus non-operative approach to dMCL repair.

ABSTRACT

Characteristics of Out-of-Hospital Shock in a National Cohort of Emergency Medical Services Agencies

TIMOTHY GEORGE *McGovern Medical School at UTHealth* *Class of 2*

Sponsored by: Henry E. Wang, MD, MS, Department of Emergency Medicine
Supported by: Office of the Dean & Department of Emergency Medicine
Key Words: Shock; hypotension; emergency medical services; paramedics; trauma

Objective: Shock from medical and traumatic conditions can result in organ injury and death. While Emergency Medical Services (EMS) personnel often provide initial care to the critically ill, only limited data describe their care of shock. We sought to describe the clinical characteristics and course of shock care in a national cohort of EMS agencies.
Methods: We used 2018 cross sectional data from ESO solutions, a national EMS electronic health record system. We included adult (≥18 yr) 911 patients with shock (initial systolic blood pressure (SBP) ≤80 mmHg). We excluded cardiac arrests and SBP=0. Using univariate odds ratios and 95% confidence intervals, we compared patient demographics, response, clinical care characteristics and etiologies between medical and traumatic shock patients. Using fractional polynomial models, we determined SBP trends during the first 90 minutes of EMS care.
Results: Among 6,156,895 adult 911 responses from 1,289 EMS agencies, shock was present in 62,876 (1.02%; 95% CI: 1.01%-1.03%), including 54,239 (86.3%) medical and 5,978 (9.5%) traumatic, and 2,650 unknown. Medical was more common than traumatic shock in women and older patients and in healthcare facilities. The most common injuries associated with traumatic shock were falls (37.6%) and motor vehicle crashes (18.7%). Mean initial and final medical SBP were 71±10 mm Hg and 99±24; SBP increased in 88.8% (mean increase 32±24) and decreased/did not change in 11.0% (mean decrease -5±7). Mean initial and final trauma SBP were 71±13 mm Hg and 105±28; SBP increased in 90.4% (mean increase 37±27) and decreased/did not change in 9.6% (mean decrease -4±6). On fractional polynomial modeling, trauma SBP increased higher and faster than medical shock.
Conclusion: In this national series, 1 of every 100 EMS encounters involved shock. Approximately 1 of every 10 shock patients did not improve with EMS care. EMS must prioritize the care of shock.

ABSTRACT

Reduction of atherosclerotic plaques using BF-ELIP

SAURENDRO GHOSH *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Melvin E. Klegerman, PhD, Cardiovascular Medicine
Supported by: Melvin E. Klegerman, PhD, Cardiovascular Medicine
Dean's Office Stipend
Key Words: BF-ELIP, atherosclerosis, stem cell

SPECIFIG AIMS:
BF-ELIP will be tested as a delivery system for mesenchymal stem cells in a mouse model. BF- ELIP is hypothesized to exhibit better localization to the tissue of interest compared to nonspecific therapies (e.9., lgG-ELIP). Levels of lipid deposition in the atheromatous plaque will be analyzed in mice treated with BF-ELIP to evaluate whether lipid accumulation rates due to atherosclerotic progression are lower.

BACKGROUND AND SIGNIFICANGE:
Atherosclerosis is one of the leading causes of coronary, cerebral, and peripheral artery disease. Early lesions can progress to plaques, leading to increases in lipid oxidation and cellular necrosis, resulting in macrophages secreting inflammatory cytokines (1). Notably, monocyte recruitment is mediated by intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) (2). These molecules also serve as important markers that can aid in the therapeutic targeting of atheromatous plaques.

RESEARCH DESIGN AND METHODS:
Endothelial cells were stained with DAPI, while stem cells were stained with GFP. Samples of endothelial cells were mixed with stem cells. These samples contained either just the cells, lgG ELIP, or BF-ELIP conjugated to both anti-ICAM-1 and anti-CD146, a marker for mesenchymal stem cells. lmmunofluorescence was performed in order to check for adhesion between endothelial and stem cells.

ln order to test efficacy of BF-ELIP in vivo, APO-E knockout mice were injected with 100 microliters of BF ELIP. IgG-ELIP was used as a control. Prior to injection, ultrasound was performed in order to check aortic arch for plaques. lnjection was performed percutaneously into the retro-orbital sinus.

OUTCOMES:
BF-ELIP showed better localization of stem cells to endothelial cells compared with both lgG- ELIP and stromal cells. Work on the in vivo BF-ELIP injections is ongoing but we

anticipate lower levels of plaque deposition in the treatment group similar to work that has been done previously with hematopoietic stem cells.

REFERENCES:

1. Tabas, l. (2002). Consequences of cellular cholesterol accumulation: basic concepts and physiological implications. The Journal of clinical investigation, 1 10(7), 905-91 1.

2. liyama, K., Hajra, L., liyama, M., Li, H., DiChiar?, M., Medoff, B. D., & Cybulsky, M. l. (1999). Patterns of vascular cell adhesion molecule-1 and intercellular adhesion molecule-1 expression in rabbit and mouse atherosclerotic lesions and at sites predisposed to lesion formation. Circulation research, 85(2), 199-207.

Misapplying Autonomy: Why Patient Wishes Should not Settle Treatment Decisions

COLIN GOODMAN *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: McGovern Center for Humanities and Ethics
Supported by: McGovern Center for Humanities and Ethics
Key Words: Autonomy, physician-assisted suicide, healthy-limb amputation

What role does autonomy play in decisions regarding the appropriateness of medical treatments? Many argue that autonomy should be given more power in this process suggesting that any medical intervention can be justified if it is what the patient wants. For example, arguments made in defense of physician-assisted suicide or healthy-limb amputation often appeal to the competency of patients requesting these interventions, their persistent desire to have them, and even a right to have them based on their autonomy. But these arguments are misguided. First, they fail to distinguish the two kinds of autonomy: positive and negative. As I argue, negative autonomy (the right to refuse medical interventions) is unrestricted, but positive autonomy (the right to demand medical interventions) has its limits. More importantly, they do not distinguish between what I call the clinical and administrative contexts. The importance of this distinction has been widely overlooked in the literature, and by ignoring these contexts many authors misapply the principle of autonomy when arguing for the appropriateness of certain medical treatments. I argue for clarification of these contexts, which shows the limits of patient autonomy in decisions concerning the appropriateness of medical treatments.

ABSTRACT

Evolution of antimicrobial resistance over 5 decades in serotype III invasive infant *Streptococcus agalactiae* infections in Houston, TX

HANNAH HARVEY *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Dr. Anthony Flores
Supported by: Flores Streptococcal Lab
Key Words: *Streptococcus agalactiae,* macrolide resistance, antimicrobial resistance

BACKGROUND *Streptococcus agalactiae* (group B *Streptococcus*, GBS) is a leading cause of young infant morbidity and mortality globally. GBS is a commensal of the lower genital and gastrointestinal tract and can be vertically transmitted from mother to neonate, resulting in life-threatening infection in 1-2% of neonates. Prevention recommendations for early-onset (age 0-6 days) GBS disease includes culture screening of pregnant women and administration of intravenous antibiotic to GBS-colonized women during parturition. Penicillin (PCN) is the drug of choice for this prevention strategy because GBS remains universally PCN susceptible. However, because of PCN-allergy, use of alternative antibiotics (e.g. usually clindamycin) is not uncommon. Since 2000, increasing rates of resistance to clindamycin and erythromycin have been reported, reaching nearly 40% and 50%, respectively. We have collected infant GBS disease isolates in Houston, TX spanning 5 decades (1970-2019). We sought to determine the occurrence of clindamycin and erythromycin resistance in serotype III GBS strains, the most common cause of GBS disease in infants. **METHODS** We determined antimicrobial susceptibility to penicillin, clindamycin, erythromycin, chloramphenicol, levofloxacin, and tetracycline of 872 serotype III GBS using disk diffusion. Macrolide-resistant isolates were further categorized as having constitutive (cMLS), inducible (iMLS), or no reistance (M) to clindamycin using the D-test. **RESULTS** All 872 isolates were susceptible to penicillin. Resistance to tetracycline was most common (806/872, 92.4%), followed by erythromycin (66/872, 7.4%), and clindamycin (26/872, 3.0%). Resistance to chloramphenicol and levofloxacin was low at 5/872 (0.6%) and 1/872 (0.1%), respectively. We next determined the frequency of resistance to each antibiotic by decade. By linear regression analysis, only erythromycin (0.6% to 24.2%, P=0.035) showed a significant increase over time that was most apparent after 1999. Surprisingly, the frequency of tetracycline resistance in 2010-2019 (84.1%) was significantly lower than the preceding 4 decades (range 91.8-96.8%). Of the tetracycline susceptible strains, only 2 (2/66, 3%) were concomitantly erythromycin resistant indicating that the decrease in the rate of tetracycline resistance was independent of macrolide resistance. **CONCLUSIONS** Increased frequency of resistance to erythromycin and clindamycin was likely coincident with widespread use of these antibiotics over the same time period. That the observed decrease in the rate of tetracycline resistance was inversely correlated with macrolide resistance is worthy of further investigation regarding the genetic relationships of resistant and susceptible GBS strains and may provide novel insights on the evolution of GBS in humans.

ABSTRACT

Examining the role of Lipin1 in 5-flourouracil-induced lipid metabolism reprograming in breast cancer cells

Ezekiel Hinojosa *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Guangwei Du, PhD, Department of Integrative Biology and Pharmacology
Supported by: Guangwei Du, PhD, Department of Integrative Biology and Pharmacology
Key Words: Lipin1, 5-Fluorouracil, chemotherapy, microsome isolation

Background: 5-flourouracil (5-FU) is an antimetabolite chemotherapy agent used in numerous types of cancer. 5-FU acts as a pyrimidine analog, covalently binding to thymidylate synthase and permanently inactivating the synthesis of thymine. In addition to the previously known functions in inhibiting nucleotide and DNA synthesis, my sponsor's lab recently found that 5-FU can also decrease phospholipid synthesis. This is thought to occur by 5-FU causing a translocation of the Lipin1 protein from the surface of the endoplasmic reticulum to the nucleus, switching its function from phospholipid/triacylglycerol synthesis to a transcriptional co-activator. This pathway has yet to be exploited in chemotherapy treatment and may provide an avenue for treatment in 5-FU-resistant tumors.
Methods: The initial stage of this study was to confirm that 5-FU treatment of tumor cells did induce the nuclear translocation of the Lipin1 protein from the microsome. HCC-1806 breast cancer cell lines were treated with 200 μM 5-FU in-vitro for periods of 8, 16, and 24-hours before treatment with an HA-conjugated Lipin1 antibody for immunofluorescent staining. The cells were then viewed under an immunofluorescent light microscope and pictures were taken. Cells derived from the same line were also treated with 10 μM torin as a positive control, and another with DMSO as a control. The second stage involved determining the optimal conditions for microsome (endoplasmic reticulum) isolation to set up an in vitro assay to study nucleotide regulation of Lipin1 association with the endoplasmic reticulum. HCC-1806 cells were suspended using either a hypotonic or isotonic buffer and mechanically lysed with either a Dounce homogenizer or a Parr cell disruption vessel. The total lysate then had the nuclei, cytosol, and microsomes isolated and collected through centrifugation. These were then analyzed using a Western blot for the endoplasmic reticulum associated BIP protein, as well as the cytosolic S6K protein.
Results: Observation using an immunofluorescent light microscope showed increasing nuclear translocation of the HA-conjugated Lipin1 with increased length of treatment with 5-FU. This translocation was not found in the DMSO treated controls, but was not as complete as with the torin treatment, which is a known translocator of Lipin1. The processed Western blots exhibited an increased and isolated BIP protein in the combined Dounce homogenizer and isotonic solution condition, with a similar result for the S6K protein.
Conclusions: The nuclear translocation of Lipin1 under immunofluorescent microscopy confirms that 5-FU treatment likely increases the transcriptional co-activator function of Lipin1, as indicated by the increasing amounts of translocation with the increasing amount of treatment. The microsome isolation and Western blots present a pattern that shows that an isotonic solution with a Dounce homogenizer is the most efficient way of isolating both the nucleus and the microsome, which will be useful for future Lipin1 translocation studies.

ABSTRACT

Reorganization of language enables safe resection of tumors in and around Broca's area

EMMA HOLMES *McGovern Medical School at THealth* *Class of 2022*

Sponsored by: Nitin Tandon, MD, Department of Neurosurgery
Supported by: Nitin Tandon, MD, Department of Neurosurgery; McGovern Medical School – Office of Educational Programs
Key Words: Broca's area, glioma, reorganization, aphasia, awake craniotomy, cortical language mapping

Introduction: Since its discovery in the 1800s, Broca's area has been viewed as a critical node for language production. Previously, pathologies in this area have been considered unresectable due to concern for producing iatrogenic language production deficits. Emerging literature suggests that although acute lesions in this area can cause widespread deficits, slow growing lesions are less correlated with these deficits due to cortical language reorganization. Based on this data, we managed a cohort with Broca's area lesions with surgical resection using awake intra-operative language mapping.

Methods: All 150 awake craniotomies performed by the senior author over a twelve-year period (2006-2017) at a single institution were reviewed. For each patient the imaging was carefully evaluated to localize the neoplasm relative to pars triangularis or pars opercularis in the language dominant hemisphere. Language dominance was confirmed using WADA testing or fMRI. All patients underwent cortical language mapping using a battery of tasks coupled with cortical stimulation.

Results: A total of 31 surgeries and 29 patients (65.5% male, 86.2% righthanded) were identified. The average age was 41. Patients presented with seizures (64.5%), speech difficulties (35.5%) or headaches (19.4%). A gross or near total resection was achieved in 26/29 (89.7%) of patients. Pathological evaluation revealed grade 2 gliomas (8), grade 3 gliomas (13) and glioblastoma (9). Post-operatively, 8 (25.8%) patients had new or worsening speech deficits, all of which resolved to baseline at follow-up.

Conclusions: Broca's area lesions can be safely resected in patients using an awake craniotomy technique with language mapping. In our series, the majority of patients had gross or near total resections, few patients had new deficits, and none had permanent new deficits. Considering the increasing evidence in favor of cytoreduction to manage glial neoplasms, this technique should be employed routinely for pathologies in this area to optimize patient outcomes.

ABSTRACT

Effect of Immune Activation on the Kynurenine Pathway

CHARLOTTE P HUNT *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Sudhakar Selvaraj, MD, PhD, Department of Psychiatry and Behavioral Sciences
Supported by: Sudhakar Selvaraj, MD, PhD, Department of Psychiatry and Behavioral Sciences
Key Words: Inflammatory challenge, cytokines, interferon

Introduction: The kynurenine pathway accounts for 95% of tryptophan (TRP) metabolism. It produces metabolites collectively known as kynurenines, and studies suggest that their altered levels play a role in psychiatric and neurodegenerative diseases. The kynurenine pathway begins with the conversion of TRP to N-formyl-L-kynurenine, a rate limited reaction activated by either Trp 2,3-dioxygenase (TDO) mainly in the liver or by indoleamine 2,3-dioxygenase (IDO) outside the liver. Evidence shows that cytokines and other molecules associated with inflammation increase the activity of IDO as well as its gene expression. Further, N-formyl-L-kynurenine can be further broken down into 3-hydroxykynurenine, 3-hydroxyanthranilic acid, and quinolinic acid – all of which are free radical generators that are considered to be neurotoxic. We conducted a systematic review to assess the effect of the clinical use of immune activation treatments or experimental inflammatory challenge and measured changes in kynurenine metabolites in humans. We predict that the administration of inflammatory challenge will result in decreased TRP and elevated KYN and IDO activity index (KYN/TRPx1000).
Methods: We conducted a systematic review to study the relationship between inflammatory challenge, particularly interferon alpha, and plasma kynurenine metabolite levels. Eligibility criteria included: 1) English language articles, 2) human in vivo studies, 3) case-control studies in which an immune activation agent or inflammatory challenge is administered and serum kynurenine metabolites are periodically measured. Articles were deduplicated then assessed by two independent reviewers for eligibility. Demographic information and kynurenine metabolite data were then systematically extracted for analysis.
Results: With our search algorithm on Medline, Embase, Cochrane Library, and PsychINFO, 5082 articles were identified, of which 1281 duplicates were removed, 3740 abstracts were excluded, and 32 full text articles were excluded. Our final analysis included 10 articles, looking at the levels of TRP, KYN, and IDO activity index at baseline and 24 weeks post treatment with interferon alpha. At 24 weeks of interferon treatment, our results showed that TRP levels had a mean difference of -0.83 compared to baseline ($p < 0.001$), KYN levels had a mean difference of 0.55 ($p < 0.001$), and IDO activity index had a mean difference of 0.99 ($p < 0.001$).
Conclusion: Significant decrease in TRP and increases in KYN and IDO activity index indicate a relationship between inflammation and the increase in kynurenine metabolites. Further research can be done to evaluate the exact relationship between these metabolite levels and mood and cognition.

ABSTRACT

Anti-CD73 Therapy for Pancreatic Ductal Adenocarcinoma

AMRUTHA IMMADI *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Jennifer M. Bailey, PhD, Department of Internal Medicine – Gastroenterology, Hepatology, and Nutrition
Supported by: Jennifer M. Bailey, PhD
Key Words: CD73, Adenosine, Pancreatic Ductal Adenocarcinoma, Immunotherapy

Introduction: CD73 is an attractive molecule for cancer therapy and immunotherapy because of its history as a key enzyme involved in dampening inflammatory responses in inflamed and hypoxic tissues (conditions common to tumor microenvironments). CD73-generated adenosine has recently been shown to have profound immunosuppressive actions and pro-angiogenic activity in the tumor microenvironment and a number of pre-clinical models have shown targeting CD73 has positive anti-tumor effects. For these reasons, we hypothesized that CD73 generated adenosine is a critical promoter of pancreatic cell proliferation and that adenosine receptor signaling is important for PDAC growth.

Methods: To identify pathways upregulated on murine cell of origin PDAC models, we performed RNA-Sequencing and confirmed with western blot analysis that CD73 expression was highly expressed in tumors arising in pancreatic ducts and is highly increased in human PDAC cell lines. To define the contribution of CD73 generated adenosine and adenosine signaling in PDAC, we performed in vitro studies using CD73 and A2bR inhibitors and assessed cell proliferation with MTT assays. As an in vivo complement to our in vitro work, we treated murine pancreatic cancer models with APCP, a potent inhibitor for CD73, to determine if inhibition of adenosine generation in vivo perturbed PDAC growth.

Results:

Our unbiased RNA-Seq data and ingenuity pathway analyses identified the ecto-5'-nucleotidase (*nt5e*/cd73) and adenosine receptor *adora2b* to be highly expressed in PDAC derived from KPC^{Duct} mice. CD73 is an ectoenzyme that converts precursor nucleotides to extracellular adenosine, thereby functioning as pace-maker for extracellular adenosine generation and signaling through 4 adenosine receptors (A1, A2A, A2B and A3). In confirmatory studies using real-time PCR, western blotting, and immunohistochemistry, we verified extremely high levels of CD73 and A2B in murine and human specimens of PDAC. Using HPLC, we observed significantly elevated adenosine production in human PDAC cell lines compared to controls, indicating elevated CD73 activity in PDAC. We also observed significantly elevated Ado in the supernatant of PDAC cells compared to controls. To address the functional role of CD73 and A2B in PDAC, we used specific pharmacologic inhibitors of CD73 (APCP) and A2B (PSB1115). APCP or PSB1115 treatment significantly reduced *in vitro* proliferation of human or murine PDAC cells. Similarly, treatment with APCP or PSB1115 of KPC^{Duct} mice revealed a dramatic reduction in ductal derived murine PDAC and survival improvements.

Conclusion:

Our data support the hypothesis that targeting adenosine generation and signaling through A2B is important for PDAC development and proliferation. Future experiments will include analysis of immune cell populations in APCP and PSB1115 treated mice to determine if inhibition of adenosine alters inflammatory cell populations in vivo.

ABSTRACT

Determination of Optimal Deployment Strategy for REBOA in Patients with Non-Compressible Hemorrhage Below the Diaphragm

NICHOLAS JOHNSON *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Laura J. Moore, M.D.
Supported by: Center for Translational Injury Research (CeTIR)
Key Words: REBOA, hemorrhage, algorithm

Objective: The purpose of this study was to evaluate the efficacy of an established clinical algorithm for use of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA).
Introduction: Non-compressible truncal hemorrhage is the leading cause of potentially preventable death in trauma patients. Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a less invasive alternative to resuscitative thoracotomy for aortic occlusion in the setting of severe hypotension due to non-compressible hemorrhage below the diaphragm. Aortic zone selection strategies vary among institutions, and between civilian and military environments, without consensus on the most effective algorithm for use.
Methods: Prospective, observational study conducted at 6 Level 1 Trauma Centers over 12-months. Inclusion criteria were age >15 years of age with evidence of truncal hemorrhage below the diaphragm with decision for emergent hemorrhage control intervention within 60 minutes of arrival. An algorithm characterized by the results of Focused Assessment with Sonography in Trauma (FAST) and pelvic x-ray was assessed for efficacy. In order to directly assess the algorithm of interest, patients were excluded that indicated any of the following: no FAST exam, an indeterminate FAST exam, a positive cardiac FAST exam, or unknown primary bleeding source. This exclusion is specific only to analysis regarding the direct impact of the algorithm, leaving 58 cases for assessment. Assessment of the relationship between correct zone selection and patient outcomes requires less selective exclusion involving only patients with unknown primary hemorrhage source, leaving 72 cases for assessment.
Results: Over 12 months, 8,166 patients were screened for enrollment. In 79 patients, zone 1 or zone 3 REBOA was utilized. The algorithm accurately predicted the correct zone for REBOA deployment in 79.3% of analyzed cases. Of the 37 patients that received a zone 1 REBOA, 4 patients (10.8%) received a zone 1 that was contraindicated according to the algorithm. Patients with a contraindicated zone 1 REBOA had a mortality of 75%, while patients with an indicated zone 1 REBOA had a mortality of 63.6% (p=0.65). Of the 21 patients that received a zone 3 REBOA, 13 patients (61.9%) received a zone 3 that was contraindicated according to the algorithm. The 13 patients with a contraindicated zone 3 REBOA had a mortality of 23.1%, while the 8 patients with an indicated zone 3 REBOA had a mortality of 25% (p=0.92). With regard to zone 1 REBOA complications in patients that survived more than 24 hours after ED admission, we found that patients that received a zone 1 REBOA had a 26.1% incidence of Multiple Organ Failure (MOF) while patients that received a zone 3 REBOA had a 4% incidence (p=0.03). We also found that patients that developed MOF had a mean occlusion time of 100 minutes and those that did not develop MOF had a mean occlusion time of 41 minutes (p<0.03).

Conclusions: The evaluated algorithm, based on FAST exam and pelvic x-ray, accurately predicts the primary source of hemorrhage in patients with no association between algorithm adherence and patient outcomes, likely due to low sample size. Further large-scale study is warranted to evaluate the existence of any associations between algorithm adherence and patient outcomes.

ABSTRACT

Factors Associated with Receiving Regional Anesthesia in Pediatric Appendectomy Patients

PRANALI KAMAT *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Mary T. Austin, MD, MPH, Department of Pediatric Surgery
Supported by: Mary T. Austin, MD, MPH, Department of Pediatric Surgery; McGovern Medical School Office of the Dean
Key Words: pediatric surgery, regional anesthesia, quality of care

Introduction: Regional blocks have been shown to effectively decrease pain after abdominal surgery, and some evidence suggests they also reduce postoperative opioid consumption. Despite their valuable analgesic effects, regional blocks are not routinely used in many pediatric abdominal procedures. We aimed to identify factors associated with regional block use in pediatric appendicitis.

Methods: We performed a retrospective review of all pediatric (<18 years) patients who underwent laparoscopic appendectomy for acute appendicitis between January 1, 2018 and April 30, 2019 at a single institution. Patients who underwent open or interval appendectomies were excluded. The primary outcome was perioperative receipt of a regional block. Factors thought to influence regional block utilization were chosen a priori based on prior literature and clinical knowledge and included patient age, gender, weight, race/ethnicity, insurance status, diagnosis (simple versus complicated appendicitis), time of surgery, weekday versus weekend surgery, and case duration. Univariate analysis and multiple variable logistic regression were performed.

Results: Of 546 patients who met inclusion criteria, 103 received regional blocks (19%). Of those, 73% received a quadratus lumborum block and 24% received a transversus abdominis plane block (block type not specified in 3%). On univariate analysis, block and no-block patients were similar by age, gender, weight, race/ethnicity, insurance status, and surgical diagnosis ($p>0.3$ for all comparisons). Block patients underwent weekday surgery more frequently than no-block patients (87% vs. 68%, $p<0.001$). The majority (76%) of blocks were performed between 7am and 1pm (n=79). After adjusting for age, gender, weight, race/ethnicity, insurance status, diagnosis, case duration, weekday versus weekend, and time of day, weekday surgery was the only factor independently associated with receiving a regional block (adjusted OR 3.6, 95% CI 1.9-6.7).

Conclusion: Weekday surgery was independently associated with receiving a regional block in pediatric appendicitis patients. Availability of an anesthesiologist who is trained to perform blocks and/or time constraints may currently be the primary determinant of regional block

utilization. Training more anesthesiologists to perform blocks may increase use and improve pain control in this population.

ABSTRACT

A Wavelet Approach for Improving Signal in BOLD Latency Analysis

EMMETT KENNADY *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Dr. Manish N Shah, MD, Department of Pediatric Surgery and department of Neurosurgery
Supported by: Dr. Manish N Shah, MD, Department of Pediatric Surgery and department of Neurosurgery; McGovern Medical School- Office of the Dean
Key Words: Wavelet despiking, resting-state functional MRI, latency analysis, pediatric refractory epilepsy, BOLD, XGBoost, Machine learning

Background: One in 300 children are diagnosed with epilepsy. The mainstay treatment of these patients is anticonvulsant medications; however, one-third of these patients will be refractory to these medications and will require surgery. Developing a non-invasive screening method to rapidly detect refractory cases can greatly improve patient outcomes. One strategy to try to identify epileptic patients is through BOLD blood oxygen dependent (BOLD) signal latency analysis. We hypothesize this signal can be used to identify epileptic foci in the brain. In latency analysis the better the fMRI signal, the better the predictive value of refractory epileptic will be. The current accepted method for denoising head movement artifacts during MRI acquisition is frame scrubbing, which often removes a significant portion of data. This study implements a newly established denoising method, wavelet despiking, to improve the quality of data and ultimately create a better screening tool to identify pediatric patients with refractory epilepsy.

Methods: Pre-surgical fMRI and anatomical MRI scans were prospectively obtained from 58 epileptic patients and 322 healthy control patients from the ADHD 200 data set. The MRI scans were then processed and registered using standard MRI protocol. Latency maps of these patients were generated using voxel-wise cross-covariance BOLD signal and global mean BOLD signal. Voxel-wise latency z-score maps were created for patients using healthy control mean and standard deviation maps. The frame scrubbing method in the MRI processing pipeline was replaced with the wavelet despiking method and previous methods were repeated. Patients from both denoising methods had machine learning features extracted using principle component analysis (PCA). The XGBoost machine learning algorithm was trained on the PCA features of latency z-score maps and the hyperparameters were adjusted using validation data. Epilepsy prediction performance of algorithms were analyzed using area under the curve, accuracy, specificity, precision, and sensitivity. The statistical measures of the validation algorithms for both wavelet despiking and frame scrubbing z-maps were then averaged.

Results: Qualitative analysis of latency z-score maps using the wavelet despiking method seemed to have better localization of foci with less noise relative to the frame scrubbing method. The XGBoost validation algorithms for the wavelet despiking method (n=12500) were significantly greater ($p<0.0001$) in AUC, accuracy, precision and sensitivity over the frame scrubbing method (n=12500). The frame scrubbing method had a greater ($p<0.0001$) specificity over the wavelet despiking method.

Conclusions: Wavelet despiking has a greater sensitivity (0.73) for refractory epilepsy screening relative to frame scrubbing (0.51) likely due to superior preservation of original

signal and artifact removal. Future direction of this project is to use a standardized pre-processed data set and collect additional patient data for more powerful machine learning prediction.

ABSTRACT

Pediatric Mock Codes and Performance in Sepsis and Trauma Settings

NEIK KHANSARI *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Donna Mendez, MD EdD, Pediatric Emergency Medicine
Supported by: UTHealth McGovern Medical School, Department of Emergency Medicine
Key Words: Mock codes, intubation, antibiotics

Background: The annual incidence of pediatric codes is just 12,135. This number is very low compared to that of adult codes, which occur at 535,000 annually. A pediatric code is defined as a child who is in need of resuscitation or immediate medical attention. This is usually due to cardiac or respiratory events. Mock codes have been shown to improve confidence and knowledge of nurses and physicians. However, there is a lack of studies investigating the effect of pediatric mock codes on patient outcomes in real cardiopulmonary events.
Significance: Participation of nurses and residents in mock codes may lead to improvement in code performance in real emergency situations, specifically in sepsis and trauma settings.
Methods: Participants of this study include nurses and residents at the TMC Memorial Hermann ED. Outcome measures were analyzed before (2015) and after (2017) the start of their participation in mock codes. Some studies have included mock codes that were performed in a simulation center. In this study, mock codes were performed in the emergency department to simulate a real setting where emergencies take place.
Outcomes were measured based on two categories: time to administration of antibiotics and time to intubation. Time to antibiotics will be analyzed in sepsis patients (N=260), while time to intubation will be assessed in trauma patients (N=49). The Pediatric Critical Care Guidelines (PALS) state that the expected time to administration of antibiotics in the case of sepsis is <1 hour, while the expected time to intubation in trauma patients is within the first 15 minutes (0.25 hours).
Results: In the case of sepsis patients, median time to administration of antibiotics before mock code participation was 3.62 hours (IQR 2.23-6.42), while time to antibiotics after mock codes was 3.13 hours (IQR 1.83-6.25). Thus, time to administration of antibiotics decreased but was not statistically significant (Log-rank test P value=0.43). With trauma patients, median time to intubation before mock code participation was 0.28 hours (IQR 0.1-0.52). Time to intubation after mock codes was 0.33 hours (IQR 0.1-0.88). This increase in time to intubation was not significant (P=0.14).
Conclusions: The premise of mock codes in the pediatric emergency setting is promising and has the potential to improve performance and thus patient outcomes in real codes. Future studies should focus on the effect of mock codes on other outcome measures, such as time to chest compressions and administration of fluids.

ABSTRACT

Characterization of HDACi-Loaded Cyclodextrin Nanoparticles

BRANDON KNIGHT *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Rachael W. Sirianni, PhD, Vivian L. Smith Department of Neurosurgery
Supported by: Rachael W. Sirianni, PhD, & McGovern Medical School Dean's Office Stipend
Key Words: Cyclodextrin, Nanoparticles, HDAC Inhibitors

Background: Every year, 16,000 patients in the US die from CNS cancers, including over 1,100 pediatric cancer patients. Traditional systemic chemotherapies offer poor penetration into the CNS and produce systemic side effects. Delivery of chemotherapeutic drugs directly into the CNS, such as intrathecally (IT) (injection into the subarachnoid space), combats the negatives of systemic administration by delivering high concentrations of drug to the CNS while maintaining low systemic drug concentrations, thereby lowering systemic side effects. However, IT-delivered free drugs display expedient clearance from the CNS, as well as potential neurotoxicity from bolus administrations. Therefore, improved methods of IT drug delivery are necessary. Nanotechnology holds great promise for improving treatment outcomes in CNS cancer patients, as drugs that are encapsulated in nanoparticles show longer lifetime *in vivo*, improved tolerability, controlled release, and tissue-specific targeting capabilities.

Purpose: The purpose of this research was to characterize new formulations of HDAC Inhibitor (HDACi)-loaded Cyclodextrin Nanoparticle (CDNs). We hypothesized that multiple types of HDACi chemotherapy drugs could be loaded in CDNs, and that characterization of these would allow selection of HDACi-CDN formulas capable of optimally prolonging drug activity in the CNS while decreasing toxicity.

Methods: Four formulations of CDNs were synthesized via polymerization of Cyclodextrin and diacrylate, with the addition of amine or Polyethylene Glycol (PEG) sidechains. Comparisons of formulations include; varying length of diacrylate linkers (increasing intra-nanoparticle free volume), varying amine sidechain length (short versus long), and varying sidechain groups (amine vs PEG). Blank and HDACi panobinostat-loaded CDNs were characterized by size, zeta potential, drug loading efficiency, and timed drug release. After initial characterization, new batches of CDNs were loaded with the HDACi's quisinostat, dacinostat, and camptothecin, to measure drug loading efficiency and release profiles of those specific CDNs.

Results: Quisinostat displayed the highest panobinostat loading across all amine CDNs, while PEG CDNs loaded best with Camptothecin. Panobinostat-loaded PEG CDNs showed sustained drug release of 90% at 15 days, while two panobinostat amine CDN formulations released drug more quickly, 90% at 3 days. The PEG CDNs were found to have a neutral-mildly negative zeta potential, while the other drug loaded CDNs had positive zeta potentials. Based on these zeta potential measurements, theoretical mechanisms of CDN-drug loading were developed.

Conclusions: Cyclodextrin nanoparticles displayed high drug loading potential and extended release profiles. A library of HDACi-loaded CDNs was made to allow optimized selection of CDN-HDACi combinations for various applications.

ABSTRACT

Blood Pressure Responses to Exercise in Thoracic Aortic Disease

Jesse Li *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Siddharth Prakash, MD, PhD, Department of Internal Medicine
Supported by: Siddharth Prakash, MD, PhD, Department of Internal Medicine
Key Words: Thoracic aortic aneurysm, thoracic aortic dissection, ambulatory blood pressure

Background: Current guidelines for patients with thoracic aortic aneurysms or thoracic aortic dissections are to minimize exertion to prevent acute dissection. High blood pressures However, a safe threshold of exertion levels has not been well characterized, and a low level of activity levels in patients predisposes to other cardiovascular diseases. In this study, we aimed to characterize the systolic and diastolic blood pressure changes in patients with thoracic aortic aneurysms or dissections upon engaging in different forms of isometric and dynamic exercises compared to the blood pressure changes in a control population.

Methods: Patients were recruited from cardiology and vascular surgery clinics at Memorial Hermann and UT Professional Building. Eligible patients (n=41) were contacted by phone and consented in clinic following their appointment. Consented patients (n=12) and controls (n=15) both underwent the same exercise protocol consisting of five moderate exercises: hand grips, planks, bicep curls, stationary bicycle, and wall sit. Blood pressure values were recorded during exercise using Spacelabs OnTrak Ambulatory Blood Pressure monitors (ABPM) and analyzed using Spacelabs Sentinel software. Patients and controls also completed a questionnaire regarding demographic data and weekly exercise levels.

Results: Peak systolic blood pressures (SBP) and diastolic blood pressures (DBP) of patients and controls during exercise were compared and no significant difference was found in any of the exercises. However, patients had significantly elevated changes in SBP from baseline compared to controls (p=.04). In addition, increasing levels moderate activity levels reported in the questionnaire correlated with lower SBP and DBP in each exercise among patients upon linear regression analysis. Vigorous activity levels did not have a strong correlation with either SBP or DBP in patients for each exercise.

Conclusion: The study results suggest that most moderate exercise are safe for patients as no significant increase in SBP or DBP was found compared to controls. Also, increased amounts of moderate activity appear to correlate with lower SBP and DBP during exertion in patients, which would reduce the risk of acute dissection. However, as patients demonstrated a significant change from baseline in wall sits compared to controls, further research should be done to clarify what component of that exercise is contributing to elevated BP. This study is ongoing and a larger and more diverse sample size will help to ascertain the significance of the current findings, with the eventual aim of establishing firmer guidelines for exertion in patients with thoracic aortic disease.

ABSTRACT

10-week Pain Program in Patients with Amputations or Limb Salvage Procedures

KOMAL LUTHRA *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Danielle H. Melton, M.D., Department of Orthopedic Surgery
Supported by: Danielle H. Melton, M.D., Department of Orthopedic Surgery
Key Words: Chronic pain, phantom pain, opioids, amputations, physical therapy, neuroplasticity

Introduction: The opioid epidemic has become a major issue in the United States. According to the U.S. Department of Health and Human Services, over 130 people die every day from opioid overdose, and 11.4 million people misuse prescription opioids. Opioid dependence is common among patients suffering from chronic pain due to limb loss and limb salvage. Several pharmacological approaches have been used to address pain in these patients, but there is a need for more research to address how non-pharmacological and non-invasive methods can be used for pain management. This study aimed to determine the effectiveness of a structured 10-week pain program that takes a multifaceted approach in reducing pain. We hypothesized that patients in the pain program will show reductions in pain levels and opioid usage, and increased functional improvement compared to non-pain program individuals.

Methods: Patients between 18 to 70 years old with chronic pain from limb loss or limb salvage who are taking narcotics as a part of their medication regimen and followed up in wellness clinic were offered enrollment in the pain program as an alternative or adjuvant treatment to opioids. The 10-week pain program consisted of surveys, functional assessments, education, sensory discrimination, mirror therapy, breathing exercises, aerobic exercises, and homework activities. Patients completed the four Patient-Reported Outcomes Measurement Information System (PROMIS) surveys (pain intensity, pain interference, physical function, and satisfaction role), Prosthetic Limb Users Survey of Mobility (PLUS-M 12Q) for those with lower limb involvement or QuickDASH Disabilities of the Arm, Shoulder and Hand survey (QuickDASH 11Q) for those with upper limb involvement at 3 time points: week 1 (pre), week 5/6 (midpoint) and week 10 (post). In addition, they completed a weekly Visual Analogue Scale (VAS) based pain log and medication list. Patients were asked to create goals for functional activities, pain levels, and reduction in opioid use.

Results: 4 patients completed the program, and 2 were lost due to drop-out. There were compliance issues in the completion of surveys and attendance of physical therapy sessions consistently every week. Over the course of the study, we noticed small changes in the patient reported surveys including PROMIS, PLUS-M, and Q-DASH. The objective functional assessments showed no significant improvement in 6MWT, 10MWT, and the TUG. Lastly, there were no significant changes in opioid usage among the 4 patients.

Conclusion: Preliminary data from this ongoing study shows promise, although we are unable to draw conclusions until more patients complete the program over the coming year. Completion of this project will establish a benchmark for clinical efficacy of the program which will guide the direction of future studies. Future directions of this research program will include understanding subject rationale for compliance/non-compliance, establishing patient-centered tools to monitor their progress, and to create processes that make program completion easier for patients.

ABSTRACT

Body Composition Affects Occurrence of Chronic Critical Illness in Trauma Patients With Blunt Injury

MORGAN K. LYNCH *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Sasha D. Adams, MD, FACS, Department of Surgery
Charles E. Wade, PhD, Department of Surgery
Supported by: CeTIR
Key Words: Chronic critical illness, body composition, CT scan, trauma

Introduction
Chronic critical illness (CCI) is a condition characterized by prolonged ICU stays and persistent organ dysfunction and is commonly followed by decreased functional status and survival. Recent research suggests that the mechanism of CCI is formed by an interplay of persistent inflammation, immunosuppression and catabolism. The role of body composition in the initiation and continuation of CCI suggests the utilizing early imaging analysis to identify patients in need of more aggressive nutritional and physical intervention. For trauma patients, the use of CT scan analysis of body composition has been shown useful in prediction of patient outcomes. We hypothesize that body composition is a contributor to the occurrence of CCI.

Methods
We conducted a retrospective review of 366 trauma patients with body composition determined by admission CT scan. Aquarius radiological software was used to determine body composition values: subcutaneous fat (SubQ), visceral fat (Visc), psoas muscle (Psoas), bone density (BD). Patient demographics and outcomes were obtained from patient records. CCI was defined as an ICU stay of 14 days or longer. For the matched-pairs cohort, paired t test and Bonferroni adjustment were used for comparing body composition variables. A conditional logistic regression model was used for estimating odds ratio of Visc. All significance defined as $p<0.05$.

Results
Of the 366 patients, we excluded all deaths (72), penetrating injuries (25), and patients not admitted to the ICU (62), leaving 207 for evaluation. Of those, 52 (25%) were found to have CCI. Upon multivariable analysis, we identified ISS as the dominating factor in the occurrence of CCI. We constructed 43 matched pairs of CCI with non CCI by controlling for ISS (within ±3), TBI (AIS >2), and sex. There was a significant difference in median length of ICU stay 19 (IQR 15, 23) days for CCI vs 4 (3, 10) days in non CCI, as well as more ventilation days, 13 (8, 18) vs 2 (1, 4), and longer hospital length of stay 26 (19, 46) vs 14 (7, 22) days. CCI patients had an increased incidence of complications (77% vs 33%). Visc was 1.5x greater in the CCI patients (Table). Comparison of Visc >120 vs <70 sq cm had an OR 5.01 (95% CI 1.25-20.12, p=0.023). No other differences were found in body composition that related to CCI.

Conclusions
In patients with blunt traumatic injuries, severity of injury is the main determinant of CCI occurrence. Visceral fat as measured on CT is independently associated with CCI, and CCI

patients have more ventilator days, longer length of hospital stay and increased complications.

ABSTRACT

Examination of Thromboelastograph Values in Patients with Severe Liver Disease

MANON MASSON *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Evan G. Pivalizza, MBChB, FFA, Department of Anesthesiology
Supported by: Evan G. Pivalizza, MBChB, FFA, Department of Anesthesiology
Key Words: Thromboelastograph, Liver Disease, Coagulation

Background: Patients with liver disease were long thought to be in a constant hypocoagulable state, however recent studies have proposed the concept of a compensatory response in liver patients called rebalanced hemostasis. As a result, traditional coagulation studies, such as PT/INR, can be misleading because they focus only on procoagulation factors rather than assess the entire rebalanced hemostatic system. An alternative test is the Thromboelastograph (TEG), a viscoelastic hemostatic assay that analyzes the dynamic, global properties of whole blood coagulation, including fibrin formation and clot strength. The aim of this study is to compare and correlate traditional coagulation studies with TEG measurements in patients with severe liver disease. We predicted that TEG values, when compared to traditional coagulation studies, will provide a more accurate report of overall hemostatic status in this patient population.

Method: Eligible participants include adult patients with severe liver disease presenting to Memorial Hermann TMC for a procedure requiring anesthesia from late May-July 2019. The surgery schedules were reviewed daily, and potential participants were identified for screening. Inclusion criteria were patients with recent laboratory studies that reported low platelet count (≤130,000/mm^3), elevated INR (≥1.4) and elevated aspartate aminotransferase (AST; ≥37 U/L) or alanine aminotransferase (ALT; ≥55 U/L). Exclusion criteria included use of anticoagulation medication, recent blood product transfusions, and recent hospitalization. If the patient consented to participate in the study, two vials of blood were collected from an existing arterial or venous line. The blood samples were then analyzed with the TEG.

Results: About 385 potential patients were screened, but many did not have sufficiently severe laboratory abnormalities; 10 patients met inclusion criteria, and 9 blood samples were collected (1 patient was lost due to a scheduling error). Statistical comparison analysis was limited due to small sample size. Mean age was 55.11 (SD=12.21) years with 22% being female. Liver dysfunction was notable with a mean platelet count of 71.44 (41.45) /mm^3, INR 1.6 (0.47), and mean AST and ALTs of 81.44 (49.94) U/L and 56.56 (45.41) U/L, respectively. Despite the abnormal INR, the corresponding TEG parameter, R-value, which measures clot formation time, was within normal limits (normal R-value = 3-8 min; sample mean=5.46 (1.54) min).

Conclusion: With this small study sample of patients with severe liver disease, the TEG measurements did not reveal hypocoagulability as severe as predicted by the abnormal INR. The TEG parameters, like R-value, showed more stable global hemostasis despite an

abnormal INR. However, additional subject enrollment is required to support this hypothesis. Continued enrollment would also allow for examination of the correlation between whole blood and plasma-based tests.

ABSTRACT

Gamma-Tocotrienol Increases Osteoblast Function and May Improve their Function after Exposure to Electronic Cigarette Liquid Which May Decrease Osteoblast Function

WYLIE MASTERSON *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Catherine G. Ambrose, MD, Orthopedic Surgery
Key Words: Orthopedics, Osteoblast, Electronic-Cigarette, Nicotine

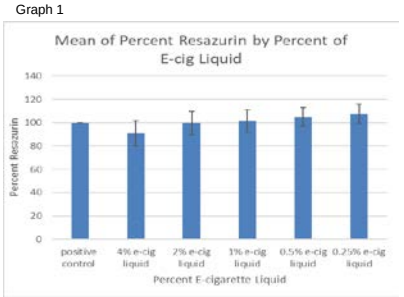
METHODS**:** Human osteoblast cells were isolated from discarded bone during surgical procedures according an IRB approved protocol. The cells were then cultured in media containing in 2/3rds low-glucose and 1/3rds high glucose DMEM with 10% FBS and 1% antibiotic/antimycotic. The media was changed every 48 hours. The cells at passage 2, 3, and 4 were plated into two 96-well plates. When the plates were 80% confluent, one plate that came from each flask was incubated in 1uM gamma-tocotrienol in new culture media for 24 hours while a second plate from each flask was cultured with media that did not contain gamma-tocotrienol. After the incubation period, all plates were analyzed with a resazurin assay to assess metabolism, lysed, and frozen. The plates were thawed and total protein (TP) and alkaline phosphatase (AP) assays were run to assess cell's synthetic ability. To determine the effect of e-cigarette liquid, cells at passage 2, 3, and 4 were plated into two plates grown to 80% confluence and incubated in 4%-0.02% e-cigarette liquid for 24 hours. After a 24 hour incubation period with e-cig liquid, one of the plates from each flask was incubated in 1uM gamma-tocotrienol while the other plate from each flask was incubated without tocotrienol.

RESULTS: Human osteoblasts incubated in 1 uM gamma-tocotrienol had significantly increased cell viability, percent total protein, and percent alkaline phosphatase (p=0.001, p=0.029, p=0.001) see table 1. The AP production normalized by TP content was not significant. Osteoblasts treated with e- cig fluid demonstrated a dose dependent decrease in viability, TP, and AP at different e-cig fluid concentrations, but the differences were not significant (see Graph 1). While it appeared that treatment with gamma-tocotrienol after nicotine resulted in higher viability, AP, and TP values (see Graph 2), the differences were not significant.

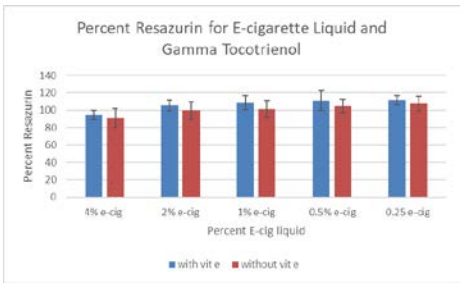
DISCUSSION: The data demonstrate that osteoblasts treated with gamma-tocotrienol significantly increased their proliferation, which is consistent with the current literature on the effect of tocotrienol on osteoblasts and fracture healing. There is more work to be done with e-cig fluid. Our data suggest that e-cig fluid could have a dose dependent effect, which is consistent with current literature that nicotine at high concentrations decreases viability and at low concentrations increase viability. Future studies will investigate multiple types e-cig fluid, study a wider range of e-cigarette fluid concentration and will also increase the nicotine incubation time to 48 and 72 hours.

Table 1		Mean	Std. Deviation	p-value
Percent Resazurin	positive control	100.00	0.00	0.001
	gamma-	109.91	9.08	
Percent AP	positive control	100.00	0.00	0.001
	gamma-tocotrienol	121.40	20.43	
Percent TP	positive	100.00	0.00	0.029
	gamma-tocotrienol	125.03	17.46	
Percent AP/Percent TP	positive control	1.00	0.00	0.290
	gamma-	0.91	0.16	

Graph 1



Graph 2



ABSTRACT

The Minimal Clinically Important Difference of an Abdominal Wall Quality of Life Survey

NIHARIKA NEELA *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Mike Liang, MD; General Surgery Department
Supported by: Mike Liang, MD
Key Words: Minimal clinically important difference for abdominal wall QOL

Introduction:
The minimal clinically important difference (MCID) is the smallest change in patient derived scores that represents a clinically important change to the patient and not just variation due to repeat testing. The MCID is a better indicator for change in health status than statistical significance. Hernias are known to impact abdominal wall quality of life (AW-QOL). We previously reported the MCID for a validated, hernia-specific AW-QOL survey, the modified activity assessment scale (mAAS), ranged from 7-14 based upon statistical distribution of a one-time measurement of 150 patients. Therefore, we sought to validate the MCID of the mAAS, using both a patient centered and statistical approach.

Methods:
This is a prospective observational study. On this survey, 1 = poor and 100 = perfect QOL. Patients were surveyed prior to undergoing computed tomography abdomen/pelvis scans and resurveyed one year later. Both anchor (patient-centered) and distribution (statistical) based approaches were used to estimate the MCID. Prior to re-survey a year later, patients were asked if they had a worsening or improvement in their AW-QOL, which established the basis of the anchor-based approach. Patients who reported no change were the control (no clinical difference) and the patients who reported a change (improved or worsened) were considered in the study groups (clinically important difference). The MCID was calculated by taking a weighted average of the difference between the control and study groups. Distribution-based approach was also performed using a widely accepted method of calculating one-half of the standard deviation in the change of quality of life of the entire cohort.

Results:
Overall, 181 patients were followed at 1 year: 95 (52.8%) self-reported no change (control), 71 (39.2%) reported improvement, and 15 (8.3%) reported worsening of their AW-QOL. The control group's mean (standard deviation) change was -1.3 (31.4) while those who self-reported improvement changed by +2.4 (32.9), and those who worsened declined by -6.3 (23.3). The weighted average difference in AW-QOL between control and study groups was 4 for the anchor-based approach. Utilizing the distribution-based approach, the overall change in AW-QOL was -0.3 (31.4) and the MCID was 16.

Conclusion:
Our study results refine and validate prior work demonstrating similar ranges of the mAAS MCID. Understanding the MCID is important when comparing the effectiveness of treatments on patient-centered outcomes. Utilizing weighted averages of current and published MCIDs, we recommend standardizing and adopting MCID of 5 and 15 for minor and major changes when assessing AW-QOL using the mAAS.

ABSTRACT

Supplementing Gross Anatomy Curriculum with Anatomy Reference Sheets

DANIEL NGO *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Len Cleary PhD, Office of Educational Programs at McGovern Medical School at UTHealth
Han Zhang MD, Department of Neurobiology and Anatomy at McGovern Medical School at UTHealth
Supported by: Len Cleary PhD, Office of Educational Programs at McGovern Medical School at UTHealth
Key Words: Streamlining Anatomy Education

Introduction: Gross anatomy is a fundamental part of medical education, intertwining with the understanding of basic physiology and disease pathology. It is the foundation upon which a large portion of medical knowledge is based, requiring a significant portion of the time spent in school to learn, and years to master. For the current gross anatomy curriculum at McGovern Medical School, we rely on many of these different resources that play separate roles in the learning process. The multitude of resources can be overwhelming for new students, who are often already having difficulties navigating the large workload that comes with medical school. It can be taxing to sift through and determine what information is the most important to learn, and nearly impossible to cover all the information during the anatomy curriculum. We developed a set of Anatomy Reference Sheets to highlight difficult structures and concepts, standardizes the dissection process, and provide useful clinical correlates and study tips on a single page, thereby minimizing the amount of time spent parsing through resources and more time learning the information. By the end of the anatomy curriculum, students should be able to identify tagged anatomical structures, recall common clinical correlates, and integrate broad anatomical concepts with the system blocks to derive how different pathologic processes may be related.
Methods: Each reference sheet is broken up into four parts. The procedure overview is pulled from the structure lists, which in turn were made by the McGovern Medical School Department of Neurobiology and Anatomy. The clinical correlates are compiled from several different resources including McGovern's previously used anatomy syllabus, the course lectures and related materials, and the recommended textbooks including Moore's Essential Clinical Anatomy, First Aid, and Bate's Guide to Physical Examination. The dissection tips and study tips will come from student and faculty input. Once the sheets have been written each will be reviewed by a small group of students and faculty in order to make adjustments and improvements to better align with the goals of the anatomy curriculum.
Conclusions: The reference sheets have been implemented in the anatomy curriculum for the current first year medical students. Based on preliminary feedback, students have been able to standardize and learn helpful mnemonics, and primarily seem to find the clinical correlate portions most helpful. Further data is being collected after the first exam to assess the efficacy of the reference sheets as well as student feedback through a survey.

ABSTRACT

Parent Perceptions of a Pre-Induction Checklist After Implementation of a Parent-Centered Script

ALI A. NOORBAKSH *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Dr. KuoJen Tsao
Supported by: Dr. KuoJen Tsao – Department of Pediatric Surgery
Key Words: Surgical, Safety, Checklist, Pediatric

Introduction
The 3-phase surgical safety checklist (SSC) was created to reduce perioperative adverse events. Increased SSC adherence has been associated with improved patient outcomes. In pediatric patients, higher parent engagement has been correlated with improved pre-induction SSC adherence by the perioperative team. We created a parent-centered script for the pre-induction SSC to promote involvement of parents. We aimed to evaluate parent perceptions of the pre-induction SSC process before and after implementation of the script.

Methods
A parent-centered script was created to involve parents in checklist items relevant to their knowledge: patient identity, weight, allergies, last oral intake, planned procedure, and surgical site. A survey was conducted in English or Spanish over two 8-week periods before (June-July 2018) and after (June-July 2019) the script was introduced. Parents of children (<18 years) undergoing non-emergent surgeries were surveyed after the pre-induction SSC was completed. Questions addressed parents' involvement in the preoperative process, perceptions of the care team, and safety concerns. If patients underwent more than one surgery during the study period, only the first survey was included. Descriptive statistics and univariate analyses were conducted.

Results
Of 232 surveys, 100 (43%) were administered before and 132 (57%) were administered after the script was implemented. Parent demographics were similar across time periods. Most respondents were mothers (81%), spoke English (80%) and identified as white (63%). Half of those surveyed identified as Hispanic (50%). After script implementation, there was a significant increase in the percentage of parents who strongly agreed that the perioperative team verified their child's identity (89% vs 77%), made sure their child did not receive medications she/he was allergic to (88% vs 77%), verified their child's weight with the parent (79% vs 65%), and discussed postoperative plans with the parent (80% vs 67%, $p<0.05$ for all comparisons). Parents did not report feeling more comfortable asking questions or expressing concerns, but these differences were not statistically significant (Table).

Conclusion
Parents reported significant improvement in several areas after introduction of the parent-centered script; however, parents did not report feeling more comfortable with the perioperative team, and their pre-induction experience remained variable. Further research is

needed to understand parents' preoperative experience and identify perceived barriers to communication with perioperative staff.

ABSTRACT

Choices Matter: Impact of Skin Management on Patient Reported Outcomes after Emergency Laparotomy

Hannah Ortiz *McGovern Medical School at UTHealth* *Class of 20*

Sponsored by: Lillian S Kao MD, MS, Department of Surgery, Division of Acute Care Surgery
Supported by: Center of Translational Injury Research (CeTIR)
Key Words: Emergency Laparotomy, Patient Reported Outcomes, Quality of Life

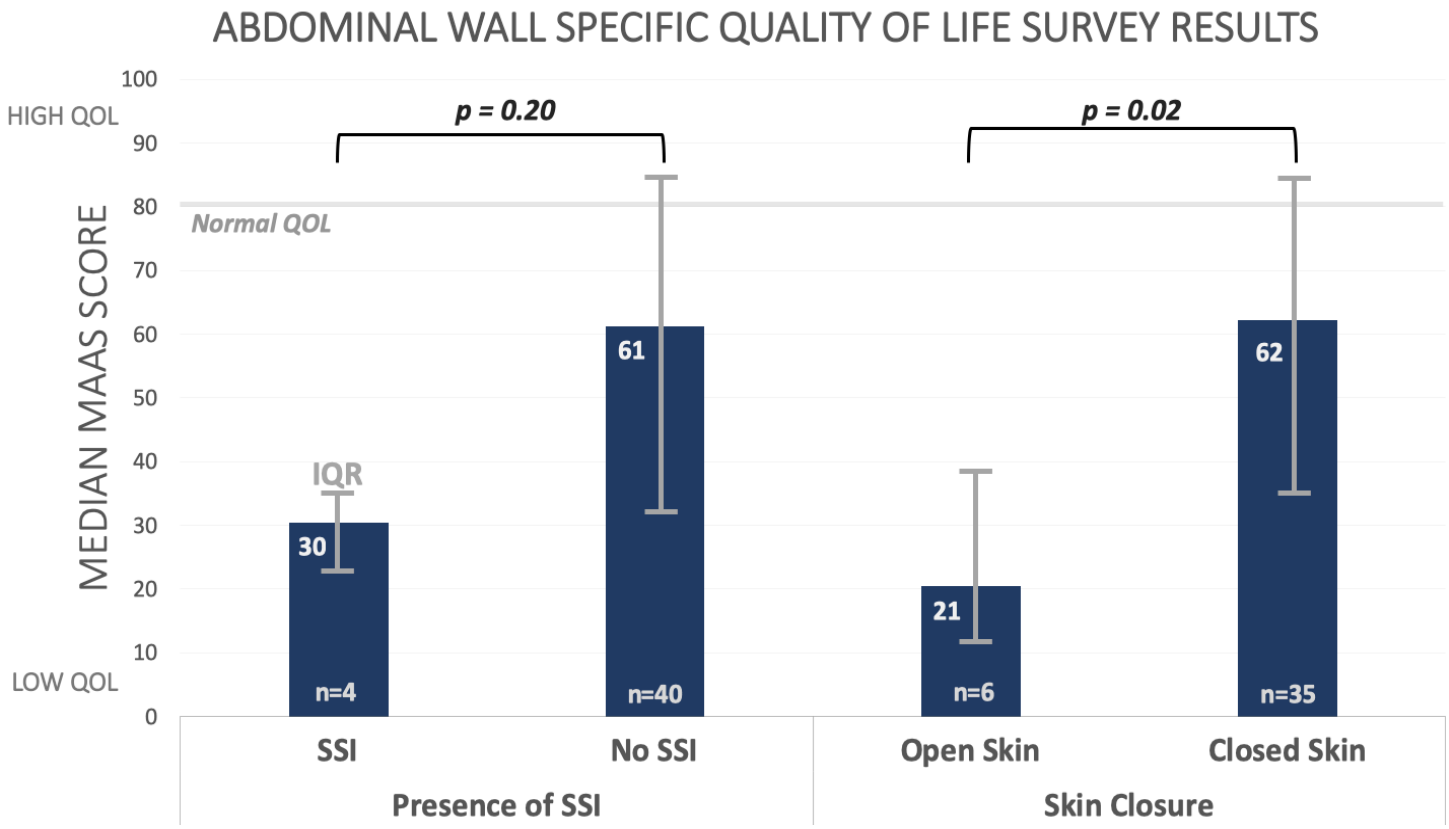
Introduction
Clinical decision-making during emergency laparotomy for injury or illness is often driven by the desire to prevent complications such as surgical site infections (SSIs). Patient-reported outcomes (PROs) provide important information regarding physical, mental, and social health and are increasingly being measured post-operatively. However, there is limited information about the effects of complications such as SSIs and of intraoperative decisions such as skin management strategies on PROs after emergency laparotomy. We hypothesized that among patients undergoing emergency laparotomy, PROs measured by an abdominal wall specific quality of life (QoL) survey would be worse with both SSIs and an open skin management strategy.

Methods
A single-center observational study of patients ≥16 years who underwent emergency laparotomy between 6/2018 and 7/2019 by the emergency general or trauma surgery services was performed. Patients requiring initial damage control laparotomy were excluded. Patients were surveyed using the modified Activities Assessment Scale (mAAS) in the outpatient clinic or by phone between 2 weeks and 3 months postoperative. The mAAS is a validated 12-question abdominal wall specific QoL survey that captures pain, function, and mental health. The cumulative responses are normalized to a scale of 1, representing poor QoL, to 100, representing high QoL. Based on prior studies, a score of 80 or above is normal. Demographics, operative details, and SSI outcomes were collected by chart review. The Center for Disease Control definition of superficial SSI was applied. Patients were stratified by development of SSI and skin management. Univariate and multivariable Poisson analyses were performed.

Results
Of 72 eligible patients, 44 completed surveys. The median patient age was 38 (IQR 24-59). The majority of patients were male (64%), white (43%), and suffered traumatic injury (68%). The median mAAS score was 51 (IQR 24-81). Normal QoL was reported by 13 patients (30%). On univariate analysis, a higher QoL was associated with absence of SSIs and with closed skin management (**Figure**). After adjusting for age, sex, and time from surgery to the survey, absence of SSI (RR 1.8 95% CI 1.0-3.2, p=0.06) and closed skin management (RR 2.1 95% CI 1.2-3.5, p=0.01) were associated with better QoL.

Conclusions

The majority of patients recovering from emergency laparotomy reported poor abdominal wall specific QoL in the early post-operative period. Closed skin and absence of SSI were associated with better postoperative QoL. PROs should be measured after emergency surgery to improve patient-centered decision-making



ABSTRACT

The Co-Localization of Huntington Protein and Huntington-Associated Protein 40

SREELEKHA PALADUGU *McGovern Medical School at UTHealth* *Class of 20*

Sponsored by: Sheng Zhang, PhD, Center for Metabolic and Degenerative Diseases
Supported by: The Brown Foundation Institute of Molecular Medicine
Key Words: Huntington's disease, Huntington (HTT), HAP40, co-localization

Background and Significance: Huntington's disease (HD) is an autosomal dominant genetic disease characterized by a progressive breakdown of medium spiny neurons primarily in the striatum. HTT is a large (348-kDa) scaffold protein that interacts with a variety of proteins known as Huntington-associated proteins (HAPs). HAP40 is of particular interest due to growing evidence in its role as a central regulator of HTT. HAP40 is primarily α-helical and binds HTT by hydrophobic and electrostatic interactions. Biochemical and genetic studies in *Drosophila* and mammalian cells have demonstrated that HAP40 has a conserved role for the stability and functions of HTT. In vivo, HTT and HAP40 actually bind in a 1:1 molar ratio to form a well-defined globular complex. Interestingly, in the absence of Hap40, HTT forms dynamic oligomers that are subject to aggregation. The stable physical association between HAP40 and HTT indicates that the regulatory relationship that HAP40 has with HTT might hold the answer to many questions regarding the cellular roles of HTT itself and the mechanism by which mutant HTT causes selective neurotoxicity. Investigating the gross tissue, cellular and subcellular localizations of HAP40, HTT and the HAP40-HTT complex is essential in understanding this mutant HTT-induced toxicity. This may be pertinent in the development of targeted gene therapies that would prevent neuronal cell degeneration.
Methods: Immunofluorescent co-labeling on endogenous HTT and HAP40 proteins were performed with mouse anti-HTT (mAb2166) and rabbit anti-HAP40 (HPA046960) primary antibodies on fixed adult mouse brain tissue, followed by staining with Dylight 567-Goat-anti-Mouse and Dylight 488-Goat-anti-Rabbit secondary antibodies. DAPI staining was used to visualize the nucleus. Imaging and analysis of the tissues was done with Cytation™ 5 Cell Imaging Multi-Mode Reader and Leica TCS SP5 confocal microscope.
Results: Preliminary results indicate that HTT and HAP40 co-localize with each other primarily in the cytoplasm, concentrated in the striatum region of the brain. In particular, numerous punctate cytoplasmic granules positive fro both HTT and HAP40 were found clustered around the nucleus at all microscopic levels. However, in negative controls (i.e., tissues processed in parallel but without primary antibodies), we observed a similar staining pattern, raising the question on the specificity of the signals.
Conclusion: Although the current results could potentially be interesting, additional studies are needed to clarify the issue of signal specificity. The non-specificity of the staining signal could be due to autofluorescent of mouse brain tissues or the promiscuous binding of the secondary antibodies. Ultimately, the staining conditions need to be further optimized to clearly define the relationship between HTT and HAP40 at subcellular levels, including to test more primary and secondary antibodies and to examine controls of HAP40 knockout and HAP40 overexpression tissues. For better understanding of HTT, we need to have a clear

picture of the physiological role of its close partner HAP40, which ultimately requires a systematic investigation of the proteins at subcellular, cellular and tissue levels in the brain.

ABSTRACT

Clinical Implications of CD73 and *CTNNB1* mutations in patients with endometrial cancer

Luan Phan *McGovern Medical School at THealth* Class of 2022

Sponsored by: Jessica L. Bowser, Ph.D., Department of Anesthesiology

Supported by: Jessica L. Bowser, Ph.D., Department of Anesthesiology
Key Words: Endometrial cancer, β-catenin, biomarker, translational research

Introduction: Somatic missense mutations in the gene encoding β-catenin (*CTNNB1*) are associated with poor prognosis in endometrial cancer (EC) patients with low-grade, low-stage tumors. However, despite identifying patients at higher risk for disease recurrence, its utility in managing clinical care has been limited, as not all patients with *CTNNB1* mutant tumors will recur and corresponding biomarkers have not yet been identified. Previous work by our laboratory has identified cell surface 5'nucleotidase, CD73 to regulate β-catenin. In this study, we assessed the relationship between CD73 and mutant β-catenin in EC.
Methods: **q**RT-PCR for *CD73* was performed on 32 frozen EC tissues validated to have *CTNNB1* mutation by next generation sequencing. Immunoistochemistry for CD73 and β-catenin was performed on 11 cases.
Results: *CD73* expression was higher in patients with no recurrence, whereas patients with recurrence *CD73* expression was low. CD73 mRNA levels were not significantly different with clinical stage or lymphatic and vascular space invasion, indicating that *CD73* expression may independently predict disease recurrence in patients with tumors with *CTNNB1* mutations. In stratifying tumors by $CD73^{High}$ or $CD73^{Low}$ mRNA levels, a trend in decreased progression free survival (P = 0.132) and overall survival (P = 0.080) was also seen with patients having $CD73^{Low}$ tumors. However, these data did not reach significance due to limited statistical power of the dataset. All deaths were patients having $CD73^{Low}$ tumors. Immunohistochemistry studies with formalin-fixed paraffin-embedded sections of tumors with *CTNNB1* mutations showed a strong association between CD73 expression and mutant β-catenin location in EC cells. Tumors that express membrane CD73 largely express mutant β-catenin at the membrane. Whereas, tumors with CD73 loss or cytoplasmic CD73 expression, mutant β-catenin staining in the nucleus was increased.
Conclusion: CD73 expression may serve as an independent biomarker for disease recurrence in EC patients with *CTNNB1* mutations and movement of mutant β-catenin into the nucleus may depend on the loss of CD73.

ABSTRACT

DIFFERENTIATING THE ROLES OF ENTEROCOCCUS FAECALIS CARDIOLIPIN SYNTHASES IN DAPTOMYCIN RESISTANCE

VINATHI POLAMRAJU *McGovern Medical School at THealth* *Class of 2022*

Sponsored by: Cesar A. Arias, MD, MSc, PhD, Professor, Department of Internal Medicine, Division of Infectious Diseases
Supported by: Cesar A. Arias, MD, MSc, PhD, Professor, Department of Internal Medicine, Division of Infectious Diseases
Key Words: Antimicrobial resistance, daptomycin, enterococcus faecalis, cardiolipin

Introduction: Vancomycin-resistant enterococci causes over 1,300 deaths annually. One of the few remaining options for therapy is daptomycin, however, emergence of resistance to DAP (DAP-R) is threatening its utility. Mutations in genes encoding the LiaFSR system (a three-component cell envelope stress response system) and cardiolipin synthase (Cls1, producing the anionic phospholipid (APL) cardiolipin) are associated with DAP-R. Activation of the LiaFSR response has been associated with redistribution of APL microdomains away from the septum to bind DAP at non-lethal locations. Data from other organisms suggests that cardiolipin is a major component of these APL microdomains. However, there are two putative *cls* genes found in *E. faecalis*, namely *cls1* and *cls2*. There are no data on the characterization of these synthases and their role in DAP-R. This project will further characterize these two enzymes in terms of gene expression and evaluate their contribution to DAP-R.

Methods: DAP-S and DAP-R derivatives of *E. faecalis* OG117 carrying mutations in *cls1* and *cls2* (*Efs* OG117, *Efs* OG117Δ*cls1* and *Efs* OG117Δ*cls2, Efs* OG117Δ*liaX* and *Efs* OG117Δ*liaX*Δ*cls2*) were grown overnight and cultures were diluted 1:50 in tryptic soy broth for daptomycin susceptibility. RNA extraction for cell pellets collected at t=1-8h was performed with the PureLink RNA extraction kit (Invitrogen). Residual genomic DNA was cleaned with Turbo DNase (Ambion), and cDNA synthesis was carried out on 200ng of RNA with SuperScriptII Reverse Transcriptase (Invitrogen). Expression of *cls1* and *cls2* was evaluated using qRT-PCR (Bio-Rad CFX-96) with 50ng of cDNA per well run in triplicate followed by a melt curve analysis. Relative gene expression was analyzed with the Pffafl method relative to the reference gene (16S rRNA).

Results: Relative to *Efs* OG117, *cls2* gene expression in the DAP-S *Efs* OG117Δ*cls1* (lacking *cls1*) markedly increased at all time points, suggesting a compensatory response. However, relative to *Efs* OG117, *cls1* gene expression in the *Efs* OG117Δ*cls2* only increased during mid exponential phase and was reduced during stationary phase. When comparing the DAP-R *Efs* OG117Δ*liaX* to DAP-S *Efs* OG117, *cls1* has significantly higher expression during late stationary phase while there is significant downregulation of *cls2* expression. When *cls2* is deleted in this DAP-R background, *cls1* expression further increases relative to both OG117 and OG117Δ*liaX,* supporting a compensatory role of this enzyme.

Conclusion: These data suggest that *cls1* may play an important role in maintaining the stationary phase of DAP-R strains, particularly in the absence of *cls2*. Additionally, deletion of *cls1* in *Efs* OG117 causes a compensatory increase in *cls2* expression at all growth phases, however, *cls1* expression only seems to compensate for the deletion of *cls2* in mid to late exponential phase. Overall, this suggests phase-specific roles for Cls1 in the expression of the DAP-R phenotype.

ABSTRACT

A Prospective Comparison of Surgical Site Infection Risk and Skin Management after Trauma Laparotomy

Luciano Posada *McGovern Medical School at UTHealth* *Class of 2022*

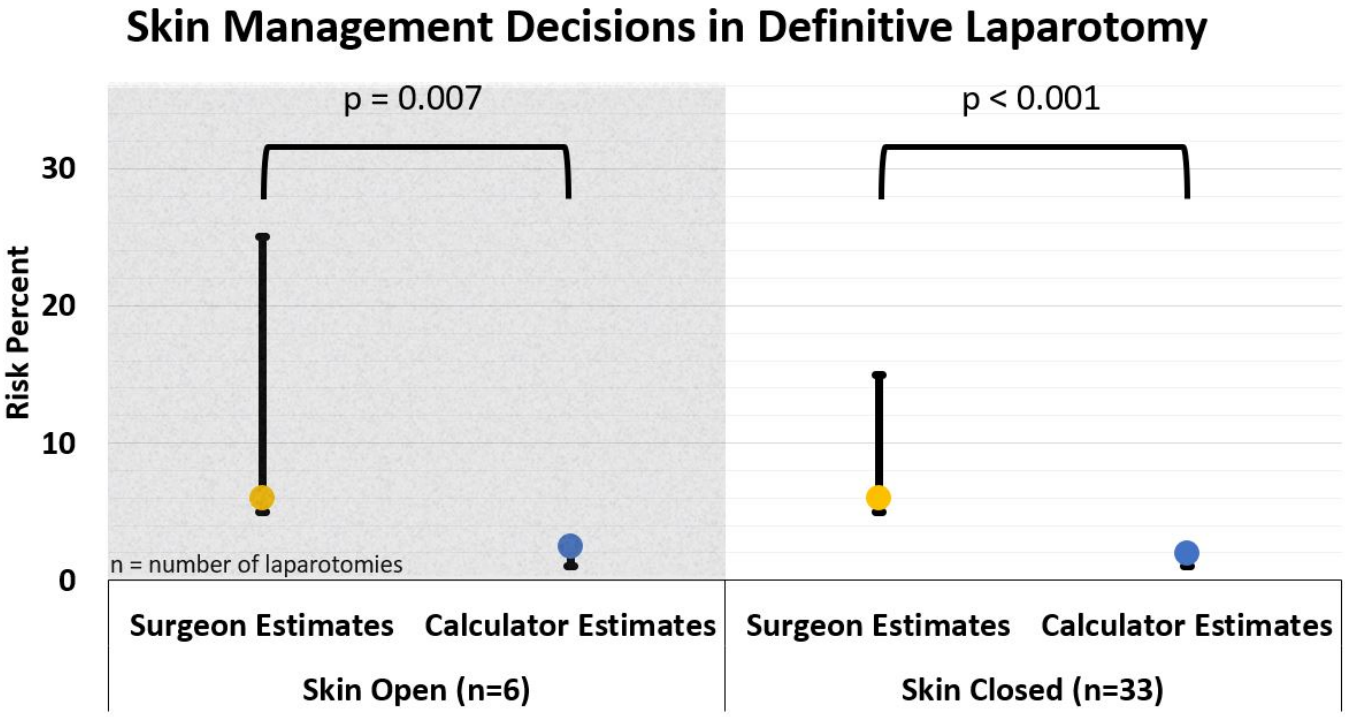
Sponsored by: Lillian S Kao MD, MS, Department of Surgery, Division of Acute Care Surgery
Supported by: Center of Translational Injury Research (CeTIR)
Key Words: Exploratory Laparotomy, Surgical Site Infection, Wound Management

Introduction: Clinical decision-making regarding skin management during trauma laparotomy is focused on preventing surgical site infections (SSI). Open skin may be chosen in lieu of a more cosmetic closure when the surgeon believes the patient has a high risk of SSI. A Bayesian risk calculator for superficial SSI was previously developed at our institution utilizing factors available upon abdominal closure and most patients' SSI risk is between 1 and 5% after definitive laparotomy. Two hypotheses were evaluated in this study: (1) there is a discrepancy between surgeon and calculator-generated SSI risks and (2) surgeons' skin management strategies are not associated with risk estimations.

Methods: A prospective, observational study of surgeons performing trauma laparotomy on adult (≥16 years) patients was performed June-August 2019. Patients who died <48 hours from admission or had a delayed index laparotomy were excluded. Surgeons who scrubbed into an index trauma laparotomy were asked to estimate the patient's superficial SSI risk in percent within 24 hours. Clinical data were collected by chart review. Calculator risks were generated using operative factors and compared to surgeon estimated risks. Additionally, surgeon estimated and computer generated risks were considered separately and were compared among skin management groups: open or closed. Univariate and one-way random effects reliability analyses were performed.

Results: Of 122 estimation requests for 50 index laparotomies, 72 estimations were obtained for 45 laparotomies. Most patients were young (median age 28, IQR 20-39), male (71%), and suffered penetrating trauma (56%). Of 39 patients who underwent initial definitive laparotomy, 33 were managed with closed skin. Two SSIs (4%) occurred, both in patients whose skin was closed. Surgeons' SSI risk estimates demonstrated moderate interrelater reliability (ICC 0.58) and were higher and more variable than calculator-generated risk estimates across groups (**Figure**). The ranges of calculator estimated risks were 1-3% in patients with skin left open and 1-9% in patients with closed skin (p=0.67). The ranges of surgeon estimated risks were 0-75% in patients with skin left open and 1-30% in patients with skin closed (p=0.43).

Conclusions: Surgeons routinely estimated higher SSI risks compared to a risk calculator. Additionally, decision-making with regards to skin management did not appear to be consistent or to be based on perceived SSI risk. A trial evaluating if the addition of a calculator-based decision aid would improve outcomes, compared to surgeon judgement alone, is warranted.



ABSTRACT

Unusual Neoplasms Causing Epilepsy

AZIM POTHIAWALA *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Nitin Tandon, MD, Department of Neurosurgery
Supported by: Nitin Tandon, MD, Department of Neurosurgery; McGovern Medical School – Office of Educational Programs
Key Words: Low-grade neuroepithelial tumors, Intractable Epilepsy, Angiocentric Glioma,
Mengioangiomatosis

Introduction: Low-grade neuroepithelial tumors (LGNTs) are well known to be associated with epilepsy, and resection of these lesions is thought to be highly curative. Angiocentric glioma and mengioangiomatosis, a hamartomatous formation, are two rare lesions with clinical presentations and long-term prognoses that are not well-defined. The slow growing nature of these tumors allowed them to be cured surgically and here we report on the clinical features and outcomes following such resections.
Methods: We compiled a list of all patients treated at Memorial Hermann Hospital in the Texas Medical Center by a single neurosurgeon from 2004 to 2019. Patients were included if they had a histologic confirmation of a low-grade tumor. For the patients that met these criteria, relevant clinical and demographic data were compiled. Patients for whom pathology reports were not available, such as patients who underwent laser thermal ablation, were excluded. From our database we identified, among other LGNTs, 4 angiocentric gliomas and 2 mengioangiomatosis. To further evaluate the key clinical features of these lesions, an expanded search to include patients from two other neurosurgeons at Memorial Hermann Hospital. The final patient list consisted of 4 angiocentric gliomas, and 5 mengioangiomatosis.
Results: Three of the four patients with an angiocentric glioma presented with intractable epilepsy as the leading clinical symptom. These 3 patients underwent a gross total resection (GTR). All were seizure-free after surgery with an Engel classification of 1a. Of note, the remaining fourth patient, presenting only with right hand tremors, was found to have an angiocentric glioma in the L. thalamus, a presentation rarely described in the literature. All 5 patients with a mengioangiomatosis presented with intractable epilepsy and underwent a GTR of their lesion. Only 3 were completely seizure-free following their operation with an Engel classification of 1a. Of the remaining 2 patients, 1 was classified as 1D and the other 2D. Two of the patients were found to have an overlying mengioma, an association well described in the literature.
Conclusions: Consistent with previously reported outcomes of angiocentric glioma and mengioangiomatosis, the majority the patients in our study were seizure free following resection. While 1 of the patients suffered from a focal neurological deficit following resection, the majority reported no complications with one patient showing improvement in mood. Studying the clinical presentations and post-surgical outcomes may have implications for delineating epileptic pathways for these lesions and how they may relate to other LGNTs

ABSTRACT

Mothers with prenatal diagnosis of Trisomy 13 or Trisomy 18 choice of postnatal care and survival outcomes in Houston

AYESHUM RASOOL *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Suzanne Lopez, M.D, Department of Pediatrics
Supported by: McGovern Medical School at UT Health, Suzanne Lopez, M.D, Department of Pediatrics
Key Words: Trisomy 13, trisomy 18, genetic counseling, postnatal care, survival outcomes

Background: Trisomy 13 and 18 are well-known lethal chromosomal anomalies, with infants usually dying within the first few days of life. While survival outcomes have been well documented, there is limited information in Texas for recent parental choice of postnatal care, including the effect of genetic counseling.

Methods: We conducted a retrospective chart review of maternal patients referred to high-risk prenatal clinics around the Houston area between 2016 and 2018 with a prenatal diagnosis of Trisomy 13 or 18 identified via a positive screening or abnormal ultrasound. Maternal and neonatal demographics, postnatal care choice and neonatal outcomes were obtained using the Fetal Center data base, Care4, and Viewpoint. Kaplan-Meier survival analysis was utilized for neonatal survival. Maternal demographics were compared to known outcomes of Texas on previously reported survival information in this population.

Results: 97 maternal patients were identified with a positive screening for Trisomy 13 or 18 and/or an abnormal ultrasound. Regarding postnatal care choice, 40% were undecided or had unknown management, 37% chose to terminate, 17% chose comfort care, 5% chose full intervention, and 1% chose expectant management. As the number of genetic counseling sessions increased, more parents chose comfort care. Regarding neonatal outcomes in the 97 patients, 37% were terminated, 23% died in-utero, 11% were liveborn, and 29% had unknown outcomes due to loss of follow-up. Out of 53 pregnancies with Trisomy 18 diagnosis, only 9 were liveborn, with a median age of death of 6 days. Out of 16 pregnancies with Trisomy 13 diagnosis, 2 infants were liveborn, with a median age of death of 1 day.

Conclusion: Survival for Trisomy 13 and 18 has not increased over time compared to previous Texas studies. A majority of parents choose termination, with the second largest choosing comfort care, and a very small number chose full intervention. As genetic counseling was associated with increasing number of parents choosing comfort care, early counseling may be important for these maternal patients.

ABSTRACT

Effects of TXA on Human Osteoblasts

William D Rieger *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: James F Kellam, MD, Department of Orthopedic Surgery
Catherine G Ambrose, PhD, Department of Orthopedic Surgery
Supported by: James F Kellam, MD, Department of Orthopedic Surgery
Key Words: Tranexamic Acid, TXA, Osteoblasts, Cell Metabolism, Drug Exposure

Tranexamic acid (TXA) is a popular antifibrinolytic drug used to prevent blood loss and transfusion risk in surgical settings, but there is a current lack of information regarding the effects of TXA on osteoblasts and bone healing. This knowledge should be expanded before TXA is used widely in orthopedic trauma situations where bone healing is of tantamount importance. Herein, we seek to determine TXA's effect on in vitro human osteoblast (HOB) viability and metabolism, which will act as a basic surrogate for fracture healing. We hypothesize that as TXA concentration and exposure time increase, HOBs will be increasingly negatively affected metabolically, but that at most "typical" surgical concentrations, no effect will be seen. To test this hypothesis, primary HOBs were cultured from explants of multiple patients undergoing either a TKA or THA. The HOBs were seeded in 96 well plates and cultured with media containing 2:1 low glucose to high glucose DMEM to simulate normoglycemic body conditions, with 10% FBS and 1% antibiotic/antimycotic under standard conditions. At 80% confluence, cells were exposed to a filter-sterilized PBS/media-dissolved TXA solution at 100, 50, 25, 12.5, 6.25, 3.125, 1.563, 0.7813, 0.3906, and 0.1953mg/mL concentrations for 3, 6, 12, or 24 hrs. Cells were then assessed for viability using a resazurin assay. The cell lysate was used to determine the amount of bone-specific alkaline phosphatase (AP) and total protein (TP) present via respective assays. The data was collated with outliers (from concentration/data columns per plate) removed. As expected, HOB viability and metabolism decreased as TXA concentration and exposure time increased. However, HOB viability and metabolism increased at low TXA concentrations and exposure times. Negligible osteoblast viability was seen at a concentration of 100mg/mL at a 24hr exposure time, suggesting a lack of HOB survival, but this concentration impaired HOB viability and metabolism below the positive control to 74.42% and 94.42% even at 3hrs exposure via resazurin and AP/TP ratio data, respectively. A TXA concentration below 56.44mg/mL at any exposure time was shown via resazurin not to effect HOB viability below the positive control, indicating that these concentrations will likely not affect fracture healing. At low TXA concentrations (≤ 12.5mg/mL, resazurin; ≤ 0.78125mg/mL, AP/TP) at all exposure times, there is an increase in cell viability and metabolism respectively, with 6hrs or less exhibiting a more dramatic increase. We both partially reject and partially accept our hypothesis, for we did see an increase in degradation of HOB metabolism as TXA concentration increased, but at low TXA concentrations we observed an improvement. We defined a concentration and exposure time that impaired HOB to the point of metabolic cessation, 100mg/mL of TXA at 24hrs of exposure. Regardless, this concentration of 100mg/mL led to HOB impairment at all exposure times and is clinically relevant, though it is near the upper limit currently reported in surgical settings with the "point of negative effect" at 56.44mg/mL being even more possible clinically. Therefore, we recommend the use of IV TXA when possible, as well as limiting concentrations to a conservative 50mg/mL when applied topically.

ABSTRACT

Engaging Parents to Improve Patient Safety

IBIS ROJAS *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Akemi Kawaguchi, M.D., Department of Pediatric Surgery
Supported by: Akemi Kawaguchi, M.D., Department of Pediatric Surgery
Key Words: Parental Engagement, Medical Errors, Reporting System, Patient Safety

Authors: Ibis A Rojas, BSA, Nutan B Hebballi, BDS, MPH, Jennifer Rizzi, BSN, RN, CPN, Kuojen Tsao, MD, Akemi L Kawaguchi MD, MS

Introduction: Medical errors remain one of the leading causes of morbidity and mortality in hospitals across the United States. Parents and families can play a vital role in improving patient safety. We hypothesized that parents and families can reliably identify patient safety events related to their hospitalized children and that an electronic parental variance reporting system would facilitate parent participation in patient safety.

Methods: We conducted a cross-sectional study of parents/families whose children were hospitalized on the surgical floor of a tertiary children's hospital between May-July, 2019. Prior to discharge, parents were administered a 24-question paper-based survey in English and Spanish, based on the validated Safety Attitudes Questionnaire, which was designed to assess patient demographics and parental perception of teamwork, communication, patient safety culture at the hospital. Open-ended questions were also included in the survey to capture the top three safety concerns in the hospital. In addition to the survey, a new electronic parental variance reporting system was introduced to half of the survey participants to anonymously report incidents/feedback regarding their child's safety in the hospital. Survey results were analyzed to determine whether the electronic reporting system had an impact on the parent's perception of patient safety reporting.

Results: Of the 224 surveys distributed, 68 (31%) were completed, including 34 (65%) English and 24 (35%) Spanish. The most common reasons for hospitalization included appendicitis, burns, and trauma and the median length of stay was 2.9 days (IQR 1-11 days). The results of the survey were largely positive (87%) and 99% of parents felt safe having their child treated at the hospital. Spanish speaking parents/families had more difficulty in speaking up (32%) if they perceived a problem with their child's care. The top three concerns parents had were regarding hygiene (32%), communication (21%), and bed related issues (11%). Parents who had access to the electronic parental variance reporting system were more knowledgeable about reporting of hospital safety events.

Conclusion: Parental feedback is a valuable source of information for improving patient safety. The electronic variance reporting system provided an avenue for parents to report their safety concerns. Future directions include further dissemination of the electronic reporting system to all parents and comparing variance submitted by parents and hospital staff.

ABSTRACT

Natural History of Occult Hernias in Adults at a Safety-Net Hospital

ALEXIS RONDON *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Mike K. Liang, MD, Department of General Surgery
Supported by: Dr. Mike K. Liang, Department of General Surgery
Key Words: Occult hernia, natural history, emergent repair, risks

Introduction

Half of all Americans have an occult hernia, a hernia seen on radiologic imaging but not felt on physical exam. Despite the high prevalence of occult hernias, little is known about the natural history of this disease. Our aim was to study the natural history of patients with occult hernias.

Methods

This was a prospective study of patients who underwent a CT abdomen/pelvis from 2016-2018. Primary outcome was change in abdominal wall quality of life (AW-QOL) using a hernia-specific, validated survey (where 1=poor and 100=perfect QOL). Secondary outcomes included elective and emergent hernia repairs.

Results

A total of 131 patients with occult hernias completed follow-up with median follow-up of 15.4 months (IQR 22.5). Nearly half of patients (56,44.7%) had a decrease in their AW-QOL, 34 (30.0%) were unchanged, and 41 (31.3%) reported improvement. Overall, there was a slight mean decrease in AQ-QOL (-0.5, 36.2).

One-fourth of patients (36, 27.5%) underwent abdominal surgeries during the study period: 28 (21.4%) were elective surgery not primarily to treat their hernia, 6 (4.6%) were elective hernia repairs, and 2 (1.5%) were emergent hernia repairs. Those who underwent abdominal surgeries experienced an improvement in AW-QOL (+7.6, 41.6) while the non-surgical group reported a worsened AW-QOL (-3.6 33.7).

Discussion

When untreated, patients with occult hernias experienced a decrease in their AW-QOL over time. Additionally, there was a small but real risk of incarceration with strangulation. Further research is needed to identify the optimal management strategy of patients with occult hernias.

ABSTRACT

Expression and Analysis of Complement Proteins in Brain Tumor Patient Tissues

SHAYAK SEN *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: John F. de Groot, Department of Neuro-Oncology, MD Anderson Cancer Center
Supported by: John F. de Groot, Department of Neuro-Oncology, MD Anderson Cancer Center
Key Words: Brain Tumors, Complement, qPCR, IHC/IF

Background: Glioblastoma (GBM) is the most common and aggressive primary brain tumor affecting adults. Despite advancements in treatment, the median survival of GBM patients remain unchanged. One challenge GBM has presented is that the tumor micro-environment (TME) may modulate immune cells to support the tumor instead of attack it. The complement cascade is a major mediator of the innate and adaptive immune system. Recent reports have shown the tumor promoting role of complement in many solid cancers. However, the role of complement proteins in GBM tumor microenvironment remains elusive. In this work, we aimed to study the expression of complement proteins in brain tumor tissues to understand their role in tumor promotion or therapy response in brain tumors.
Methods: *Quantitative PCR (qPCR)***:** GBM frozen tissue samples were subjected to total RNA isolation using RNeasy Mini Kit and were reverse transcribed to cDNA using High Capacity cDNA Reverse Transcription Kit. The quantitative real time expression of complement proteins was carried out by using 7500 Fast Real Time PCR system.
Immunohistochemistry (IHC)/Immunofluorescence (IF): Paraffin embedded human GBM tissue sections (4 μm) were subjected to deparaffinization and graded rehydration. Then, sections were incubated with antigen retrieval buffer followed by incubation in blocking buffer, then incubation with primary antibody overnight at 4°C. The following day, the sections were incubated with appropriate HRP/fluorescent secondary antibody for 1 h at room temperature and the staining's were analyzed by using Zeiss microscope.
Results: The results for the qPCR experiments and IF/IHC experiments showed that there is abundant expression of complement in brain tumor tissues. We tested six different patient samples for multiple complement genes (C3, C3AR, C5, C5AR, and C1QB). Of the tissues two were GBM, two were grade II astrocytomas, and two were grade II oligodendrogliomas. All samples tested showed elevated expression of complement expression in comparison to the non-cancerous normal brain tissue. Furthermore, the qPCR results were confirmed with IHC. GBM samples showed positive membrane staining for complement receptors C3AR and C5AR. Additionally, double IF staining with microglia marker IBA1 confirmed that the complement receptors are expressed in cancer cells.
Conclusion: Based on these findings, we can conclude that complement proteins are expressed in brain tumor samples. There is significant RNA and protein expression of complement proteins in brain tumor patient samples. These preliminary findings suggest that complement proteins may play a crucial role in brain tumor progression. However ongoing studies will identify the mechanistic role of complement proteins in the brain tumor microenvironment.

ABSTRACT

The Role of Social Factors in Perinatal Depression

JASPERINA SHEI *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Sudhakar Selvaraj, M.D., Ph.D, Department of Psychiatry and Behavioral Sciences
Supported by: Saltzberg Summer Research Program
Key Words: perinatal depression, postpartum depression, maternal mortality, social factors

Perinatal depression is a heavy burden of disease and a common pregnancy complication in the United States. It affects 12-20% of pregnant and postpartum women, and accounts for 20-25% of maternal deaths. Maternal mortality is a rising concern in the United States, which currently has the highest rate in the developed world. However, studies place depression treatment rates among symptomatic mothers as low as 12%. Despite the chronic consequences of perinatal depression on maternal, child, and family health and strong recommendations for evidence-based pharmacological and psychological therapies, new mothers are not getting the care they need.

Extensive research has been conducted to identify the social risk factors for the development of perinatal depression. These studies have subsequently been used to increase screening and preventative efforts among high-risk women. However, relatively little has been done to identify the role of social determinants in treatment outcomes. Social factors are major contributors to the mental healthcare treatment barriers faced by new mothers. To break down these barriers, increase care access, and narrow gaps in treatment, it is essential to identify the relevant modifiable social factors for more effective and comprehensive maternal healthcare. This paper will review the evidence for the roles of partner support, social support, employment, health insurance, and housing instability in perinatal depression development and treatment. Increased incorporation of these five determinants into maternal mental healthcare will be crucial in addressing the maternal mortality crisis in the United States.

ABSTRACT

Optogenetic Approaches for Vision Restoration

TELAVIVE TAYE *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: John O'Brien, PhD, UTHSC Visual Sciences and Ophthalmology
Supported by: William Stamps Farish Foundation
Key Words: Optogenetics, retina degeneration, zebrafish, channelrhodopsins

Background: In pathologies such as Retinitis Pigmentosa and macular degeneration the first layer of light sensitive neurons in the retina degenerate, resulting in vision loss. One strategy to restore vision is to render remaining neurons light-sensitive. Research in the field of vision restoration has demonstrated the utility of rhodopsin channels to regulate signal transduction in salvageable retinal neurons. Bipolar cells, among non-photoreceptors found intact in retinal degeneration, can be used to transmit vision restoring signals, retaining the ON/OFF modulation observed in natural light signal transmission for image formation.
Objectives: We are working on initiating channelrhodposin (ChR)-induced depolarization in bipolar cells of cone degenerate zebrafish mutant (*pde6c*^{w59}). Our goal is to separately express cation and anion ChR in On and Off bipolar cells.
Methods: We injected zebrafish single-cell embryos (30 minutes post fertilization) with a Tol2 transposon-based plasmid containing cation PsChR driven by a *ribeye* promoter and containing an mCherry heart marker. We checked for mCherry expression in the heart of five day post fertilization (5 dpf) embryos for delivery of plasmid and selected the viable embryos. We sacrificed some larvae at 7 dpf, fixed the sample in OCT blocks and took micrometer slices. We visualized ChR expression in wildtype and *pde6c*^{w59} retina using confocal microscopy. We studied visual motor response of *pde6c*^{w59} and wildtype zebrafish at 7 dpf in 12-well plates using ZebraBox.
Results: In the visually-guided behavior study, we observed *pde6c*^{w59} movement is less frequent than in wildtype. We were able to deliver the plasmid into the embryos; however, we did not detect PsChR expression in the retina. We have started working on expressing a reporter gene, GFP, downstream the *ribeye* promoter to determine first if the construct's fault is in the promoter. We have not seen expression of the reporter gene. Additionally, we have determined a battery of OFF-promoter candidates for the anion ChR and have started building constructs.
Conclusion: We are determined to develop viable plasmids with anion channelrhodopsins so our current work has been using different OFF-bipolar cell promoter candidates. Similarly, we are working to configure the appropriate plasmid with the ON-bipolar cell promoters.

ABSTRACT

Exploring Therapeutic Inertia in Hypertension Management

MUBEEN TEJANI *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Deevakar Rogith, MBBS, PhD, Assistant Professor, UTHealth School of Biomedical Informatics, Houston, TX
Supported by: UTHealth School of Biomedical Informatics
Key Words: Hypertension, Therapeutic Inertia, Pattern Analysis

Importance Therapeutic inertia contributes to prevalence of uncontrolled hypertension. It accounts for about 19% variance in blood pressure. However, there have been no clear measures describing the epidemiology of therapeutic inertia. Identifying and characterizing therapeutic inertia is difficult due to its multifactorial nature, and thus it is difficult to quantify outcomes.

Objective To explore therapeutic inertia in hypertension patients and summarize temporal features of therapeutic inertia.

Design, Setting, and Participants We analyzed patient data from ambulatory care clinics in Texas. Patients with a billing diagnosis of hypertension (HTN) from March 1, 2019 to May 31, 2019 were analyzed. Therapeutic inertia was defined as periods with consecutive over target BP measurements at least 30 days apart without any change to anti-hypertensive medication within 7 days of the elevated BP measurements. We mined for periods of inertia and calculated temporal measures.

Main Outcomes and Measures We identified therapeutic inertia periods in selected patients with a primary billing diagnosis of HTN. We calculated incidence of inertia, duration of inertia and grouped by patient characteristics, provider characteristics and clinical visit characteristics.

Results Of the 13,735 patients with a primary billing diagnosis of HTN analyzed, 7,733 had an incidence of therapeutic inertia in their patient history. 4,479 patients had more than one inertia event. Most patients had inertia events lasting longer than 150 days and the most common cause of inertia event cessation was controlled BP, followed by up-titration of already prescribed medications, followed by prescription of new medications.

Conclusion and Relevance This preliminary study demonstrates how to identify therpaeutic inertia in EHR data, and its distribution. This is a pilot study to uncover patterns and contributing factors of therapeutic inertia, and their impact on patient outcomes in hypertension.

ABSTRACT

Understanding Operative Delays and Same-Day Cancellations in Pediatric Surgery

JEFFREY VEHAWN *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: KuoJen Tsao, MD, Pediatric Surgery
Supported by: KuoJen Tsao, MD, Pediatric Surgery
Key Words: Pediatric surgery, delays, cancellations

Introduction:
Operative delays and cancellations reduce efficiency and waste resources, while decreasing patient/guardian satisfaction. We hypothesized that the majority of pediatric same-day cancellations and operative delays at our institution are preventable. We aimed to describe current rates and causes of operative cancellations and delays.

Methods:
We conducted a retrospective review of all outpatient pediatric surgeries scheduled November 2018-April 2019. All pediatric surgeries were included except for fetal surgeries. Cancellations were defined as cancellations on the same calendar day as the scheduled surgery. Delays were defined as patient arrival in the operating room >5 minutes after the scheduled start. Only first-start cases were evaluated for delays, as later delays may be secondary to a first-start delay. Cancellations and delays were classified as readily preventable, potentially preventable, or non-preventable. Readily preventable factors were defined as those that occurring due to a flaw in or lack of adherence to the current system. Potentially preventable factors were defined as those that would require a new system in order to prevent them. Descriptive statistics were used.

Results:
Of 1129 scheduled operations, 102 (9%) were cancelled. Cancellations were attributed to changes in patient health status (41%), parent/patient request (24%), patient no-show (19%), surgeon request (5%), need for additional workup (3%), and financial/insurance reasons (3%). Of 469 first-start cases, 82 (17%) were delayed. Reasons for delay included surgeon tardiness (20%); documentation issues, including missing preoperative note or consent (20%); parent questions (15%); need for medical care unrelated to the planned procedure (11%); equipment problems/unavailability (9%); patient tardiness (7%); and need for an interpreter (4%). The remaining cancellations and delays were due to infrequent reasons (n≤2). Readily preventable factors accounted for 33% of cancellations and 75% of delays. These included tardiness (patient or surgeon), no-shows, need for additional workup, surgeon request, financial/insurance reasons, parent questions, and issues with documentation, equipment, or interpreters. Potentially preventable reasons included change in patient health status and parent/patient request. No reason for cancellation or delay was found to be non-preventable.

Conclusions:
Many cancellations and delays were avoidable, with 33% of cancellations and 75% of delays determined to be readily preventable. Modification of the preoperative process at our institution, such as using automated reminder texts and/or calls, may drastically reduce no-shows and late arrivals. Penalizing surgeons for their contribution to tardiness or incomplete

documentation may improve surgeon-related factors. Other factors, such as a change in the patient's health status prior to surgery, may require more complex interventions.

ABSTRACT

Highlighting the Incidence of Meniscus Root Tears in Acute ACL trauma

ANDREW WANG *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Dr. Manickam Kumaravel, MD, Diagnostic and Interventional Imaging
Supported by: Dr. Manickam Kumaravel, MD, Diagnostic and Interventional Imaging
Key Words: Meniscus root tear, grade 3 ACL tear, wrisberg rip, humphrey rip

Background
ACL tears are among one the leading causes of sports-related injuries. There are often additional secondary ligamentous, cartilage, or meniscal injury associated with full-thickness ACL tears that may play a significant role in the prognosis of these patients. Meniscus root tears are increasingly recognized as an important subset of meniscal injury. These injuries are difficult to evaluate radiologically and arthroscopically, hence often go under-recognized. The purpose of this study is to evaluate the association between acute Grade 3 ACL tears and the characteristics of secondary meniscal root tears to increase diagnostic accuracy, awareness, and improve patient outcomes.

Material and Methods
Following institutional IRB approval, a list of 109 patients with established grade 3 ACL tears from 2016-2018 was retrospectively reviewed. The clinical notes, radiology reports, MRI images, and post-operative reports were all evaluated. Using arthroscopy as a "gold standard", the pre-operative MRI reports were authenticated. The etiology, grade of meniscal injury, location, type of tear, type of surgery performed, and prognostic factors were recorded. The observations were documented by an orthopedic surgeon, upper level radiology resident, and a musculoskeletal fellowship trained radiologist.

Results
Of the 109 patients who had full thickness ACL tears, 27.52% (30/109) had only a lateral meniscus root tear and 11.01% (12/109) had only a medial meniscus root tear. It was rare for a patient to have a root tear on both medial and lateral menisci (2/109). The location of the root tears were overwhelmingly observed on the posterior horn attachment, as the lateral meniscus had 84.28% (27/32) and the medial meniscus showed 100% (14/14). Additionally, medial root tears were most commonly observed concurrently with complex meniscus tears 35.71% (5/12), while lateral root tears were most commonly observed concurrently with radial meniscus tears 25% (8/32).

Conclusion
Root tears are increasingly recognized as an important subset of meniscal injury associated with ACL trauma. These injuries alter the knee biomechanics and increase the likelihood of meniscal extrusion and accelerated osteoarthrosis. Highlighting the incidence and etiology of these injuries will allow physicians to become more aware of the different patterns in acute ACL tears with secondary meniscal injuries. This will ultimately allow for more efficient diagnosis and surgical planning for patient

ABSTRACT

Surgical Intervention for Epilepsy caused by Recurrent or Residual Meningiomas

JEVONS WANG *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Nitin Tandon, MD, Department of Neurosurgery
Supported by: Nitin Tandon, MD, Department of Neurosurgery
Key Words: Epilepsy, Seizures, Meningioma, Residual

Meningiomas are a common form of brain tumor, the presence of which is often associated with seizures. Following incomplete surgical resection of epileptogenic meningiomas, or consequent to damage to surrounding cortex produced by the meningioma or by its resection, the epilepsy related to these neoplasms, persists. In this investigation, we describe the risk factors, natural history, surgical management, and outcomes following surgery for recurrent or residual epileptogenic meningiomas. Through retrospective chart reviews, we identified patients with persistent epilepsy following incomplete resection or recurrent cases of meningiomas over a 14 year interval. Eighty-five patients with intracranial meningiomas were identified, 25 of whom presented with incidental seizures, and 21 presenting with epilepsy. Overall, parasagittal meningiomas were observed to be more likely to have subtotal resection than meningiomas with other intracranial locations ($p = 0.003$), likely due to the operative difficulty in achieving radical resection of lesions of this location with minimal brain manipulation. Two patients undergoing anterior temporal lobectomy for treatment of intractable temporal lobe epilepsy were found to have incidental convexity-located meningiomas intraoperatively. Two patients who underwent gross total resection of convexity-located meningiomas developed subsequent intractable epilepsy, which was addressed with anterior temporal lobectomy, yielding seizure control (Engel Ia, IIIa). Eleven patients were identified with new-onset epilepsy following surgical resection, 8 of whom were able to obtain seizure control following gross total resection of the meningioma (4 Parasagittal, 3 Skull base, 1 convexity) and subsequent anticonvulsant therapy, and 3 of whom were able to obtain seizure control after sub-total surgical resection followed by adjuvant radiotherapy of the meningioma (1 Parasagittal, 2 Skull Base) and subsequent anticonvulsant therapy. Six patients of note (4 Male, 2 Female) were identified with new-onset intractable epilepsy following subtotal resection and recurrence of 5 parasagitally located and 1 frontoparietal convexity-located meningiomas. Patients presented with an average of 2 failed antiepileptic drugs prior to re-resection of lesions. Follow-up surgery involved resection of residual/recurrent meningioma in all 6 patients and resection of surrounding areas of electrocorticography-proven epileptogenicity in 4/6 patients. Subsequent histopathology of resected epileptogenic lesions revealed gliosis (4/4), cortical scarring (1/4), hemosiderin deposits (2/4), and leptomeningeal fibrosis (2/4) consistent with prior surgical interventions. Two of 6 patients received adjuvant radiotherapy for cases of sub-total re-resection, and all patients were continued on anti-convulsants for seizure prophylaxis. Patients were able to obtain seizure improvement following resection of these lesions with Engel Ia (3/6), IIc (1/6), and IIIa (2/6) outcomes. These cases highlight the risk involved in management of parasagittal meningiomas and offer modalities for the treatment of subsequent complicating intractable epilepsy.

ABSTRACT

High Fat Diet Increases Alkaline Phosphatase Activity of Murine Blood in Conjunction with Hypercholesterolemia, Atherosclerosis and Cardiac Dysfunction

JACOB WATSON *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Yong-Jian Geng, MD, PhD, Department of Internal Medicine
Supported by: Yong-Jian Geng, MD, PhD
Key Words: Atherosclerosis, Calcification, Alkaline Phosphatase, Apo E-/-, LDL Cholesterol

Introduction: Alkaline phosphatase (ALP), a critical enzyme for bone morphogenesis and tissue calcification, has been implemented to be a contributing factor to atherosclerotic coronary arterial disease. This study used a murine model to test the hypothesis that high fat diet elevates ALP activity as well as induces hypercholesterolemia and atherosclerosis.

Methods: C57BL/6J (n=14) and APO-E -/- (n=15) mice (10-18 months and both sexes) were fed normal chew or high fat diet for 8 weeks. Blood pressure (BP), body weight, and echocardiograms were measured. Blood plasma LDL cholesterol and ALP levels were measured by spectrometry.

Results: APO-E-/- mice under normal chew already developed much higher levels of ALP (>0.1 U/mL) and LDL-cholesterol (above 200 mg/dL). High fat feeding markedly increased the ALP activity in both wild type and APO-E-/- mice. The high fat diet-increased ALP activity was accompanied by elevation of blood plasma LDL cholesterol levels in wild type by 2 folds and APO-E -/- mice by 8 folds. Both wild type C57BL/6J and APO-E -/- mice on high fat diet gained 20-25% body weight over eight weeks. Compared to wild type, APO-E-/- mice showed decreased cardiac performance evidenced by reductions in stroke volume, left ventricular ejection fraction, and cardiac output. Furthermore, APO-E -/- mice had reduced aortic valve cusp separation and ejection velocity, while their aortic intimal thickness increased significantly. However, there was little change in blood pressure levels in the two groups of mice.

Conclusions: Increased ALP activity is prominent in mice fed high fat diet. APO-E -/- but not wild type mice developed hypercholesterolemia and aortic intima thickness. High fat diet induced poor cardiac performance and aortic stenosis, suggesting the presence of aortic valve disorder and calcification.

References:

1) Tonelli, M., Curhan, G., Pfeffer, M., Sacks, F., Thadhani, R., Melamed, M. L., . . . Muntner, P. (2009). Relation Between Alkaline Phosphatase, Serum Phosphate, and All-Cause or Cardiovascular Mortality. *Circulation,120*(18), 1784-1792. doi:10.1161/circulationaha.109.851873
2) Li, J. W., Xu, C., Fan, Y., Wang, Y., & Xiao, Y. B. (2014). Can serum levels of alkaline phosphatase and phosphate predict cardiovascular diseases and total mortality in individuals with preserved renal function? A systemic review and meta-analysis. *PloS one*, *9*(7), e102276. doi:10.1371/journal.pone.0102276
3) Kabootari, M., Raee, M. R., Akbarpour, S., Asgari, S., Azizi, F., & Hadaegh, F. (2018). Serum alkaline phosphatase and the risk of coronary heart disease, stroke and all-cause mortality: Tehran Lipid and Glucose Study. *BMJ Open,8*(11). doi:10.1136/bmjopen-2018-023735
4) Panh, L., Ruidavets, J. B., Rousseau, H., Petermann, A., Bongard, V., Bérard, E., . . . Ferrières, J. (2017). Association between serum alkaline phosphatase and coronary artery calcification in a sample of primary cardiovascular prevention patients. *Atherosclerosis,260*, 81-86. doi:10.1016/j.atherosclerosis.2017.03.030

ABSTRACT

Emergency Department Visits Associated with Hemodialysis by Uninsured Patients in Texas

JULIANNA WEST *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Henry E. Wang, MD, Department of Emergency Medicine
Supported by: Department of Emergency Medicine and Dean's Office of McGovern Medical School
Key Words: Uninsured, Hemodialysis, Emergent Dialysis

Background: Medicare covers chronic scheduled hemodialysis (HD) treatment for patients with end-stage renal disease (ESRD) in the United States. However, for uninsured patients with ESRD, such as undocumented individuals, HD through the Emergency Department (ED) may be the sole treatment option. In this study we sought to characterize ED visits associated with HD for an acute indication by uninsured patients in the state of Texas.
Methods: We performed a cross-sectional analysis using the 2017 Texas Emergency Department Data Set. We included all ED visits by patients ≥18 years old with a length of stay (LOS) ≤1 day and identified ED visits associated with HD treatment by the International Classification of Diseases-10p and the Healthcare Common Procedure Coding System/Current Procedural Terminology codes. The primary exposure was insurance status, with Medicare, Medicaid, commercial, and Tricare as insured and self-pay, charity, and indigent status as uninsured. We identified differences between insured and uninsured individuals using logistic regression with odds ratios and 95% confidence intervals.
Results: Of 6,968,438 adult ED visits with a LOS ≤1 day, HD was associated with 33,829 ED visits: 10,390 were uninsured (incidence 1.24 per 1,000 adult ED visits, 95% CI: 1.22-1.26) and 23,439 were insured. Most of the ED visits associated with uninsured HD originated from the Arlington (66.1%) and Houston (20.4%) regions. Uninsured HD patients were more likely to be younger (OR 4.73, 95% CI: 4.19-5.35), of white race (OR 7.09, 95% CI: 6.45-7.81), and Hispanic ethnicity (OR 5.05, 95% CI: 4.75-5.37). Most HD patients were discharged to home or home health (98.1%). Total hospital charges for uninsured HD visits totaled $91M.
Conclusion: These results highlight the large health care system burden posed by uninsured HD patients in Texas. Strategies are needed to optimize care for uninsured HD patients.

ABSTRACT

Diffusion Tensor Tractography of the Dorsal Thalamo-Hypothalamic Pathway using High Spatial Resolution DTI

LINDSAY WILKEN *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Arash Kamali, MD, Department of Diagnostic and Interventional Imaging
Supported by: Arash Kamali, MD, Department of Diagnostic and Interventional Imaging; McGovern Medical School – Office of The Dean
Key Words: Thalamus, Hypothalamus, Limbic System, DTI Tractography

Background: The thalamus is known to be involved in sensory processing by directing sensory information to various cortical and subcortical structures throughout the brain. While it is not conventionally considered to be part of the limbic system, several tracts have been identified between the thalamus and limbic structures, indicating that it is integral to limbic function. Anatomical animal studies have revealed connections between the thalamus, hippocampus and hypothalamus that suggest a separate thalamo-hypothalamic pathway from the known ventral mammillothalamic tract.

Methods: High spatial resolution DTI data from forty-five healthy adults (ages ranging from 24 to 37 years) at 3.0 T were used to reveal a dorsal pathway between the thalamus and hypothalamus. Written informed consent was obtained from all subjects prior to use of the data. Fifteen of the forty-five subjects were scanned in-house using a single-shot multislice 2-D spin-echo diffusion sensitized and fat-suppressed echo planar imaging (EPI) sequence, with the balanced Icosa21 tensor encoding scheme. DTI acquisition was repeated three times and averaged to enhance SNR. The fiber assignment by continuous tracking (FACT) algorithm was used in DTI studio with a fractional anisotropy threshold of 0.22 and an angle threshold of 608.

Results: We identified a tract between the thalamus and hypothalamus that we named the dorsal thalamo-hypothalamic tract. The tract originates in the posterior nuclei of the thalamus then projects laterally through the fornix of the hippocampus and turns anteriorly and medially into the anterior hypothalamic and septal nuclei.

Conclusion: Experimental studies on the thalamus and its association with the limbic system in both animal models and humans have revealed a range of possible functions that are supported by this dorsal thalamo-hypothalamic tract. These functions include arousal and attention processing, social behavior, migraine allodynia and photophobia, feeding behavior (including overeating and anticipation), circadian rhythm synchronization, auditory stress response and fear learning during life-threatening events. The tract also appears to be involved in Parkinson's disease autonomic dysfunction. The dorsal thalamo-hypothalamic tract elucidates the role of the thalamus in limbic system function and could potentially serves as a diagnostic tool for its dysfunction.

ABSTRACT

Comparison of Patient-level Charges Between Surgical Settings for Elective Outpatient Total Shoulder Arthroplasty

TAYLOR WILLENBRING *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Ryan J. Warth, MD, Department of Orthopedic Surgery
Supported by: Volunteer Status
Key Words: Total shoulder arthroplasty, charge analysis, outpatient

Background: Elective outpatient total shoulder arthroplasty (TSA) has shown increasing demand alongside increasing patient-level charges. These charges may be prohibitive in underserved and rural populations. In this study, we compared the charges between TSA performed in hospital outpatient departments (HOPD) and ambulatory surgical centers (ASC).

Methods: A total of 1,048 records were analyzed from the Texas Healthcare Information Collection (THCIC) database, a publicly available comprehensive collection of all documented clinical encounters in the State of Texas. Comparisons of itemized patient-level charges were made between TSdAs performed at HOPD and ASC. Statistical analysis was performed using one-way ANOVA with post-hoc Tukey analysis. P-values less than 0.05 were considered statistically significant.

Results: The mean total charges for HOPD (N=944) and ASC (N=104) were $60,482 ± $39,063 and $62,454 ± $32,153, respectively with no significant statistical difference. For all categorical sub-charges, HOPD charged significantly more ($p<0.05$) except for radiology and outpatient services. The outpatient services charge is ASC specific with a mean value of $36,184 ± 31,873. This non-specified charge comprised 57% of all ASC charges.

Conclusions: We conclude that there is no significant difference in the total charges between the two surgical settings for elective outpatient TSA. However, the large amount of ambiguous "outpatient service charges" billed from ASCs accounts for the majority of the charge differences between ASCs and HOPDs. Further studies should be done to evaluate the transparency of billing procedures and regulatory reporting for ASCs in the State of Texas.

ABSTRACT

Patient Demographic Effects on Antibiotic Decision Making

JUN YAN *McGovern Medical School at UTHealth* *Class of 2022*

Sponsored by: Deevakar Rogith, MBBS, PhD, School of Biomedical Informatics
Supported by: Deevakar Rogith, MBBS, PhD, School of Biomedical Informatics
Key Words: Antimicrobial, demographics, EHR data, clinical decision making

Importance: A key step toward effective antibiotic stewardship is to study the patterns of antibiotic prescription in the clinic and identify factors that contribute to the clinician's decision making when prescribing antibiotics.

Objective: The aim of this study is to identify key demographic factors affecting the diagnosis and treatment course of patients with infections where antibiotic use is clinically indicated.

Design: Analysis was performed on electronic health record (EHR) data. Encounters relevant to antibiotic prescription were identified by the authors via encounter diagnosis (identified via International Classification of Diseases 9th (ICD 9) or 10th revisions (ICD 10)).

Setting: Data was obtained from a clinical data warehouse containing clinical data from multiple ambulatory encounters in Texas from 2010 to end-of-year 2018.

Patients: All patients with an office visit with a relevant diagnosis were included in the analysis.

Main Measures: We identified discreet clinical decisions: what to diagnose, whether to prescribe, and what to prescribe. We compared the physician's diagnosing behavior (diagnosis indicating antibiotics vs. not indicating antibiotics) and antibiotic prescribing behavior (whether to prescribe antibiotics, and whether to prescribe broad-spectrum antibiotics) by demographic the patient factors race, age, sex, gender, and insurance status (public vs. non-public).

Results: Black patients, older patients, and patients with public payer health insurance were diagnosed with an antibiotic indicating diagnosis at a lower rate than the average patient. Regardless of diagnosis indication, black patients and patients on public payer insurance plans received antibiotics at a lower rate. Stratification between antibiotic-indicating and non-indicating diagnoses revealed that the disparity between black patients and nonblack patients when antibiotics were not indicated is larger than when antibiotics were indicated. Younger patients were diagnosed with respiratory infections at a higher rate compared to older patients but received antibiotics for these diagnoses at a lower rate.

Conclusions: Differences in diagnosis and treatment based on patient demographic characteristics reveal patient characteristics which influence clinical decision making.

UTHealth | McGovern Medical School

The University of Texas Health Science Center at Houston

Undergraduate Students

UTHealth | McGovern Medical School

The University of Texas Health Science Center at Houston

International Students