UTHealth
The University of Texas
Health Science Center at Houston

McGovern
Medical School

2018 SUMMER RESEARCH PROGRAM
STUDENT ABSTRACTS

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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

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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.

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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)."

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ABSTRACT

Immunofluorescence Staining of Oncostatin M in Human Dorsal Root Ganglion

JAMES ABERCROMBIE *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Patrick M. Dougherty, PhD; Yan Li, PhD; The University of Texas MD Anderson Cancer Center; Division of Anesthesiology, Critical Care, and Pain Medicine

Supported by: The Role of ENF Loss, TLR4 and Spinal Plasticity in Paclitaxel CIPN — CA200263

Key Words: Oncostatin M, Human Dorsal Root Ganglion, Neuropathic Pain

Oncostatin M (OSM), a member of the IL-6 family of cytokines, was first discovered in 1986 when it was shown to inhibit the growth of human cell lines, such as neuroblastoma and malignant melanoma. OSM binds to its membrane receptor, OSMR, to activate the JAK/STAT and MAPK pathways to regulate transcription.

In a previous study, a significant difference was identified between patients with nociceptive axial pain without radicular pain and patients with unilateral or bilateral radicular pain. The first group was composed of patients without radicular pain (Group 1), the second with unilateral radicular pain (Group 2), and the third with bilateral radicular pain (Group 3). In the study, it was shown that radicular pain was strongly associated with nerve root compression (North et al, 2018). RNA sequencing data reveal that OSM is upregulated in patient groups with radicular pain due to nerve root compression when compared to patients without radicular pain.

In the present study, immunofluorescence staining was employed to determine the location and level of expression of OSM in human dorsal root ganglion (DRG). A polyclonal antibody raised in rabbit against the human OSM was used to stain human DRG samples collected from patients undergoing spinal root compression neurosurgery. It is necessary to further divide the previous Group 2, patients with unilateral radicular pain, into patients with a unilateral ganglionectomy on the non-painful side, patients with a unilateral ganglionectomy on the painful side, and patients with a bilateral ganglionectomy (both painful and non-painful sides). Unilateral ganglionectomy patients on the non-painful side exhibited weak staining of OSM in human DRG. Unilateral ganglionectomy patients on the painful side shows strong staining of OSM on the DRG neurons. Bilateral ganglionectomy patients with DRG collected from both the painful and non-painful sides reveals strong staining of OSM on the painful side when compared to the non-painful side.

The present study supports that radicular pain in patients can occur due to nerve root compression and connects OSM as an important mediator. Further investigations are necessary in order to determine if OSM plays a causative or secondary role in the development of neuropathic pain.

ABSTRACT

The Effects of E-Cigarettes on Fracture Healing

TRAVIS ALFORD *McGovern Medical School at UTHealth* Class of 2021

Sponsored by: Catherine G. Ambrose, Ph.D. Department of Orthopaedic Surgery
Supported by: Foundation for Orthopedic Trauma
Key Words: Fracture, Bone, Healing, Electronic Cigarettes

Purpose of Study
Cigarette smoking has been shown to delay fracture healing. Cigarettes have additional detrimental effects on bone health such as increased rates of bony non-union, lower bone mineralization density and weaker bony strength tests. Many orthopaedic surgeons, therefore, insist on smoking cessation prior to elective surgery. Electronic cigarettes represent a popular new alternative to traditional cigarettes. The literature is currently uncertain regarding the compound within cigarette smoke that leads to a decline in bone health, however, current theory suggest nicotine may be implicated. Electronic cigarettes and traditional cigarettes both contain this chemical, thus it is important to determine if electronic cigarette vapors produce a similarly detrimental response in bone healing. If they do not, they may represent a safer alternative nicotine delivery system for patients undergoing orthopedic surgery.
Methodology
Sprague-Dawley rats (male, 260g, N=48) were divided into three groups (N=16) for either ambient air, cigarette or e-cigarette exposure. The TE-2 Manual Smoking machine (Teague Enterprises) was used for experimental exposure. The e-cigarette group was exposed for twenty minutes twice daily. The cigarette group was also exposed for two, twenty-minute sessions, and consumed a total of four cigarettes per session. After one week of exposure, an orthopaedic traumatologist surgically created a midshaft femur fracture in the right thigh of each animal. The smoking or ambient air exposure subsequently continued daily until euthanasia. Half of the animals were euthanized at three weeks to provide insight into the time course of bone healing and the other half were euthanized at six weeks. After euthanasia, contact radiographs were gathered and judged by two blinded orthopaedic surgeons using a modified RUST scoring system. Micro CT data was collected and used to assess measures of bone mineralization density. Statistical analyses were run to determine between group differences.
Results
There were significant correlations between the modified RUST scores and the analyzed microCT data. Fracture healing was increased at 6 weeks compared to 3 weeks for all three groups. Three weeks after fracture, most outcome measures showed that the control group had higher healing than the cigarette group, with the e-cigarette group measuring between the 2 other groups. At 6 weeks after fracture, the animals in the e-cigarette group has persistent callus formation which was higher than the animals in the other 2 groups. At this time, mechanical testing results are still being analyzed.
Conclusions
It appears that the effects of cigarette smoke exposure on fracture healing are more significant than the effects of e-cigarette exposure, but data analysis is ongoing.

ABSTRACT

Parental Engagement in Patient Safety

KYLIE ANTHONY *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Akemi Kawaguchi, MD, Department of Pediatric Surgery
Supported by: Akemi Kawaguchi, MD
Key Words: parental engagement, patient safety, health policy

Background and Hypothesis:
While patient safety research often focuses on the perspective of healthcare providers and patients, the parents of pediatric patients also play a significant role in their children's healthcare. We hypothesized that parents will offer unique observations on their children's healthcare safety that may be useful to improve patient care.

Methods: We conducted a cross-sectional study on a medical-surgical pediatric unit within a tertiary children's hospital. Over a ten-week period, English-speaking parents and legal guardians were asked to complete a paper or electronic survey about patient safety adapted from the validated inpatient Safety Attitudes Questionnaire. The survey contained 20 questions on a 5-point Likert scale representing three domains: safety climate, perception about management, and teamwork. Two additional open-ended questions were included to identify their top three patient safety issues and viewpoints on patient safety in the hospital.

Results: 150 of the 168 (89%) patient families approached agreed to participate. 58 of the 150 surveys were returned (39%). 53 were paper surveys and 5 were submitted electronically. Patients had a median length of stay of 3 days (range 1-17 days), with 48% a first hospitalization, and a wide variety of diagnoses. Overall, 96% of the responses were slightly or strongly positive. Safety climate statements were 95% positive, teamwork statements were 98% positive, and perception of management statements were 97% positive. The statements with the least positive parental responses are listed in the table below. The top three most common parental responses to the open-ended questions included concerns about security at the entrance of the floor, handwashing by staff, and bed height for pediatric patients.

Conclusion: Parents have a unique perspective on safety concerns regarding their child's care while in the hospital. A focus on improving communication, improving information exchange, and empowering parents to speak up for their child's care may be useful to help improve the care of pediatric patients.

Table 1. Least positive parental survey responses

	Positive Responses			Negative Responses		
Statement	N	Strongly Positive (%)	Slightly Positive (%)	N	Slightly Negative (%)	Strongly Negative (%)
I know where I can direct questions about my child's safety in this hospital (Safety Climate)	46	79.5	14.2	3	4.1	2.0
In this hospital, it is difficult to speak up if I perceive a problem with my child's care. (Safety Climate)	40	69.5	17.3	6	2.2	10.9
Problems often occur in the exchange of my child's healthcare information when moving to different parts of the hospital. (Teamwork)	36	79.4	12.8	3	5.1	2.6
Communication with physicians about my child is difficult.	47	83.3	3.7	7	7.4	0.0

ABSTRACT

A Systematic Review of Reported Funding Sources and Industry Affiliations in Randomized Clinical Trials of Biologic Treatments in Sports Medicine

HAYDEN ANZ, HEBA AHMAD *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Ryan J. Warth, MD, Department of Orthopedic Surgery
Supported by: Johnny Huard, PhD, Department of Orthopedic Surgery
Key Words: Biologics, systematic review, funding, sports medicine, orthopedics

Purpose/Hypothesis: The purpose of this study was to evaluate relationships between clinical outcomes and industry affiliations in randomized clinical trials of biologic treatments in sports medicine. We hypothesized that the industry affiliations will be associated with reporting of favorable results when compared to studies without industry affiliations.
Methods: A systematic search of the PubMed and Embase databases was performed to identify sources of funding and favorability of conclusions reported for all Level I and Level II randomized clinical trials that investigated the treatment of sports medicine-related injuries using a biologic treatment compared to a standard treatment. Industry affiliation was defined as a funding source or author affiliation with the company that provided the biologic product being studied. The terms used for database search included "platelet rich AND randomized" and "marrow aspirate AND randomized". Data were extracted from each study in duplicate by two independent reviewers; these data included the reported purpose, conclusion, sources of funding, researcher industry affiliations, sample size, minimum follow-up, and the outcomes metrics utilized. Two-tailed t-tests were used to compare frequencies of favorable results according to body region, industry affiliation, and funding source. Logistic regression analyses were performed to identify interactions between body region, industry affiliation, funding source, and favorability of conclusions with respect to the biologic treatment. Regression coefficients are reported as odds ratios (ORs) and statistical significance was declared when $p<0.05$.
Results: Systematic literature search provided 2,241 records after removal of duplicates. Ninety-two studies met our inclusion criteria and included a total of 5,618 subjects (2,691 males [47.9%]) with an average minimum follow-up of 10.0 months (standard deviation [SD], 8.0 months; range, 6 weeks-24 months). The studies investigated shoulder issues (n=24; 26.1%), knee issues (n=33; 35.9%), foot and ankle (F&A) issues (n=17; 18.5%), and elbow issues (n=12, 13.0%). Only 43 of the 92 studies (46.7%) reported the source of study funding. In total, 71 of the 92 studies (77.2%) reported favorable results (**Figure 1**) and 17 of these studies (18.5%) reported industry affiliations (**Figure 2**). Published studies of knee pathology were significantly more likely to report results in favor of the biologic treatment ($p=0.006$). Logistic regression analyses indicated no statistically significant relationships among body region, industry affiliation, or funding source and the reported favorability of the biologic treatment ($p<0.05$; all ORs include 1.0).
Conclusion: Our results indicate little-to-no interactions among body regions, funding sources, or reported favorability of the biologic treatment being studies. However, knee studies were significantly more likely to report favorable results regarding biologic treatment. Clinical reports

of randomized trials should emphasize reporting of funding sources to ensure data transparency and interpretability of results.

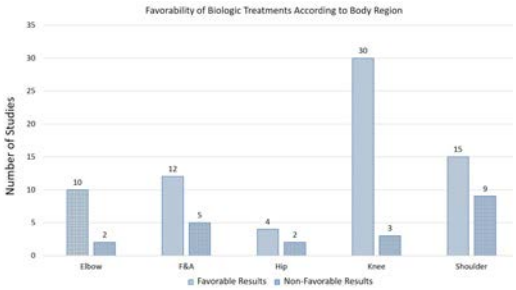

Figure 1

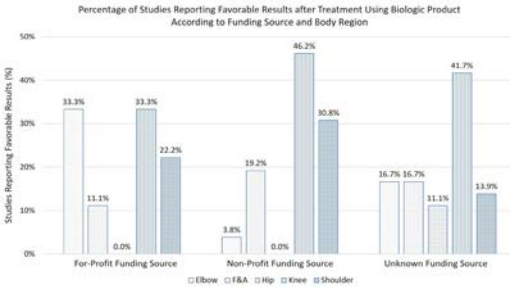

Figure 2

ABSTRACT

Analysis of Neuronal Network Changes Following Operant Conditioning in *Aplysia*

PANAYOTIS APOKREMIOTIS — *McGovern Medical School at UTHealth* — *Class of 2021*

Sponsored by: John H. Byrne, PhD
Supported by: Dean's Stipend and NIH Grant "Analyses of the Distributed Representation of Associative-Learning in an Identified Circuit Using a Combination of Single-Cell Electrophysiology and Multicellular Voltage-Sensitive Dye Recordings, "R01 NS101356 to Dr. John H, Byrne
Key Words: *Aplysia*, Extracellular nerve recording, Operant Conditioning, Spike Sorting

Background

Adapting behavior based on the consequences of one's actions (operant conditioning) is a basic and essential form of learning. However, little is known about the neuronal network changes induced by this learning. I focused on the analysis of extracellular nerve recordings of the buccal ganglion, which controls feeding behavior in *Aplysia* and its modification by operant conditioning. As a first step in analyzing learning-induced changes in the network, it is necessary to identify the individual neurons contributing to the extracellular activity. To do this, I implemented the spike sorting algorithm KiloSort.

Methods

KiloSort is a template-matching algorithm used on nerve tracings to cluster action potentials from the same neuron. To validate that the action potentials clustered by Kilosort were derived from an individual neuron, I analyzed and compared nerve tracings of neuronal activity from the radula nerve (Rn) with simultaneous intracellular recording of B8, a neuron known to project through Rn, as a ground truth.

Results

Theoretically, each of the 32 templates produced by Kilosort corresponds to an individual neuron, and each action potential clustered to that template come from the same neuron. In practice, some templates captured noise, so 12 templates on average corresponded to unique waveforms that have a high likelihood of being unique neurons.

Of all of the intracellularly recorded action potentials from B8, KiloSort correctly detected and clustered 67% of the corresponding action potentials in Rn into one template. Of all of the action potentials clustered to that template, 55% of them did not correspond to an intracellular action potential from B8 and were therefore incorrectly assigned.

Conclusion

These percentages are acceptable because there are 4 different B8 neurons that project through Rn. Distinguishing between their action potentials is challenging and not relevant because they perform the same function. With the addition of KiloSort, we will increase number of neurons we can analyze, and any neuron identified by KiloSort can be analyzed for longer durations of time. Moving forward, we will use KiloSort in conjunction with voltage-sensitive dye imaging to identify the changes in the neuronal activity of the buccal ganglia that encode the learning for operant conditioning.

ABSTRACT

Traditional versus Realistic Bleeding Control Training Models

MARIA JOSE ARAUJO *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Sasha D. Adams, MD, Department of Surgery
Supported by: Center for Translational Injury Research
Key Words: Simulation, education, trauma

Purpose of study

Uncontrolled bleeding is the main cause of preventable traumatic death and the arrival of first responders may be delayed due to safety concerns. The Hartford Consensus education program "Stop the Bleed" was created to train non-medical bystanders with skills to control hemorrhagic wounds until first responders arrive, potentially saving lives. Prior studies found that 1-hour hands-on instruction an effective method to teach these techniques. We hypothesized that a realistic bleeding simulator would improve the quality and impact of this training.

Study design, analyses, materials used

Third year medical students (MS3) and non-medical summer students (NMS) underwent "Stop the Bleed" training. Each student was given an anonymous identifier to track results and were randomized into standard "DRY" model or realistic "WET" bleeding simulator groups. After a didactic lecture by a certified instructor they each had hands-on training to pack wounds and place tourniquets. Students completed pre and post surveys to evaluate baseline knowledge, teaching effectiveness, and willingness and preparedness to intervene to help a bleeding stranger. They were observed placing a tourniquet and packing a wound, timed and evaluated on technique. Statistical significance, defined as $p<0.05$, was analyzed using T-test and the Likert scale by Wilcoxon-signed ranked test.

Summary of results

Students (n=360) were trained in bleeding control techniques (241 MS3, 119 NMS) and stratified between WET (n=171) and DRY models (n=189). Results were excluded if unpaired or incomplete. While both groups demonstrated improved average correct of 5 knowledge questions after training (MS3 3.9 to 4.8, NMS 3.3 to 4.2) there was a significant difference in the NMS compared to the MS both before and after. Both groups had a similar and significant increase in willingness and preparedness to help a bleeding stranger after training, irrespective of the method. Compared to the DRY teaching model, students on the WET model needed more correction on technique and required significantly more time for tourniquet placement (DRY: 50 sec, WET: 62 sec). For wound packing, however, students on the WET model were faster (DRY: 72 sec, WET: 62 sec), but this could be attributed to different packing spaces between models.

Conclusion

Students receiving training in bleeding control techniques are confident and empowered to aid a bleeding victim irrespective of the teaching method. Students on the WET tourniquet model voiced anxiety due to the active "bleeding", and were visibly fumbling, which may account for

the longer time to placement. This may be a better representation of the real world experience, and may help them overcome those anxieties to intervene while still in a training situation.

ABSTRACT

Laser Treatment of Burn Scars

JANET R. ASHLEY *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: David J. Wainwright, MD; UT Physicians Plastic and Reconstructive Surgery
Supported by: UT Physicians Department of Plastic and Reconstructive Surgery
Key Words: Ultrapulse laser, burn scars, patient satisfaction

Background: The Ultrapulse CO2 laser is a useful tool for scar management. Studies have shown that use of a fractionated CO2 laser in scar revision is safe and yields improvement in both scar gross and histological appearance. Patients have reported positive changes in skin thickness, relief, and pliability.

Objectives: The purpose was to determine which scar characteristics prompted patients to undergo laser treatment for their burn scars and how well this modality meets their needs. We also assessed the immediate post laser experience in burn patients undergoing Ultrapulse Laser scar modification.

Methods: Patients undergoing laser treatment for their burn scars were selected for the study. Three questionnaires were created. 1. To determine the primary patient problem; 2. Patient perceived effectiveness; 3. Patient experience including pain, wound care, and the effect on other scar management techniques. The scar characteristics evaluated were itching, pain, redness, stiffness/dysfunction, pigmentation, appearance, thickness, irregularity, and dryness.

Results: 19 patients were enrolled in the study. Patient demographics and burn injury details were gathered on all of the patients. 50% of patients were Hispanic, 25% were Caucasian, 13% were Asian, 6% were African American, and 6% were unknown. The average age was 40 (19-64). 63% of patients were male. Patients had an average of 36% burn area with a range of 3% to 89%. The most common problematic burn scar characteristics were itching (94% of patients) and pain (88% of patients) and these were also the primary reasons for seeking laser treatment in most patients. Despite this, patients perceived thickness as the most severe burn scar characteristic. Itching and pain were the burn scar characteristics that patients reported the laser to be most effective. Patient experience was evaluated in twenty patients. Eighteen patients reported pain associated with laser treatment of their burn scars, and this was typically moderate. Most (80%) patients reported superficial wounds associated with laser treatment, with the majority closed by 8 days. Wounds were typically dressed with xeroform and bacitracin ointment. Moisturizer and scar garments were typically resumed 13 and 15 days after laser treatment for their burn scars, respectively. Of the four patients who use silicon, it was resumed 17 days after laser treatment. Overall patient experience with laser treatment was positive and many (80%) patients said they would recommend this modality of burn scar treatment to others.

Conclusions: Itching was the most common burn scar characteristic prompting burn patients to seek laser treatment and, along with pain, showed the most improvement. Laser treatment is generally well tolerated and interferes minimally with other scar treatment modalities.

ABSTRACT

Audit and Feedback Accelerates Reduction in Opioid Prescriptions in Pediatric Surgical Patients

JOHN-PAUL BACH *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: KuoJen Tsao, MD, Department of Pediatric Surgery
Supported by: KuoJen Tsao, MD
Key Words: Opioids, Pediatrics, General Surgery, Prescribing Practices

Introduction: Opioid prescriptions, commonly written for post-operative pain, are an important component of the opioid epidemic. While physician awareness of excessive opioid prescribing has increased, few surgeon-level interventions for prescription reduction have been described. The aim of this study was to evaluate the impact of a simple audit and feedback intervention on pediatric surgeon opioid prescriptions in post-operative appendectomy patients at discharge.

Methods: Pediatric (<18 years) patients who underwent appendectomy for simple appendicitis from October 2016 through May 2018 were included in a retrospective review of discharge opioid prescriptions. Patients were discharged from a tertiary care Children's Hospital located in a state in which only fully-licensed (primarily attending) physicians can prescribe out-of-hospital opioids. Prescription data were captured from a state prescription monitoring program database. At the end of October 2017, discharge opioid prescriptions for simple appendectomies over the previous 6 months were audited. These data were fed back to attending pediatric surgeons in a 10-minute presentation, providing descriptive statistics of their opioid prescribing patterns as a group. No specific guideline was established regarding opioid prescribing. The Cochran-Armitage test for trend was used to evaluate for prescription trends over time. Student's t-test, Wilcoxon rank sum and test for trend were used to compare pre- (10/1/16-10/31/17) and post- (11/1/17-5/31/18) intervention dosing.

Results: Amongst the nine attending pediatric surgeons, opioid prescriptions at discharge for pediatric patients with simple appendicitis decreased significantly over time, ($p<0.005$) from a zenith of 84% of patients receiving a prescription in January 2017 to 0% receiving a prescription in February and March 2018. Morphine milliequivalents per day (mme/d) prescribed also declined significantly in mean dose (20.5 mme/d ± 12.7 pre-intervention vs. 16.5 mme/d ± 13.6 post-intervention, $p<0.005$). Number of days for which opioids were prescribed also decreased from a median of 5 days (IQR 3-6) to a median of 3 days (IQR 3-4), $p=0.05$.

Conclusion: Although the rate of opioid prescription was already falling, a simple educational intervention dramatically accelerated the rate of decline. Audit and feedback of individual or local group prescribing practices may help prescribers recognize their contribution to unnecessary opioid use.

ABSTRACT

Exploring the Genetic Association of Valve Morphology in Bicuspid Aortic Valve Disease

PRESTON BAKER *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dr. Siddharth Prakash MD, PhD, Ellen Regalado MS, CGC, Department of Medical Genetics
Supported by: Dr. Siddharth Prakash MD, PhD
Key Words: Heritability of Cusp Orientation

Introduction: Bicuspid aortic valve (BAV) is the most common adult congenital heart defect and is associated with thoracic aortic aneurysms (TAA) and aortic valve degeneration requiring surgical repair. The penetrance and age of onset of cardiovascular complications are variable and are difficult to predict in sporadic cases. Clinical studies indicate that BAV cusp orientation may predispose to adverse outcomes. While 10% of cases are familial, the heritability of cusp orientation is not proven. We hypothesize that genetic factors regulating the bicuspid morphology of the aortic valve are heritable and may predict BAV-related clinical manifestations in familial cases.

Methods: I ascertained eligible families for analysis from the UTHealth Bicuspid Aortic Valve Research Registry and the Division of Medical Genetics. Families were included if there were at least two relatives with documented BAV. I abstracted data on clinical and demographic characteristics, BAV cusp orientation, valve function, congenital heart defects and surgical repair from all available family members into a customized database. I constructed detailed pedigrees to illustrate the heritability of cusp orientation and cardiovascular outcomes.

Results: 21 families with a total of 55 affected individuals were included in the study; I will present data from three representative families. Family 1 included 8 individuals with BAV and TAA in two generations. Valve morphology was not concordant: 3 had R-L (Type 1) and 3 had R-N (Type 2) orientations. However, diffuse aortic dilation involving the root and ascending aorta was present in all affected individuals. Family 2 included one father with Type 2 cusp orientation and two sons with Type 1 orientations, but all three affected individuals presented with isolated ascending aneurysms and required aortic valve replacements due to aortic insufficiency. Family 3 consisted of two siblings with concordant Type 1 cusp orientations. However, their clinical presentations (mitral valve prolapse and TAA) were discordant. I found no correlation between aortic morphology and cusp orientation in any of the investigated families.

Conclusions: Valve and aortic anatomy and complications are variably concordant in BAV families. Inherited patterns of BAV morphology and disease may provide insight into the genetic landscape of BAV. I am currently analyzing additional families to replicate these observations.

ABSTRACT

Effectiveness of Prehospital Dual Sequential Defibrillation for Refractory Ventricular Fibrillation and Ventricular Tachycardia Cardiac Arrest

Lauren Beck *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Henry E. Wang, MD, MPH, MS, Department of Emergency Medicine
Supported by: Henry E. Wang, MD, MPH, MS, Department of Emergency Medicine; McGovern Medical School at UTHealth – Office of the
Key Words: Dual sequential defibrillation, out-of-hospital cardiac arrest, refractory ventricular fibrillation

OBJECTIVE: Dual sequential defibrillation (DSD) – successive defibrillation with two separate defibrillators – offers a novel approach to refractory ventricular fibrillation and tachycardia (VF/VT). The effectiveness of DSD is unknown. We evaluated the association of DSD with outcomes in refractory VF/VT out-of-hospital cardiac arrest (OHCA).

METHODS: We used data from Houston Fire Department, a large metropolitan fire-based EMS service. We included all adult OHCA during 2013-2016 with refractory VF/VT after ≥3 standard 360J defibrillations. Online physicians authorized subsequent DSD use, consisting of rapid successive 360J rescue shocks delivered by two separate defibrillators (PhysioControl LIFEPAK® 12/15) with pads placed anterior-lateral and anterior-posterior. Evaluated outcomes included return of spontaneous circulation (ROSC), survival to hospital admission, survival to 72 hours, and survival to hospital discharge. Using multivariable logistic regression, we evaluated the association between defibrillation type (DSD vs convention) and OHCA outcomes, adjusting for patient demographics and event characteristics.

RESULTS: We included 310 patients in the analysis, including 71 patients receiving subsequent DSD, and 239 receiving conventional defibrillation. Patient demographics and event characteristics were similar between DSD and conventional defibrillation. ROSC was lower for DSD than standard defibrillation: 39.4% vs 60.3%, adjusted OR 0.46 (95% CI: 0.25-0.87). There were no differences in survival to hospital admission (35.2% vs 49.2%, adjusted OR 0.57 [95% CI: 0.30-1.08]), survival to 72 hours (21.4% vs 32.3%, adjusted OR 0.52 [95% CI: 0.26-1.10]), or survival to hospital discharge (14.3% vs 20.9%, adjusted OR 0.63 [95% CI: 0.27-1.45]).

CONCLUSIONS: Compared with conventional defibrillation, DSD was associated with lower odds of ROSC. Defibrillation type was not associated with other OHCA endpoints. DSD may not be beneficial in refractory VF/VT OHCA.

ABSTRACT

Elevated Neutrophil to Lymphocyte Ratio (NLR) in Cocaine Use Disorder (CUD) as a Marker of Chronic Inflammation

AMBER BERUMEN *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: *Scott D. Lane, Ph.D.*, Professor & Vice Chair for Research, Department of Psychiatry & Behavioral Sciences
Dr. Joy M. Schmitz, Ph.D., Louis A. Faillace Professor at the Department of Psychiatry and Behavioral Sciences, Director for the Center for Neurobehavioral Research on Addiction (CNRA)
Supported by: Saltzberg Summer Fellowship Award in Psychiatry
Key Words: Chronic inflammation, Cocaine, Aging, Biomarker

Elevated Neutrophil to Lymphocyte Ratio (NLR) in Cocaine Use Disorder (CUD) as a Marker of Chronic Inflammation

Background: Recent studies have used NLR as an inflammatory marker to predict incidence, morbidity, and mortality in both systemic and psychiatric disorders. Evidence of increased inflammation in CUD supports the premise for evaluating NLR as a potentially significant inflammatory marker, however this has not been evaluated in aging CUD populations, who may be at increased risk. Aging is associated with a decline in immune system function, and this process is often complicated with proinflammatory comorbidities prevalent in older adults, such as diabetes and hypertension. This project sought to examine whether chronic cocaine use adds exacerbated inflammatory burden among older adults (50-65 years old) with CUD relative to a nationally representative sample of non-cocaine users. Common age-related conditions such as diabetes, hyperlipidemia, and hypertension were included in the dataset, but known inflammatory conditions were excluded. Specifically, we hypothesized increased NLR in patients with CUD vs. matched controls. Within CUD, we predicted significant associations between NLR and markers of addiction severity, social function, and cognitive function.

Methods: The dataset included 107 participants meeting standardized diagnostic criteria for CUD who were participating in cocaine treatment trials. NLR values were derived from routine complete blood count tests. Additional variables of interest (within the CUD group) included cocaine severity, social functioning, and cognitive functioning. We used the National Health and Nutrition Examination Survey (NHANES) to extract data from adults (50-65) without CUD. A doubly robust propensity score method (inverse-probability-weighted regression adjustment, or IPWRA)was used to estimate group differences on NLR while controlling for potential confounding variables (age, gender, race, income, smoking, marijuana and alcohol use). All subjects with immunocompromising conditions were excluded from the analyses (e.g., HIV, STDs, TB, active infections). Relationships between NLR and addiction-related variables were tested via linear regression.

Results: The propensity score model estimates revealed a significant difference in NLR between the groups $\beta = 0.67$, robust S.E. = 0.14, Z-score = 4.88, $p < .0001$. The means and standard errors for the groups were CUD = 2.38 (± 0.13); controls = 1.71 (± 0.02). The β weight of 0.66 indicates

a moderate effect size, confirming the initial hypothesis of greater inflammation in CUD subjects aged 50-65 versus an age matched nationally representative sample. Within the CUD group, there were no identified associations between NLR and the addiction-related variables.

ABSTRACT

Chemoprevention in breast cancer subtypes *in vitro* with NSAIDs and phosphatidylcholine-associated NSAIDs

SHELLEY BURGE *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Lenard M. Lichtenberger, Ph.D., Department of Integrative Biology and Pharmacology
Supported by: Lenard M. Lichtenberger, Ph.D
Key Words: Breast cancer, NSAIDs, Aspirin, Indomethacin, Phosphatidylcholine

Introduction: Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to reduce incidence, progression and mortality of several cancers in epidemiological studies. The Lichtenberger lab has found that phosphatidylcholine (PC) associated NSAIDs are even more effective than NSAIDs alone in inhibiting tumor growth *in vitro* and *in vivo*. Studies of aspirin's effect on breast cancer have had mixed results. Aspirin's purported activity against breast cancer is typically attributed to inhibition of COX-2, which is overexpressed in some breast tumors. Thus, the current study was carried out to investigate whether the inhibitory effect of NSAIDs and PC-NSAIDs would vary for specific breast cancer subtypes, and whether these impacts could be correlated to COX-2 expression in each subtype.

Methods: Human breast cancer cell lines were obtained representing three major breast cancer subtypes: MCF-7 (hormone receptor (HR) +, HER2-), SKBR3 (HR-, HER2+) and MDA-MB-231 (HR-, HER2-). To assess cell proliferation, cells were plated in 24-well plates for 8 days in culture medium containing a test drug and 5% FBS, with one change of medium on day 4. Test drugs were aspirin 0-1 mM, phosphatidylcholine-associated aspirin (aspirin-PC) 0-1 mM, indomethacin 0-50 μM and indomethacin-PC 0-50 μM. A control of phosphatidylcholine (PC) alone was run for each drug and cell line. After 8 days, proliferation was assessed with an MTT assay. Cell culture supernatant collected on day 4 was assayed for prostaglandin E2 (PGE2) activity as a marker of COX-2 expression.

Results: Tukey's HSD test was used to determine significant reductions in cell proliferation relative to an untreated control. Aspirin significantly inhibited proliferation of MDA-MB-231 and SKBR-3 cells at high concentrations (0.4-1 mM), but did not inhibit MCF-7 cells. Proliferation of all cell lines was significantly and dramatically inhibited by aspirin-PC even at low concentrations. Unexpectedly, PC alone inhibited cell proliferation as effectively as aspirin-PC. Indomethacin and indomethacin-PC significantly reduced proliferation of all cell lines. Indomethacin-PC inhibited proliferation more effectively than indomethacin or PC alone for all cell lines. Native expression of PGE2 was low for all cell lines, with less than 30 pg/mL present in supernatant collected from control cells. NSAIDs reduced PGE2 expression only minimally.

Conclusion: NSAIDs and PC-NSAIDs reduced *in vitro* proliferation of cell lines representing three major breast cancer subtypes. Indomethacin-PC was particularly effective on all three lines, making it a promising candidate for further study. COX-2 inhibition did not account for the anti-tumor effects of NSAIDs in this study.

ABSTRACT

CT Scan Analysis Indicates Nutritional Status in Trauma Patients

FRANK CAI *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Sasha D. Adams, MD, McGovern Medical School, Surgery, CeTIR
Supported by: Charles E. Wade, PhD, CeTIR
Key Words: Dietician assessment, sarcopenia, malnutrition, average psoas area

Introduction:
More than 2 million people are hospitalized in the US annually for traumatic injuries. These patients are at risk for malnutrition due to prolonged preoperative fasting and minimal intake due to ileus or intestinal injury, and their injuries increase metabolic demands. The gold standard diagnosis for malnutrition is a dietician interview and physical exam to assess ASPEN/AND malnutrition consensus criteria. Weight loss, loss of muscle mass and fat are commonly used as indicators, along with calorie intake history, however, this requires time, resources and training. Given the prevalence and accessibility of CT imaging in trauma admissions, morphometric analysis has the potential to be an indicator of admission nutritional status. We hypothesized that admission CT scans can identify individuals at high risk of being malnourished on arrival, and this early identification can target them for aggressive nutrition supplementation.
Methods:
We did a retrospective review of adult (>15 years) patients with traumatic injuries admitted to our level I trauma center. We included patients with admission abdominal CT scans and a dietician nutritional assessment within 3 days. Patients were stratified by gender, age (Young<65 years, Older≥65 years), and nutritional status, designated as non-malnourished (NM) or moderate-severe malnourished (MSM). CT images were analyzed using Aquarius TeraRecon software to calculate the average psoas area at the level of 4-5thlumbar disc. Statistical significance was determined by stepwise selection modeling and set at $p<0.05$.
Results:
Images were analyzed in 120 patients, of which 58% were male. The mean age was 53.6 ± 21.6 and 37% were Older (n=44). The median average psoas area in NM Young males (n=47) was 18.6 cm^2, compared to a median of 12.9 cm^2 in the MSM. For Young females (n=29), the medians were 10.6 cm^2 in the NM and 9.2 cm^2 in the MSM. When looking at the older population, Older males (n=23), had a median of 12.1 cm^2 in the NM and 9.7 cm^2 in the MSM. Older females (n=21) had a median of 8.4 cm^2 in the NM and 6.6 cm^2 in the MSM. With stepwise selection modeling, we found that gender and psoas size each had a significant effect on the nutritional status. Age by psoas size demonstrated an interaction on nutritional status, but did not reach significance.
Conclusion:
Our data show that average psoas area significantly decreases in patients diagnosed with malnutrition. Gender is also associated with a significant increased risk in having malnutrition. In trauma patients with admit CT scans, psoas area analysis can potentially be used to trigger a more aggressive nutrition supplementation plan upon admission, even before dietician assessment.

ABSTRACT

Microglial Response to Probiotic Treatment Following Traumatic Brain Injury

FANNI B. CARDENAS *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Charles S. Cox, Jr., MD, Department of Pediatric Surgery
Supported by: Charles S. Cox, Jr., MD, Department of Pediatric Surgery; McGovern Medical School at UTHealth, Office of the Dean
Key Words: Traumatic brain injury, TBI, microglia, microbiome, gastrointestinal dysfunction

Introduction: Traumatic brain injury (TBI) has widespread effects on the body, including gastrointestinal dysfunction. Morbidity from TBI results from chronic inflammation propagated by activated microglia. Probiotics alter the gut microbiome and may reduce inflammation, but studies of probiotic effects following TBI are limited. While activation of brain microglia indicates an inflammatory response, microglia expressing M1 markers propagate inflammation, while M2 microglia are associated with repair and anti-inflammation following injury. We aimed to understand the role of probiotic treatment post-TBI by characterizing the microglial immune response via M1/M2 inflammatory profiles. We hypothesized that probiotic treatment would reduce gut dysbiosis, thereby mitigating the overall inflammatory response to TBI.

Methods: Controlled cortical impact (CCI) injuries were given to Sprague-Dawley rats, which were then treated with a single strain probiotic, LR 17938, for 21 days. Sham animals were included to allow for normalization of data. LR 17938 was cultured every 2-3 days in deMan-Rogosa-Sharpe (MRS) media for 24 hours. Rats were individually housed to prevent cross-contamination. On Day 21, brains were harvested to undergo dissociation into single cell suspensions. Immune-phenotyping was performed via flow cytometry (LSRII, BD Biosciences) for isolated microglia. Cells positive for CD45+, CD11+, and P2Y12+ were classified as activated microglia. CD32+ and CD86+ markers were used to classify microglia as M1 phenotype, while CD200R+, RT1B+, and CD163+ were markers of M2-type microglia.

Results: CCI animals treated with probiotics had significantly increased microglial activation ($p<0.01$) in comparison to untreated CCI animals. M1/M2 profile analysis showed that CCI probiotic animals had significantly more activated cells exhibiting the M1 CD86 inflammatory marker than CCI animals without treatment ($p<0.001$). M2 CD200R expression was significantly higher in CCI probiotic animals in comparison to untreated animals ($p<0.001$). The M1/M2 ratio was shifted towards an M2 phenotype in animals that received probiotics when normalized to their respective shams.

Conclusion: Probiotic treatment resulted in increased microglial activation, leading to an increased overall inflammatory response. Yet, analysis of M1/M2 markers revealed an association between probiotic use and M2-exhibiting microglia. Thus, probiotic use may indeed attenuate the inflammatory response post-TBI through upregulation of M2 microglia that serve to reduce inflammation and potentiate repair following injury.

ABSTRACT

Evaluation of the benefit of AHCC® supplementation in men and women with low risk human papillomavirus (HPV) infections

RACHEL E. CARLSON *McGovern Medical School at UTHealth* *Class of 2021*

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Supported by: WHIM Research Philanthropic Funds.
Key Words: HPV-11, HPV-6, AHCC, active hexose correlated compound, treatment

Background: Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide. HPV types 6 and 11, otherwise known as low-risk HPV, are associated with 90% of all genital lesions. Current treatment modalities for low-risk HPV focus on removal of genital lesions, but are inadequate in eradicating the underling HPV infection, therefore there is a high rate of recurrence. Previous *in vivo* and *in vitro* studies demonstrated that AHCC®, an extract prepared from the mycelium of *Lentinula edodes* mushrooms, has immunomodulatory capabilities such as increasing the number and activity of dendritic cells and natural killer cells. It is proposed that modulation of host immune response via AHCC supplementation will elicit eradication of HPV, thus clearing or reducing the number of genital lesions. The objective of this study is to evaluate the benefit of AHCC supplementation in men and women with low-risk HPV infections with active genital lesions.

Methods: A total of 100 patients (ideally 50 men and 50 women) will be recruited to this open-label, single arm phase II clinical trial and seen in the UT Physicians (UTP) Women's Center – Texas Medical Center (TMC) and UTP Internal Medicine Clinic (TMC). Study subjects with active genital lesions from low-risk HPV strains will take AHCC 3g once daily on an empty stomach for 16 weeks. On initial visit, a blood sample is drawn to measure baseline interferon-beta (IFN-β) levels, a skin biopsy is taken to assess HPV status, and the number of skin lesions is recorded in a quadrant-like fashion. Study participants return to clinic every 4 weeks to repeat blood draws and skin biopsies, and record genital lesions. At each visit, the participants receive the next month's supply of AHCC. Participants record self-compliance and adverse effects in a medication log, which is reviewed at each visit. Following 16 weeks of AHCC supplementation, the participants are monitored for an additional 12 weeks. Participants return every 4 weeks for the 12 weeks to have blood samples drawn, skin biopsies taken, and lesions recorded.

Results: The study is ongoing with enrollment anticipated to conclude in March 2019. To date, patient enrollment should begin in September 2018. Adverse effects are monitored throughout supplementation, and thus far, no adverse effects have been observed. Analysis of response to AHCC supplementation via HPV status, number of genital lesions, and IFN-β levels will be collected and preliminary results presented during poster session.

Conclusion: This study could elucidate a potential treatment for low-risk HPV and associated genital lesions, which can be painful and distressing to those affected. As a natural supplement, AHCC could be a readily available and easily accessible form of treatment.

ABSTRACT

Parent Perceptions of the Pre-Induction Surgical Safety Checklist

ALEXANDRIA CHILDS *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: KuoJen Tsao, MD Department of Pediatric Surgery
Supported by: KuoJen Tsao, MD
Key Words: Parental engagement, pediatric surgery, surgical safety checklist

Background: The surgical safety checklist (SSC) is a 3-phase tool introduced by the World Health Organization to reduce surgical morbidity and mortality. The pre-induction portion of the SSC is intended to facilitate the exchange of critical information prior to surgery; it is typically conducted by the anesthesiologist and circulating nurse, and involvement of the patient or guardian of pediatric patients is recommended. Previous work at our institution has shown a dramatic improvement in pre-induction checklist adherence when parents are present for and engaged in the SSC process. However, little is known about parent perceptions of their involvement in the pre-induction checklist. The purpose of this study was to understand parent perceptions of their participation in the pre-induction SCC and to identify facilitators and barriers to parental engagement.

Methods: Parents or guardians of children (<18 years) undergoing surgical procedures were asked to complete a 32-question survey after the pre-induction SCC was performed. The survey included questions about their involvement in the pre-induction checklist, their perceptions of the pre-operative experience, and demographics.

Results: 100 surveys were completed from June-July 2018. Six surveys were excluded due to failing to complete at least half of the questions (n=2) or giving the same answer to every question (n=4), yielding a total of 94 surveys. Most participants were white (55%), English-speaking (79%), non-Hispanic (53%), mothers (86%), and did not have a college degree (51%), and half of respondents reported that their child had a previous surgery. The most common surgical specialty was otorhinolaryngology (26%), followed by general surgery (16%), neurosurgery (15%), and urology (14%). In response to the statement "the team included me in my child's care," 87% chose "strongly agree" and 12% chose "agree". When asked to grade their overall preoperative experience on a scale of A to F, parents were highly satisfied with 97% selecting "A" (n=90).
Parents were confident that staff had confirmed child's NPO status (100%), surgical site (99%), identity (98%), and drug allergies (98%). Two survey items assessed parents' comfort when interacting with perioperative staff: "I would have felt comfortable speaking up and asking the team questions" and "I would have felt comfortable speaking up to the team if their information was incorrect." Most participants strongly agreed or agreed with these statements (91% and 87%, respectively). All participants who chose "disagree" or "strongly disagree" were mothers; however, there were no trends regarding race, ethnicity, primary language, or level of education.

Conclusions: The majority of parents are satisfied with the preoperative experience and appreciate their involvement in the SCC. A small minority of mothers do not feel confident

raising issues with perioperative staff, and further study is needed to determine how best to increase their comfort level.

ABSTRACT

Characterization of Phenotypes Associated with Heritable Vasculopathies

ISABELLA CIUFFETELLI *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dianna Milewicz, M.D. Ph.D., Department of Internal Medicine
Supported by: Division of Medical Genetics
Key Words: Grange syndrome, Alagille syndrome, moyamoya disease, thoracic aortic disease

Background

Rare mutations in genes can predispose to early onset or unusual vascular diseases. Once mutations in a gene are identified to be associated with a condition, further analyses are necessary to define the full spectrum of both mutations and clinical phenotype associated with pathogenic variants of a gene. To address the full range of mutations and clinical presentations associated with known vascular disease genes, I collected and analyzed medical records and genetic data from patients with novel mutations in *YY1AP1* and *JAG1*.

Results and Conclusions

Grange Syndrome is an autosomal recessive condition with severe early onset vascular disease, characterized by stenosis of the renal, cerebral, and abdominal arteries, with variable penetrance of brachydactyly, syndactyly, bone fragility, and learning disabilities. Homozygous or compound heterozygous loss-of-function variants in *YYA1P1* have been identified in patients with Grange syndrome from four unrelated families. We recently identified a novel homozygous *YYA1P1* missense mutation in a 51-year-old female patient presenting with features typical of Grange syndrome: long-standing hypertension, syndactyly, bilateral internal carotid stenosis with extensive collateralization of cerebral arteries, stenosis of the left renal artery, and stenosis of the celiac trunk and superior mesenteric arteries. Compared to the cases with loss-of-function variants, this missense case presented with a milder phenotype, characterized by later presentation of cerebrovascular event (42 years of age as compared to a median of 18) and later onset of secondary hypertension (25 years of age as compared to a median of 15). The patient also had tortuosity of cerebral and coronary arteries, raising the possibility that this could be a late onset feature of the condition.

JAG1 mutations are found in 94% of patients with Alagille syndrome, a highly variable autosomal dominant disorder presenting with neonatal liver disease, congenital heart defects, posterior embryotoxon, vertebral abnormalities, and characteristic facies. Cerebral and abdominal vascular anomalies are described in Alagille syndrome patients and account for 34% of the mortality in these patients. We assessed a 15-year-old male with ascending aortic dilation and left pulmonary artery stenosis and identified a novel *de novo JAG1* frameshift mutation. To assess if *JAG1* variants further cause vascular disease in the absence of syndromic features of Alagille syndrome, we are analyzing *JAG1* variants identified in 3 patients with moyamoya disease and 5 patients with thoracic aortic disease to assess their pathogenicity. In summary, we suggest: (1) *JAG1* sequencing should be considered in patients who present with early onset thoracic aortic disease or moyamoya disease; and (2) further evaluation of genetic and vascular

phenotype data on patients with Alagille syndrome to further understand the extent and outcomes of vascular diseases in these patients

ABSTRACT

Surgical Safety Checklist Adherence Improves Outcomes in Pediatric Patients

MAILE E CURBO *McGovern Medical School at UTHealth* *Class of 2021*

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Supported by: KuoJen Tsao, MD, McGovern Medical School at UTHealth, Department of Pediatric Surgery, Houston, TX, USA
Key Words: Surgical Safety Checklist Outcomes

Introduction: The surgical safety checklist (SSC) is a 3-phase tool created to reduce morbidity and mortality. Adult studies have demonstrated improved outcomes associated with SSC utilization. However, the pediatric surgical population has very low morbidity and mortality, therefore the association between SCC adherence and outcomes has been difficult to establish. The purpose of this study was to evaluate whether SSC compliance was associated with improved 30-day post-operative outcomes in pediatric surgical patients.

Methods: An observational study of non-emergent pediatric surgical cases in a children's hospital was performed by trained observers (2017-2018). Degree of adherence (verbalization and confirmation by 2 or more parties) was defined by the proportion of checklist items completed. Pre-induction, pre-incision and debriefing phases were observed. Total adherence score was the proportion of items completed from all 3 phases combined. Thirty-day outcomes were determined by retrospective chart review and included surgical site infection, wound dehiscence, readmission, emergency department (ED) visits, unplanned reoperations, pneumonia, and urinary tract infection. The primary outcome was a composite of any complication. Logistic regression was used for analysis.

Results: 510 cases were observed for SSC adherence. Patients had a median age of 4.1 years (IQR 1.1-9.8 years). Most observed cases were performed by Pediatric General Surgery (26.9%), Otorhinolaryngology (24.9%), or Urology (21.6%). Cases had a median operative time of 33.9 minutes (IQR 19.7-68.8 minutes). Median total adherence score was 86.2 (IQR 66.7-96.0). SSC adherence differed by phase: pre-incision phase was highest at 100% (96-100), followed by debriefing at 90.9% (IQR 72.7- 100), then pre-induction at 84.6% (IQR 53.8-100). Complications occurred in 11.2% (n=57) of patients; ED visits were most common (64.9%), followed by readmission (38.6%), and surgical site infection (19.3%). Case length and age were not associated with presence of a post-operative complication. However, surgical specialty, higher pre-induction adherence, and higher total adherence were associated with reduced likelihood of any complication on univariate regression. After adjusting for age, case length, specialty and total adherence to the SSC, only higher total adherence remained associated with decreased post-operative complications ($p<0.02$), with pre-induction as the only significant phase.

Conclusions: This is the first study to demonstrate that increased SCC compliance is associated with improved patient outcomes in pediatric surgery. These data suggest that improving pre-induction checklist adherence may prevent patient harm.

ABSTRACT

A Novel Link between Chronic Inflammation and Pancreatic Cancer

JOY DAVIS *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Tien C. Ko, MD and Yanna Cao, MD, MS, 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 Cancer, Chronic Pancreatitis, Gremlin1, Macrophage

Background: Chronic pancreatitis (CP) is a major risk factor of pancreatic ductal adenocarcinoma (PDAC), one of the most lethal malignancies in the United States. However, how chronic inflammation promotes pancreatic tumorigenesis is unclear. A characteristic feature of PDAC is a prominent desmoplasia in the tumor microenvironment, composed of activated fibroblasts and immune cells such as macrophages. Activated macrophages can be categorized as classically activated (M1) and alternatively activated (M2), with tumor inhibiting and promoting functions, respectively. The macrophages found in CP, the precursor lesion PanIN (pancreatic intraepithelial neoplasia), and PDAC are all reported to show an M2 preferential phenotype. M2 macrophages can promote pancreatic cancer progression and are correlated with a poor prognosis. We hypothesize that within the pancreatic tumor microenvironment, chronic inflammation-induced expression of a key pro-fibrogenic factor Gremlin1 (Grem1) by fibroblasts stimulates alternative activation of macrophages (M2) and promotes pancreatic tumorigenesis. **Methods**: Three commercially acquired human pancreatic tissue microarrays were used, containing a spectrum of different pancreatic disease states, including 13 cases of CP, 11 cases of PanIN, and 97 cases of PDAC with different pathological tumor stages from 1-4. Grem1 RNA *in situ* hybridization was performed and scored 0-4 based on increasing Grem1 expression. Immunohistochemistry was performed using a myofibroblast marker, α-smooth muscle actin (SMA), and an M2 marker (CD163). For each case, the most densely stained area was imaged and the positively stained cells were counted. All data were acquired by investigators blinded to case identification. **Results**: Grem1 RNA expression overlaps with α-SMA, indicating an exclusive expression of Grem1 by fibroblasts. $Fibroblasts^{Grem1+}$ significantly increase from CP to PanIN to PDAC (1.09±0.52, 2.67±0.43, 3.25±0.48, p=0.035). $Fibroblasts^{Grem1+}$ positively correlate with pathological tumor stages in PDAC (r_s=0.230, p=0.024). The $M2^{CD163+}$ cells do not progressively increase from CP to PanIN to PDAC (98.41±24.45, 60.94±12.89, 118.13±48.07, p>0.05), nor have a significant correlation with pathological tumor stages in PDAC. However, $Fibroblasts^{Grem1+}$ positively correlate with $M2^{CD163+}$cells in PDAC (r_s=0.228, p=0.025). **Conclusion**: $Fibroblasts^{Grem1+}$ increase progressively from CP to PanIN to PDAC, and correlate with $M2^{CD163+}$ macrophages and pathological tumor stages in PDAC. These results suggest that $Fibroblasts^{Grem1+}$ may play a critical role in alternative activation of macrophages during the development of PDAC. Further investigation of the effect of $Fibroblasts^{Grem1+}$ on macrophage activation status is warranted, with aim of potential novel therapeutic development.

ABSTRACT

A case of undiagnosed pseudocholinesterase deficiency and a resulting normal dibucaine number

Karen Delgado *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Acsa M. Zavala, MD, Anesthesia Department, MD Anderson Cancer Center
Key Words: Pseudocholinesterase deficiency, Dibucaine Number

Introduction

Pseudocholinesterase deficiency (PD) is an autosomal recessive condition caused by a mutation in the butyrylcholinesterase (BCHE) gene that is responsible for the breakdown of choline ester drugs, such as succinylcholine and mivacurium. With an incidence of up to 1 in 5,000, most cases are diagnosed only after exposure to choline ester-class medications result in residual paralysis (1). We present the case of a successful perioperative anesthetic management in a patient with undiagnosed PD.

Case Report

A 55 year-old man with a BMI of 39 and history of obstructive sleep apnea presented for transpupillary thermotherapy to his left eye for uveal melanoma. There was no family history of complications with anesthesia. Upon airway evaluation, it was expected that the patient would be a difficult intubation given his neck circumference of 48 cm, so a C-MAC® was planned for the intubation. After administration of propofol 250mg, succinylcholine 100 mg was used as the muscle relaxant of choice to promptly secure the airway, which was easily accomplished. Upon completion of the thermotherapy, the patient had spontaneous respiratory effort on pressure support, but his tidal volumes were minimal. Nerve twitch monitoring showed 4/4 twitches without fade and sustained tetanus. The patient became hypertensive, tachycardic, and continued to show signs of residual paralysis. He was administered midazolam 2mg as well as a propofol infusion of 150 mcg/kg/hr, remained intubated and was transported to recovery to allow for the residual paralysis to resolve. Upon discussion with the family, it was discovered that the patient's sister had PD. The patient was intubated for 8 hours and extubated when he regained muscle strength. He was discharged home the next day with no complications. His pseudocholinesterase level was received 4 days later at a decreased level of 1694 (normal 3100-6500), and a normal dibucaine number of 83.

Discussion

In the event of delayed muscle strength recovery in which PD is suspected, one must wait until the effects of the muscle relaxant resolve by maintaining the patient intubated and sedated. It is important to note the importance of neuromuscular monitoring to avoid premature awakening with residual paralysis, resulting in distress to the patient (2). Whenever a patient is confirmed to have a PD, it should be advised that immediate family members take part in genetic testing to determine whether a genetic enzyme variance is present. Additionally, the patient should be counseled on the condition and future implications and a medical bracelet should also be recommended. Although this patient had a family history of PD, his dibucaine number was normal, usually suggesting that the cause is not genetic in origin. However, there are other genetic variants of the deficiency as well as combinations of variants making the expected response to succinylcholine variable. There are other tests including fluoride and chloride which can identify different variants of the deficiency including A-variant, F-variant, and S-variant (4).

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ABSTRACT

Spatial and functional neurocartography of *Aplysia* buccal ganglion

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Sponsored by: John H. Byrne, Ph.D., Department of Neurobiology & Anatomy
Supported by: NIH Grant "Analyses of the Distributed Representation of Associative-Learning in an Identified Circuit Using a Combination of Single-Cell Electrophysiology and Multicellular Voltage-Sensitive Dye Recordings," R01 NS101356 to Dr. John H. Byrne
Key Words: Neurocartography, voltage-sensitive dye (VSD) imaging, homologous neurons, *Aplysia*

When analyzing recordings of any nervous system, it is important to ensure that comparisons made between different subjects are meaningful—a metric referred to as "*correspondence*"—in order to make any conclusions about the anatomical or physiological properties of the system. Classically, the knowledge of characterized neurons has been used to surmise the properties of neurons less well-known. However, we are somewhat limited in our ability to grossly distinguish neurons by relying on unique characteristics that may or may not be obtainable; while a neuron may not possess a characteristic exclusive to it, it appears that many neurons, instead, possess unique *combinations* of features that, individually, are shared among many others and that these neurons are distinct enough that they, too, can be characterized. Building on the work of Frady et al. (2016), we aim to assess the similarity of these potentially characterizeable neurons using the buccal ganglion in *Aplysia* as a model test system. We attempted to represent spatial and functional features of neurons in the most efficacious manner and assess the usefulness of these features; these include neuronal involvement and intensity of activity in various motor pattern phases, as well as classifying axonal projection into nerves *Rn*, *iBn2*, *iBn3* and *cBn2* based on delay and rise time. All of these features proved useful in discriminating neurons from each other, in addition to spatial information such as size and position within the ganglion. We then algorithmically (Hungarian) matched homologous neurons between pairs of experiments (i.e. pairwise matches) using their specific combination of features, which were often consistent with the matches we could intuit. From here, we are currently implementing a cyclic matching algorithm to assimilate these pairwise matches into a set of "canonical" neurons, which altogether form a "canonical atlas" that can be used to augment our ability to assess correspondence between subjects and to better our understanding of the nervous system being studied. Our approach is novel, in that we attempt to remove the necessity of prior knowledge in order to derive a spatial and functional map of the system. We expect that this technique will be advantageous when investigating the roles of specific neurons not currently characterized in behavioral networks, such as in *Aplysia*. Furthermore, addressing the issue of correspondence using neurocartography could facilitate the targeting of specific brain areas for medical therapy.

ABSTRACT

Outcome of Enhanced Recovery After Surgery (ERAS) Implementation

MARCO DOMINGUEZ *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dr. Keyuri Popat, MD, Department of Anesthesia and Peri-Operative Medicine
Supported by: MD Anderson Cancer Center
Key Words: ERAS, Exparel, Opiod Consumption

Objective:
The Enhanced Recovery After Surgery (ERAS) protocol was initiated in a trial capacity at MD Anderson cancer center for participating major spine surgery patients. The ERAS protocol involves the use of a multimodal approach to patient care preoperatively, intraoperatively and postoperatively. It has been shown that its use has resulted in shorter length of hospital stay by 30% to 50% and similar reductions in complications, while readmissions and costs are reduced [1]. The aim of the research conducted was to find if there was a change in patient post-operative opioid consumption and pain scores when liposomal bupivacaine (Exparel) was used for wound infiltration intraoperatively as opposed to no Exparel used. The research hypothesis is that there will be a lower incidence of opioid use and hospital stay in the operative cases that used Exparel compared to those that did not.

Methods:
The Redcap database was used to analyze and undertake a retrospective abstraction of data. The source of information from which patient information was drawn to be used in the database was from the EPIC system and the MD Anderson institutional EMR. All of the cases analyzed were open spine surgery and no minimally invasive surgeries were included. The open spine surgeries were classified as either laminectomy, instrumentation or vertebrectomy. The variables chosen to be used in analysis were median average pain scores for post-operative day (POD) 1, 2, and 3, median date of discharge and morphine equivalent daily dosing for POD 0 and POD 1-3.

Results:

Surgery	ME0	ME1-3	AP-1	AP-2	AP-3	AP-D	Total Pts
Vertebral Resection- exparel	72	336	2.9	3.1	2.1	2	32
Vertebral Resection- no exparel	63.2	295	2	2	2	0.29	32
Stabilization-exparel	78.7	459.7	3.7	3.3	2.5	2	48
Stabilization-no exparel	67.5	295	2.8	2	2.2	0.94	40
Laminectomy-exparel	87	467	3	2.3	3	1.85	58
Laminectomy-no exparel	55	273	2.4	2.5	2	0.66	54
Lam+Stab-exparel	107	580.5	3.69	3.25	3	2	36
Lam+Stab-no exparel	64.5	291	2.8	2	2.83	1	34
Lam+Stab+Vert-exparel	110	514.5	2.8	3.2	3	2	21
Lam+Stab+Vert-no exparel	71.2	295.5	2	2	3	1	25

Conclusion:

The use of liposomal bupivacaine (Exparel) had no impact on opioid consumption in POD 0 or POD 1-3, as well as no impact on the average pain scores for POD 1-3 compared to patients on whom it was not used.

References:

1. Enhanced Recovery After Surgery: A Review. Ljungqvist O, Scott M, Fearon KC. JAMA Surg. 2017 Mar 1; 152(3):292-298

ABSTRACT

Role of ribosomal S6 kinase (RSK) in long term enhancement of electrical excitability in sensory neurons of *Aplysia*

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Sponsored by: John H. Byrne, Ph.D., Department of Neurobiology and Anatomy
Supported by: Analysis of the Neural Control of Behavior NIH NS019895-35
Key Words: Ribosomal S6 kinase, *Aplysia*, sensory neuron excitability

Background
The formation of long-term memories involves modulation of gene expression necessary for the growth and structural changes of neural synapses. In *Aplysia* sensory neurons (SNs), these cellular changes are mediated by several serotonin (5-HT)-activated second messenger cascades, including cAMP/PKA and MEK/ERK. These cascades ultimately lead to long-term synaptic facilitation (LTF) and long-term enhancement of excitability (LTEE), where excitability is defined as the number of action potentials (APs) the pre-synaptic neuron fires in response to a given current stimulus. Both of these cellular mechanisms contribute to long-term memory formation. It has recently been shown that ribosomal S6 kinase (RSK) is also activated by ERK in *Aplysia* SNs and knock down of RSK levels within the SNs attenuates LTF. Coffin-Lowry syndrome (CLS), caused by a mutation in the gene encoding human RSK2, presents with cognitive defects. Consequently, the *Aplysia* SNs may serve as a model system to gain insights into CLS. This project aimed to determine the effects of RSK inhibition on LTEE, thus elucidating its role in long-term memory formation and offering a possible therapeutic target for CLS.

Methods
SNs obtained from pleural ganglia were cultured for *in vitro* electrophysiological recording. Excitability and changes in excitability were assessed as the number of APs elicited at a given level of current injection. LTEE was induced in the SNs by applying five, 5-min pulses of 5-HT. Inhibition of RSK activity was achieved by treating cultures with the drug BI-D1870 (BID). SN excitability was measured prior to 5-HT treatment (pre-test), and 24 h after treatment (post-test) in four groups: 1) Vehicle control, 2) 5-HT alone, 3) BID alone, and 4) 5-HT + BID. For analysis, the percent change in the number of APs elicited between pre- and post-test was determined for each individual neuron within each treatment group.

Results
As expected, application of the vehicle control and BID alone produced little changes in excitability (37.6% ± 12.1, n=7; 1.9% ± 22.2, n=6, respectively). In contrast, 5-HT treatment led to a 300.8% ± 81.1 (n=7) increase in excitability. However, 5-HT treatment in the presence of BID only produced a 168.1% ± 31.7 (n=8) increase. Although further experiments are necessary, these results suggest that inhibition of RSK partially inhibits 5-HT-induced LTEE in *Aplysia* SNs, and that RSK plays a role in both LTF and LTEE, thus impacting the formation of long-term memories.

ABSTRACT

Validation of D-Dimer as an Indicator of Progressive Hemorrhagic Injury Following Traumatic Brain Injury

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Sponsored by: Jessica C. Cardenas, PhD, Department of Surgery
Supported by: Dean's Office stipend, Department funds to J. Cardenas
Key Words: Traumatic brain injury, Progressive hemorrhagic injury, Fibrinolysis

Introduction:
Progressive hemorrhagic injury (PHI), the early expansion of intracranial hemorrhage (ICH) following a traumatic brain injury (TBI), is associated with a five-fold increase in the risk of neurological decline, complications, and mortality. Our lab, and others, had previously demonstrated fibrinolysis to be an important mechanism underlying PHI and that admission levels of D-dimer, a byproduct of fibrinolysis, may be used to screen for PHI. In this study, we aimed to independently validate the previously proposed D-dimer of 3.6 µg/mL threshold for PHI identification and hypothesized it would accurately differentiate patients with PHI from those with stable hemorrhage (SH).
Methods:
This was a single institution, retrospective analysis of prospectively collected data between September 2013 and March 2018. All highest-level trauma activation patients between ages of 18-55 years, with an initial head CT scan at admission showing severe TBI, defined as presence of ICH, and a repeat scan within 6 hours following, were included. This limit on age was set to minimize inclusion of patients on anticoagulants. Prisoners, pregnant women, and patients with non-survivable head injury were excluded. Differentiability of D-dimer was evaluated by receiver operating curve analysis. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for the previously identified cut point of 3.6 µg/mL.
Results:
From September 2013 to March 2018, 244 patients between 18-55 years old were admitted to Memorial Hermann Hospital with severe TBI. An additional 75 patients were excluded due to non-survivable injuries, lack of CT scan, did not consent, or plasma was not obtained. This left 169 patients for analysis. Of those, 54% had SH and 46% had PHI. Patients who developed PHI received more red blood cell transfusions ($p = 0.02$) and had significantly fewer ventilator-, intensive care unit-, and hospital-free days compared to SH patients (all $p < 0.01$). Furthermore, PHI patients had significantly higher D-dimer levels than those with SH (8.1 (4.6, 17.1) µg/mL vs 5.7 (1.8, 11.7) µg/mL, respectively, $p < 0.01$). The D-dimer threshold of 3.6 µg/mL yields a sensitivity of 0.83 (95% CI 0.74-0.91), specificity of 0.40 (95% CI 0.30-0.50), positive predictive value of 0.53 (95%CI 0.44-0.62), and negative predictive value of 0.74 (95% CI 0.61-0.86).
Conclusion:
Clinical use of D-dimer on admission in TBI patients could provide a sensitive screening tool to identify patients at high risk for PHI. Such a tool could be used for early administration of life-saving interventions for high risk patients and also eliminate costly, invasive screening procedures for patients at low risk of PHI.

ABSTRACT

Expression Profiling of Exosomal miRNAs Between C57BL/6 and MRL/MpJ (Super Healer) Muscle-Derived Stem Cells

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Sponsored by: Sealy Hambright Ph.D. Department of Orthopaedic Surgery
Supported by: Start-up funding from Dr. Johnny Huard Lab
Key Words: Muscle-Derived Stem Cells, Exosomes, Regeneration

INTRODUCTION: The mouse strain MRL/MpJ, also known as super-healer, has an increased ability to spontaneously repair various tissues, including digits, retina, ears, cartilage, and skeletal muscle after injury. Several studies indicate that MRL/MpJ mice have increased cell proliferation and differentiation capacities, and reduced cell apoptosis, which facilitate their high healing capacity post-injury. The circulating factors that enhance muscle regeneration in the super-healer mouse is not well known. Exosomes are lipid bilayer extracellular vesicles of 50-150nm in size, which are secreted by all cells and function as key paracrine regulators of key cellular processes. Exosomes contain multiple regulatory factors, including nucleic acids (mRNA, non-coding miRNA's, and DNA), proteins, and lipids. We hypothesize that circulating exosomes confer increased regenerative potential in MRL /MpJ mice which may provide novel therapeutic targets for increasing muscle regeneration following injury.
METHODS: Extracellular vesicles (EVs) containing exosomes were purified from blood plasma of MRL-MDSCs and WT-MDSCs. Total RNA isolated from EVs was analyzed by the expression profiling of non-coding miRNAs using Affymetrix Gene array Chip. For *in vitro* studies, exosomes were isolated from cultured media of WT and MRL/MpJ MDSCs using established ultra-centrifugation methods. Myogenic differentiation of MDSCs were studied in the presence of exosomes. Isolated exosomes were injected in gastrocnemius muscle of progeroid Zmpste24$^{-/-}$ (Z24) mice upon muscle injury with barium chloride. Muscle tissues were harvested, sectioned, and analyzed at 5 days post injury for histological analysis. Western blot qPCR were used to analyze protein and mRNA expression
RESULTS: When WT MDSCs were treated with MRL/MpJ MDSCs, we found enhanced myogenesis of WT MDSCS indicated by elevated multi-nucleated myosin heavy chain (MHC) staining and reduction in expression of pro-inflammatory/pro-fibrogenic factors suggesting a role of muscle regeneration/repair. We found largescale differences in the miRNA profile in MRL/MpJ sera exosomes compared to WT. There was increased miRNA expression in MRL-MDSC exosomes in miR-709 (important role in skeletal muscle regeneration) with over 25-fold increase compared to WT-MDSC exosomes and miR-31-5 (important in muscle regeneration and positively regulates the proliferation of vascular smooth muscle cells). Z24 mice treated with MRL-MDSC exosomes following BaCl2 induced injury saw reduced fibrosis in early trials.
DISCUSSION: The main objective of this study was to investigate the roles of exosomes and their miRNA cargo in the regenerative potential of MDSCs derived from WT and MRL/MpJ mice *in vitro* and *in vivo.* We found a differential expression profile of miRNAs between WT and MRL/MpJ mice. In addition, we found that MRL-MDSC exosomes improved myogenic

potential *in vitro* and *in vivo.* Since our result suggest that MRL/MpJ exosomes have ability to increase the myogenic capacity of aged and progeria MPCs we posit that these exosomal miRNAs may play anabolic roles in muscle tissue repair after injury. Exosomes could be a promising therapy for enhancing musculoskeletal regeneration caused by aging and injuries.

ABSTRACT

Application of Audiovisual Learning in Gross Anatomy

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Sponsored by: Han Zhang, M.D., Neurobiology & Anatomy
Supported by: Human Structure Facility, Dept. of Neurobiology and Anatomy
Key Words: Gross Anatomy, Audiovisual, Education, Video Series

Background:
Due to the intricate ties of anatomical structure, function, and pathological alterations, the basis of every physician's medical education hinges upon an in depth understanding of normal anatomy. With the shear increase in medical knowledge and the vast number of contact hours required for medical school, creating a firm foundation in the basic sciences can be difficult. For this project, we aim to enhance the understanding of anatomy for McGovern Medical School students by creating an instructional video series that documents correct dissection procedures. The videos will serve as an aid for medical students in their own dissection.

Methods:
Prosections were performed by the UT McGovern Medical School, Department of Neurobiology & Anatomy professor, Dr. Zhang, on the designated faculty teaching cadaver. The order of prosections were scheduled in accordance with current curriculum for UT McGovern Medical School Anatomy Lab, and were documented using provided camcorders. Raw video footage was then uploaded for processing in Adobe Premiere Pro. Files were then edited for quality and content, and given labels to emphasize important anatomical structures. Finished video files were then exported and uploaded to Panopto, a student video library, for reference before Anatomy lab. To access feedback on quality of videos, a survey will be disbursed to the students in the course to assist in future improvements.

Conclusion:
This project is considered a work-in-progress and will continue throughout the remainder of the year. As of today, 2/3 of required dissections have been performed and recorded. Half of this content has been edited and provided to students. This is a long-term project that aims to produce instructional videos that will aid future generations of doctors.

ABSTRACT

Trauma, Inflammation, and Anhedonia in Cocaine Use Disorder

KIRA E. GOMEZ *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Margaret Wardle, Ph.D., UTH Psychiatry Department
Supported by: Margaret Wardle, Ph.D., UTH Psychiatry Department
Key Words: cocaine use disorder, NLR, inflammation, anhedonia, trauma

Background: Cocaine contributes significantly to global disease burden, as almost 1 million individuals meet criteria for cocaine use disorder (CUD) in the United States alone. Anhedonia, the inability to feel pleasure, predicts worse treatment outcomes in CUD. Neuroinflammation may be a biological mechanism underlying anhedonia. Activation of the innate immune system leads to biochemical and behavioral changes meant to fight infection, such as social withdrawal. This may be maladaptively activated in CUD, producing anhedonia. Neuroinflammation could be plausibly produced either simply by cocaine, as psychostimulants activate the innate immune system, or by psychological trauma. Trauma is highly common in substance use disorders, is associated with anhedonia, and could cause stress-induced neuroinflammation.
Specific Aims and Hypotheses: The present study aimed to assess the relationships between trauma, inflammation, and anhedonia in CUD. It was hypothesized that participants with higher levels of inflammation would have more severe anhedonic symptoms and that trauma would relate to both higher levels of anhedonia and inflammation. Finally, we tested on an exploratory basis whether trauma and inflammation interactively contribute to anhedonia.
Experimental Design: Data was collected from 150 treatment-seeking individuals undergoing initial evaluation for several CUD studies. Participants were excluded for inflammatory medical conditions and regular anti-inflammatory medication use. Inflammation was measured using the Neutrophil-to-Lymphocyte Ratio (NLR), a relatively inexpensive, general measure that is diagnostic and prognostic in other mental illnesses. Anhedonia was measured with the Snaith-Hamilton Pleasure Scale (SHAPS) and trauma with the PTSD Checklist (PCL). Independent sample t-tests, ANOVA, and correlations were used to identify potential confounds. Multiple linear regressions were used to assess individual relationships between inflammation, anhedonia, and trauma. Moderated regression was used to examine possible interactions between inflammation and trauma in their effect on anhedonia.
Results: Of the tested potential confounds, only lifetime cannabis use was associated with both anhedonia and inflammation - longer cannabis use related to higher inflammation, but lower anhedonia. Cannabis use was controlled for in all analyses. Unexpectedly, there were no direct relationships between inflammation and anhedonia, inflammation and trauma, nor trauma and anhedonia. However, inflammation interacted significantly with trauma, such that only in participants with high trauma symptoms did inflammation relate to greater anhedonia.
Conclusions: This was a novel study investigating NLR in substance use disorder, further contributing to its validation as a cheap, easy biomarker of inflammation, and identifying a relationship between trauma, inflammation, and anhedonia. It is possible that trauma alters functioning in ways that allow inflammation to affect to motivation and pleasure, but without a primary insult (e.g. trauma), inflammation does not cause significant change. This could focus potential anti-inflammatory treatment approaches for individuals with cocaine addiction on those who have a history of trauma, a group that is typically treatment resistant.

ABSTRACT

Olfactory Function Following Bilateral Superior Turbinate Resection in Endoscopic Transphenoidal Hypophysectomy

SHAINA W. GONG *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: William C. Yao, MD, Department of Otorhinolaryngology – Head and Neck Surgery
Supported by: Department of Otorhinolaryngology – Head and Neck Surgery; McGovern Medical School at UTHealth – Office of the Dean
Key Words: Olfaction, endoscopic, pituitary surgery, superior turbinate, Sniffin' Sticks

INTRODUCTION: Endoscopic transphenoidal hypophysectomy (TSH) has become an increasingly preferred method for removal of pituitary adenomas. While the endoscopic approach confers many advantages, reports of postoperative olfactory impairment raise quality of life concerns as it affects many aspects of daily living. One technique involves resection of the bilateral superior turbinates (ST) to allow for wider exposure.
OBJECTIVE: We sought to use Sniffin' Sticks to determine the impact of bilateral ST resection on olfactory outcomes.
METHODS: A prospective observational study was conducted on 18 English-speaking adult patients (≥18yrs) undergoing endoscopic TSH at a tertiary academic center. Olfactory function was measured using the Sniffin' Sticks on three occasions at the preoperative visit, 2-weeks and at 6-8 weeks postoperatively. Paired two-tailed *t*-test was used to compare preoperative and postoperative odor threshold (OT), odor discrimination (OD), odor identification (OI) and composite TDI scores.
RESULTS: To date, 14 patients have enrolled, with 4 completing the study. Statistical analysis was performed with the current data. There was a significant decrease in composite TDI scores (n=6, p=.018) between preoperative (28.42 ± 3.83) and 2-weeks postoperative (19.17 ± 5.63) visits. In addition, there was a significant decrease in OT (6.42 ± 2.36 vs. 2.00 ± 1.31, p=.002) and OI (12.67 ± 2.42 vs. 9.00 ± 2.19, p=.024) but no significant difference in OD (9.33 ± 2.25 vs. 8.17 ± 3.25, p=.443). Although there was an increase in composite TDI scores between 2-weeks (19.31 ± 7.00) and 6-8 weeks (25.94 ± 3.35) visits, the difference was insignificant (n=4, p=.087). Furthermore, there was no significant difference found between OT (2.06 ± 1.66 vs. 4.69 ± 1.71, p=.059), OD (7.75 ± 3.77 vs. 9.50 ± 2.38, p=.162), and OI (9.50 ± 2.65 vs. 11.75 ± 2.50, p=.153) between 2 and 6-8 weeks postoperative visits. As the study is currently ongoing and enrollment of patients is set to continue until 18 patients have completed the study, further statistical analysis remains pending.
CONCLUSION: Preliminary results show patients undergoing endoscopic TSH with bilateral ST resection experience postoperative hyposmia 2-weeks postoperatively. Although results suggest olfactory function improvement between 2-weeks and 6-8 weeks postoperatively, further data will need to be collected.

ABSTRACT

Model of Mouse Liver SIK1 Conditional Knockout and Skeletal Muscle SIK1 Overexpression

VICTOR GONZALEZ *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Rebecca Berdeaux, Ph. D., Integrative Biology and Pharmacology
Supported by: Rebecca Berdeaux, Ph. D., Integrative Biology and Pharmacology
Key Words: Obesity, mitochondrial dynamics, glucose, gene knockout

Obesity has been shown to lead to impaired insulin response as well as fat accumulation in liver and muscle. High fat diet conditions, leading to obesity, cause insulin resistance and hyperinsulinemia. Salt inducible kinases (SIK1-3) are serine/threonine kinases that are regulated by cAMP signaling in different tissues. Previous experiments in the Berdeaux lab have shown that SIK1 knock-out mice fed a high fat diet develop obesity, increase energy expenditure, and increase muscle glucose uptake despite insulin resistance. The prior experiments did not determine whether increased expression of SIK1 is sufficient to inhibit insulin stimulated glucose uptake. Expressing elevated SIK1 in lean animals will show if the data gathered (glucose tolerance, insulin levels in skeletal muscle) are present even in the absence of actual obesity and are not due a synergistic effect of SIK1 and another alteration that occurs during development of obesity. This current experiment was to establish a system for conditional knockout (CKO) and overexpression (OE) that can be used to achieve testable conditions. The CKO experiment focuses on liver tissue to see if previous results found in skeletal muscle with respect to mitochondrial metabolism are conserved in liver cells. CKO was tested using Adeno-associated virus and OE was pursued using Tetracycline-induced expression. Adeno-associated virus with Cre-recombinase promotors were used to cleave out the SIK1 gene out in liver tissue. The virus was delivered IV injection via tail-veins and tissue was harvested ≥7 days after injection. The overexpression portion was done by injecting intra-peritoneal Doxycycline once per day for 5 days to mice with reverse tetracycline-controlled transactivator (rtTA) segments. The tissue was collected after the final injection. DNA and RNA were isolated from the harvested tissue, and presence/absence of the SIK1 gene was analyzed via PCR and QPCR. Tissue was also examined under microscope for a phenotypic analysis of the CKO. The results for the CKO showed that, while the SIK1 deletion was present, there may be other non-hepatocyte cells that potentially upregulate SIK1 when it is deleted in adjacent cells. Further experiments are needed to isolate hepatocytes from non-parenchymal cells such as stellate cells and Kupffer cells. For the OE experiment, optimization of the Tet-system needs to be pursued to ensure doxycycline injections cause systemic overexpression. Further improvements on both systems will allow for analysis of mitochondrial proteins as well as ATP and glucose metabolism. The long-term goal of this experiment is to find if a drug specific to SIK1 (not SIK2 or 3) may improve glucose uptake in the skeletal muscle of obese animals.

ABSTRACT

Assessment of pediatric vaccination rates in an academic community clinic in Houston, TX

JANA GUTIERREZ *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Susan H. Wootton, MD, Department of Pediatrics
Key Words: Pediatrics, vaccination, timeliness

Background: Childhood vaccination is one of the most effective prevention methods against infectious diseases, preventing 2 to 3 million deaths each year worldwide and reducing hospitalizations and medical visits. Despite evidence supporting the effectiveness and success of vaccines, some parents are choosing to deviate from the recommended ACIP schedule by either decreasing the number of vaccines their child receives at one point (or over a period of time), delaying certain vaccines by months or years or completely abstaining from vaccines. The purpose of this study was to explore methods for documenting baseline vaccination rates at an academic pediatric clinic prior to the implementation of a vaccine clinic dismissal policy for vaccine refusers (June 2018).

Methods: Children age 0 to <5 years with at least one clinic visit during the period of January 1, 2017- May 31, 2018 were reviewed using Electronic Medical Record (EMR) data. Demographic variables and vaccination status were collected. Timeliness of each vaccination series was defined per CDC's Comprehensive Clinic Assessment Software. Patients were classified as 1) up-to-date if all age-recommended vaccine series were received on time, 2) late if at least one vaccine series was late or 3) ineligible if too young to receive any recommended vaccine series.

Results: In total, 536 children were reviewed. Mean age was 1.63 years old (range 0 to <5 yrs), 91 (18%) were Caucasian, 160 (30%) Hispanic, and 134 (25%) African American. 91 (17%) had private insurance, 236 (44%) had public insurance, and 209 (39%) were either uninsured or unknown. In total, 44 (8.2%) were up to date, 418 (78%) were late and 74 (13.8%) ineligible. Among children classified as late (n=418), 77 (18.4%) were late for 1 vaccine series, 257 (61.5%) for 2-5 series, and 84 (20.1%) for > 5 series. The most frequently completed vaccine series were Pneumococcal conjugate vaccine 13 [279 (52.1%)] Hepatitis B [271 (50.6%)], and Rotavirus [268 (50%)]. The vaccine series most frequently with ≥1 missing dose was Varicella [369 (68.8%)], Measles, Mumps and Rubella (**MMR**) [357 (66.6%)] and Hepatitis B [200 (37.3%)] vaccines. No systematic fields for refusal were noted.

Discussion: The majority of the patients were classified as late for at least 1 recommended vaccine series. Analysis is currently ongoing including dose timeliness and audits. Interpretation of results are limited by 1) age of the clinic (only open for 3 years so many children with outside records), 2) type of vaccination record reviewed (only clinic records versus), and 3) inability to capture data within text fields. This study highlights the difficulties of 1) accessing accurate vaccination and vaccine refusal rates using the EHR and 2) monitoring the impact of a new clinic dismissal policy on vaccine refusal rates. Next steps include creating standard refusal fields and exploring opportunities for linking the EHR with state vaccine registries.

ABSTRACT

The Role of Body Mass and Adipokines in Traumatic Injury Outcome

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Sponsored by: Dr. Charles E. Wade, PhD., Department of Surgery
Supported by: Center for Translational Injury Research (CeTIR)
Key Words: Trauma, Adipokines, Inflammation, Body Mass Composition

Background: Body mass index is a commonly used descriptor when describing individual patients, but it may not always be the most accurate to adequately assess severely injured patients. Adipokines are cytokine molecules that are secreted by fat and play a role in the inflammatory process. We hypothesized that in trauma patients with severe injuries, adipokines and inflammatory molecules are associated with body fat mass after admission to the intensive care unit (ICU).

Methods: A retrospective study was conducted using a subset of patients from the PROPPR study database. The PROPPR study looked at severely injured patients experiencing hemorrhagic shock that required blood transfusions. The patient's body mass composition (visceral fat, subcutaneous fat, and psoas muscle cross-sectional area) was measured using CT scans and the adipokines (resistin, adiponectin, and leptin) and inflammatory markers (IL-6, IL-8, G-CSF, MCP-1) were measured using ELISA. Multivariate analysis was done using the data collected from patients from hours 48-72 in the ICU.

Results: The patient population (n=81) had a median age (IQR) of 39 years (25, 56). The ISS, was 33 (22, 43), systolic blood pressure was 90 mm Hg (78, 110), heart rate of 107 beats/min (94, 130) and a base excess of -6.5 mmol/L (-10.0, -3.0). Compared to established controls in the lab, the cytokine inflammatory markers measured were significantly increased, as was resistin, while adiponectin and leptin were decreased. The inflammatory cytokines were not related to body composition. Resistin was significantly associated with the cytokines while adiponectin and leptin were not. Adiponectin was negatively associated with body mass index (BMI), visceral fat, and psoas muscle cross-sectional area. Leptin was positively associated with BMI, visceral fat, and subcutaneous fat.

Conclusion: Adipokines are significantly altered in response to traumatic injury with resistin increasing, following its classical inflammatory response, and adiponectin/leptin showing a reduction, but persisting in their classical relationship to body composition**.**

ABSTRACT

Platelet-rich plasma and muscle stem cell therapy for improving joint degenerative disease

MACGREGOR HALL *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Krishna Sinha, PhD, Department of Orthopedic Surgery
Ping Guo, PhD, Department of Orthopedic Surgery
Supported by: Johnny Huard, PhD, Department of Orthopedic Surgery research start up fund
Key Words: Platelet-rich plasma, muscle-derived stem cell, osteoarthritis

Introduction

Adult stem cell therapy and platelet-rich plasma (PRP) are emerging therapies in regenerative medicine for repair of musculoskeletal defects due to injury or aging. Stem cells after transplantation readily participate in tissue regeneration, while PRP provides growth factors that accelerate and enhance endogenous cells to participate in the repair process. PRP contains several growth factors, including platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-β1 (TGF-β1). Some of these growth factors can enhance healing in certain tissue lineages but may be harmful in others. Studying the tissue-specific effects of PRP while blocking certain growth factors can give us a better understanding of its biological nature and its potential utility in musculoskeletal regeneration.

Methods

Muscle derived stem cells (MDSC) were plated into 24-well plates with 5,000 cells/well. After reaching 60-70% confluency, cells were treated with 2% PRP and then induced in myogenic, chondrogenic, or osteogenic differentiation media. After 3-5 days, myogenic differentiation was analyzed by immunostaining for myosin heavy chain (MyHC) for myotube formation and DAPI for nuclear staining (Fig. 1). Chondrogenic differentiation was analyzed with Alcian Blue staining which stains proteoglycans (Fig. 2), and osteogenic differentiation with Alkaline Phosphatase which is an early osteoblast marker. Cells were also treated with PRP with neutralizing antibodies of TGF-β (PRP-αTGF-β) and VEGF (PRP-αVEGF) during myogenic and chondrogenic differentiation, respectively. To test the therapeutic use of PRP in osteoarthritis (OA), we established a rat model for OA. OA was induced with a single injection of monosodium iodoacetate (MIA) in the right knee of four 3-week old rats to develop degeneration of articular cartilage. Two weeks after MIA injection, rats were given a single injection in the same knee with 100% PRP from a healthy rat or phosphate buffered saline (PBS). Four weeks after PRP or PBS injection, the animals were sacrificed and both right and left knees were harvested.

Results

PRP enhanced the proliferation and differentiation potential of MDSC's. This study concluded that treatment with 2% PRP at the time of differentiation medium improved MDSC proliferation and differentiation into each respective tissue lineage. However, neither PRP-αVEGF nor PRP-αTGF-β showed significant enhancement of proliferation or differentiation compared to PRP alone. *PRP improved healing of articular cartilage in OA model rats.* After the OA model was

successfully established, this study concluded that PRP healed cartilage faster than the untreated (PBS) group by observing gross morphology of each rat knee (Fig. 3).

Discussion

PRP has become a popular therapy for several musculoskeletal conditions but its clinical utility has yet to be fully elucidated. This study supports the notion that PRP can enhance tissue proliferation *in vitro* and promote articular cartilage healing *in vivo.* However, further quantification of tissue differentiation *in vitro* and growth factor removal needs to be done. Histological and immunochemical analysis must also be performed on the harvested OA rat knees.

ABSTRACT

Rethinking how Commonly Prescribed Diabetic Drugs Affect Osteoblast Survival

CHRISTOPHER HAMAD *McGovern Medical School at UTHealth* *Class of 2021*

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; Bone; Osteogenesis; Osteoblast; Metformin; Pioglitazone; Canagliflozin

Purpose:
Studies have suggested that drugs used to treat type 2 diabetes have a significant impact on osteogenesis, possibly exacerbating the already-poor mineral quality of diabetic bone. The first line treatment, metformin, may promote osteogenesis, but pioglitazone (TZDs) and canagliflozin (SGLT2-inhibitors), drugs used in combination therapy, may be detrimental to osteogenesis. The primary objective of this study was to determine the in-vitro effects of pioglitazone and canagliflozin on osteoblasts cultured in standard and high glucose media from normoglycemic and diabetic patients on metformin therapy (T2DM+M).

Methods:
Discarded bone samples were collected from primary total hip and knee arthroplasties performed on three normoglycemic and four T2DM+M patients. Subjects were chosen at random, and the investigators were blinded to patient demographics with the exceptions of age, sex, and diabetes control. Patients were excluded if HbA1c>8.5%. Primary osteoblasts were harvested using the trabecular bone explant model. Cultured osteoblasts were treated with Canagliflozin (3 μM-47 μM, in 0.2% DMSO) and pioglitazone (2 μM-31 μM in 0.2% DMSO) for 48h. Cell viability, total protein (TP), and alkaline phosphatase (ALP) activity were assayed.

Results:
T2DM+M cells cultured in standard glucose medium expressed 3x higher ALP than normoglycemic cells ($p<0.0001$). T2DM+M cells cultured in high glucose media had significantly lower cell viability ($p<0.001$) and ALP ($p<0.046$), while normoglycemic cells were not significantly impacted.

In standard and high glucose media, canagliflozin dose-dependently decreased osteoblast viability in both normoglycemic and T2DM+M cells, while pioglitazone had a differential effect. In standard glucose media, Pioglitazone increased cell viability in normoglycemic and T2DM+M cells, while in high glucose media, decreased the viability of T2DM+M cells.

Conclusions:
Culture conditions significantly impacted T2DM+M cell behavior. Our data agrees with studies suggesting a negative effect of SGLT2-inhibitors on bone. Pioglitazone exhibited a differential effect; it increased cell viability at low glucose, but decreased cell viability at high glucose concentrations. These results suggest that commonly-prescribed diabetes drugs may have important effects on bone metabolism. Physicians should consider duration of hyperglycemia in combination pharmacotherapy as these drugs appear more detrimental in the presence of high glucose.

ABSTRACT

Mock Code Curriculum for Pediatric Residents, Pediatric Emergency Fellows and Emergency Medicine Residents

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Sponsored by: Dr. Donna Mendez, MD, Department of Pediatric Emergency Medicine
Supported by: Dr. Donna Mendez, MD, Department of Pediatric Emergency Medicine
Key Words: Pediatric Emergency Medicine, Mock Modules, Residency Education

Background: Pediatric emergency medicine fellows, emergency medicine residents and pediatric residents require treatment of critically-ill patients but gaining experience managing pediatric codes can be difficult due to low incidence rates. Many residency programs utilize mock code curricula to teach code management. Although studies in the past have accessed the effectiveness of mock code curricula in relation to knowledge-base and confidence, previous studies have not attempted to study implementation of a web-based educational model and failed to assess mock code curricula across multiple disciplines. Furthermore, previous studies have failed to access demographic factors such as gender, race, and level of training. This study will access the implementation of a web-based mock code curriculum across disciples (pediatric emergency medicine residents, emergency medicine residents and pediatric emergency fellows) with follow-up assessment at 6-month and 1-year intervals post curriculum completion.

Methods: Participants were recruited from the UT Health Science Center Emergency Medicine residency program, the Pediatric Emergency Residency and the Pediatric Emergency Medicine Fellowship. Knowledge was assessed using a pretest/posttest module. Follow up surveys will be administered to participants at 6-month and 1-year post module completion to further assess gender, age and level of training.

Results: Comparison of preintervention and postintervention evaluation scores showed significant improvement in knowledge-base across all included specialties. 19 residents completed mock module 1 with an average pretest score of 10.42/20 compared to an average posttest score of 15.31/20. 15 residents completed mock module 2 with an average pretest score of 12.87 compared to an average posttest score of 18.07. Comparison of pretest/posttest scores showed a 24.45% improvement ($p \leq .0001$) for mock module 1 and 26.00% improvement ($p \leq .0001$) for mock module 2. As the project is ongoing, demographic data will be collected and analyzed at 6-month and 1-year intervals post-completion of the mock modules curricula.

Conclusions: Implementation of a web-based mock code curricula showed significant increases in knowledge-base across multiple specialties. Web-based mock modules may be a successful means of teaching pediatric code management to residents across different specialties.

ABSTRACT

Clinical Hemostatic Associations in Patients with Nonpulsatile Left Ventricular Assist Device

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Sponsored by: Dr. Angelo Nascimbene, MD., Center for Advanced Heart Failure
Supported by: Dean's Office Stipend for the 2018 Summer Research Program., Center for Advanced Heart Failure.
Key Words: Left Ventricular Assist Device, Non surgical Bleeding, Thrombosis-Thromboembolism, Cerebrovascular Ischemia, Hemolysis

Background: Left Ventricular Assist Devices (LVAD) are devices that aid patients with end stage heart failure to maintain requisite cardiac output. Historically, devices were designed to maintain the heart's native pulsatile function. However, newer devices have evolved to maintain continuous blood flow via an internal rotor within the device. Despite known patient improvement of cardiac function with these devices, severe complications still persist. These complications are hemostatic in nature and include, device thrombosis-thromboembolisms, hemolysis or severe non-surgical bleeding.
Objective: To study LVAD and clinical hemostatic adverse events such as severe non-surgical bleeding, device thrombosis, hemolysis or thromboembolic strokes.
Study Design: Retrospective data collection was obtained from 50 patients who had a LVAD implanted. This study focused on either HeartMate II (ThoratecCorp.,Pleasanton, CA) or HeartWare (HeartWare Inc.,Framingham, MA) model. Patient demographics, diagnosis as well as Pre-New York Heart Association (NYHA) class was obtained at the time of admission (baseline). Patient blood samples were also collected before device implantation (baseline), after discharge, 1, 3, 6 months and one year post-implant and any readmission for suspected hemo-related adverse events. device parameters were also obtained to describe changes of device support including pulsatile index (HeartMate II only) and device rotations per minute (RPM) throughout the study. All data was stored in REDCap web-based data entry; a secure web application accessed only by study investigators and database managers.
Results: Of 50 patients, 6 patients were excluded due to either death prior to implant, transfer to outside hospital, or orthotopic transplantation. Among the remaining patients, 14 patients had severe adverse events. Of the 14 patients, 7 had 1 adverse event, 3 had 2 adverse events, 2 had 3 adverse events and 2 patients had 4 adverse events; moreover 4 patients underwent re-implantation of new devices. Of the 4 cases of re-implantation, 2 had previous hemolytic adverse events that later presented with device thromboembolism. Of the 27 cases, 23 (85.2%) were reported to be hemostatic episodes that included ten with severe gastrointestinal (GI) bleeding, thromboembolic stroke in two, subarachnoid hemorrhage in 1, device thrombosis in three, hematoma in one, hemolysis in five and, arterial non-CNS thromboembolism in one. No patient that presented with severe GI bleeding presented with hemolysis or pump thrombosis indicating two different hemostatic complications.
Conclusion: Several patients were readmitted for severe hemostatic adverse events post LVAD implantation. Patients seems to cluster in 2 distinct groups based on hemostatic complications,

either severe GI bleeding or hemolysis/device thromboembolism without significant overlap. Further studies will be needed to obtain markers able to better discriminate individuals in these two distinct clinical entities.

ABSTRACT

Psychiatric Comorbidity in Trauma Patients: A Retrospective Look at Burden and Outcomes

AARON HOCHER *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dr. Bryan Cotton, MD & Dr. Damaris Ortiz, MD, Department of Surgery
Supported by: Center for Translational Injury Research (CeTIR)
Key Words: Psychiatric comorbidity, trauma, serious mental illness

Introduction - Trauma patients with psychiatric comorbidities are a high-risk population. Both medical and surgical patients with psychiatric comorbidities have been shown to receive guideline based care at lower rates than patients with the same medical problems who lack psychiatric comorbidities. In trauma patients, studies show that patients with preexisting psychiatric illnesses are at an increased risk of in-hospital mortality, a more complicated course, and longer hospital stays. The prevalence of serious mental illness in trauma patients is not known, and existing literature suggest significant issues with patient care for this population. Thus, the purpose of this study is to better quantify the number of trauma patients with psychiatric comorbidities to describe the burden of disease as well as outcomes in this patient population. Primary outcomes include mortality, length of stay, and complications.

Methods - A retrospective chart review was performed of patients admitted to Memorial Hermann Hospital from January 1, 2016 to May 14, 2016. Inclusion criteria for the study were 1) trauma admission, 2) 18 years and older, and 3) a diagnosis of a serious mental illness or self-injury. Serious mental illness includes major depressive disorder, bipolar disorder, schizophrenia, and anxiety. Pregnant women, prisoners, patients who were transferred after their initial trauma, and patients who were readmitted for a previous traumatic injury were excluded. Patient diagnoses were pulled from the trauma registry using the ICD-10 codes and corroborated with inpatient medical records. Outpatient medical records were used to validate the psychiatric diagnosis of patients with a serious mental illness.

Results - There were 626 consecutive level-1 trauma patients entered into the Trauma Registry from 01/01/16 through 05/14/16. Of these, 541 (86%) carried no psych diagnosis and 85 (14%) had a psych diagnosis or had injured themselves. Of these 85, 16 (19%) had anxiety, 24 (28%) had bipolar disorder, 9 (11%) had schizophrenia, and 36 (42%) had depression. Self-injury occurred in 16 of the 95 (19%). Preliminary analysis of the data showed that 1) there are more males in the non-psych group (74%, <0.001), 2) psychiatric patients have significantly more blunt injury than penetrating injury (35%, <0.001), and 3) psychiatric patients had longer hospital stays (22 hospital-free days vs. 25 hospital-free days in the non-psych group; 0.001).

Conclusion - This study aimed to determine the number of trauma patients who had a comorbid psychiatric illness in order to help define the burden of disease in this population.

Preliminary analysis showed that a significant number of trauma admissions had preexisting serious mental illness or had injured themselves, comprising 14% of the initial cohort. Thus, it is a population that deserves special attention. Notable results include patients in the psychiatric group having longer lengths of hospital stay than the control group. This finding supports the existing literature. Further study should be done to identify what factors contribute to this patient population's longer length of stay. Additionally, trauma admission for patients without a diagnosis who present with self-injury may present an opportunity for psychiatric intervention.

ABSTRACT

Effect of a Pill-Based, Multi-Modal Pain Regimen on Opioid Use in Trauma Patients

JOHN HOWELL *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: John A. Harvin, M.D., F.A.C.S., Department of Surgery
Supported by: McGovern Medical School, Department of Surgery, CeTIR
Key Words: Opioid, Trauma, Pain, Analgesia, Surgery

Introduction: In 2013, surgeons at the Red Duke Trauma Institute at Memorial Herman Hospital-Texas Medical Center implemented a multi-modal pain regimen with the goal of decreasing opioid use in trauma patients. The aim of this study was to quantify the effect of this new regimen on reduction of opioid use and how this reduction affected associated pain scores reported by patients. We hypothesize that there will have been reduced administration of Morphine Milligram Equivalents (MME) per day over each year from 2010 to 2017. Also, this reduction in MME given per day will have no effect on pain scores reported by patients via the Numeric Rating Scale (NRS) over the same time-period.

Methods: All adult patients (>16 yrs) with 1 or greater rib fractures admitted to the trauma center from January 1, 2010 through December 31, 2017 were included. Data collected from the trauma registry included: age, race, sex, Injury Severity Score (ISS), opioid medication administration, and NRS pain scores. Average daily opioid use was calculated by dividing the total MME of all opioids received during hospitalization by the number of days hospitalized. Average NRS pain scores were recorded by nurses (0 = no pain to 10 = worst pain). Kruskal Wallis test was run on adjusted data by year to assess for significant changes in opioid use.

Results: 6,933 patients were included, of which approximately 2/3 were male. There was a significant decline in Caucasian patients during this time period and an increase in Hispanic patients admitted, from 18% in 2010 to 31% in 2017 ($p<0.001$). Median ISS, the percentage of patients with major trauma (ISS>15), and the percentage of patients with severe chest trauma (AIS Chest ≥3) did not change over time. There was a significant reduction in MME per day from 2010 to 2017 (2010 median MME 56 [IQR 35, 88] versus 2017 MME 37 [IQR 17, 61], $p<0.001$). This represents a 34% reduction in MME per day over the time period. Average NRS pain scores also significantly decreased over the study period (2010 median pain score 4 [IQR 3, 6] to 2017 pain score 4 [IQR 2, 5], $p<0.001$).

Conclusions: The results of this study demonstrate the multi-modal pain regimen implemented at the Red Duke Trauma Institute was successful in reducing average MME per day by 34%. There was also a decrease in the average NRS pain score. While it is unclear if the reduction in the average NRS pain score is clinically significant, the downward trend lends support to the fact that the multi-modal regimen was an effective alternative to opioid-based analgesic strategies.

ABSTRACT

The Effects of Bmi1 proto-oncogene Knock-Out on B-cell Differentiation and Proliferation in Murine Populations

ALEXANDER HUNT *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dr. Momoko Yoshimoto MD, PHD; Dr. Michihiro Kobayashi MD, PHD - Center for Stem Cell Research and Regenerative Medicine
Supported by: Dr. Momoko Yoshimoto; McGovern Medical School SRP Matching Grant
Key Words: Polycomb Repressive Complex, Bmi1 Knock Out, B Cell Development, Pro B Cells, IL7R-Cre:Bmi1-Flox Knock Out

Background and Significance: The *Bmi1* proto-oncogene product, Bmi1, is part of the Polycomb Repressive Complex that regulates the expression of genes epigenetically through the ubiquitination of histones (Wang et al., 2004). Global knock out of Bmi1 produces a phenotype with 3 abnormalities: neurological dysfunction, posterior abnormalities, and a significant decrease of hematopoietic stem cells and an impairment of proliferative response when they are exposed to mitogens. In order to study the effects of Bmi1 on hematopoiesis as it effects B cell development we sought to isolate the deletion of Bmi1 to common lymphoid progenitors (CLP) and their downstream cell stages. Preliminary data shows that there is a delay in B cell development in mice that have Bmi1 knocked out with an accumulation of CLP and pro B cells and decrease in Pre B and immature B cells. We hypothesized that Bmi1 plays a key role in regulating transcription of genes that are necessary for development of B cells. Obtaining this information gives us key insights to the epigenetic regulation of B cell development.
Materials and Methods: In order to obtain mice that are Bmi1 KO specific to CLP and their downstream stages, IL7-R $Cre^{KI/WT}$ were crossed with $Bmi1^{flox/flox}$ with the lox insertion flanking the Bmi1 gene. This produced IL7-R Cre:Bmi1-flox double heterozygous mice which were crossed with Bmi1 flox homozygous again, producing offspring who have homozygous flox and cre inserted in the same mouse (IL7-$Rcre^{KI/WT}$:$Bmi1^{flox/flox}$ mice). This was confirmed through PCR genotyping. The mice of interest and IL7-$Rcre^{WT/WT}$:$Bmi1^{flox/flox}$ mice, which was used as a control, were sacrificed and bone marrow collected. Cells were stained and sorted according stage specific markers into KSL, CLP, pro B, pre B, and Immature B cell groups. RNA was then harvested from the different cell groups and cDNA as made. Transcription factors specific for B cell development, pro-apoptotic, anti-apoptotic, proto-oncogenic, epigenetic regulation, and DNA repair genes were then ran through qPCR and the effects of Bmi1 KO on gene expression in the different B cell stages was analyzed. We then ran PCR amplifying the VDJ recombined region of the B cell receptor to assess for changes in VDJ recombination.
Results: In all samples ran we saw an expected increase in p19arf, which is a pro-apoptotic gene that is normally repressed by the polycomb repressive complex. There was a universal decrease in the transcription of IKZF1, an important B cell transcription factor. In addition to this we saw an approximate 2 fold decrease in the DNA repair genes DCLRe1 and DNA-PK in the pro B cell population. In the PCR amplification of VDJ recombined regions we saw a less intense band in the IgM^+ cell sample group in the KO population compared to the WT indicating possible less VDJ recombination occurring during that stages of development. However this is not conclusive as we did not see a less intense band in the pro B cell stage of development.
Conclusions: The universal de-repression of pro-apoptotic gene p19arf would lead to more apoptosis and less B cells phenotypically. However, this does not explain the accumulation of the early B cell stages CLP and pro B. Bmi1 plays a role in regulating the development of B cells which could possibly be related to the decreased gene expression of IKZF1. Further studies need to be done to confirm the relationship between DCLRe1c, DNA-PK, and Bmi1 and possible decreases in VDJ recombination.

ABSTRACT

The Role of TSPO in Mitophagy Failure and NLRP3 Inflammasome Activation in Bipolar Disorder

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Supported by: McGovern's Dean's Matching Fund
Key Words: Bipolar Disorder, Mitochondria, Mitophagy, Inflammasome, TSPO

Purpose: The outer-mitochondrial membrane Translocator Protein, TSPO, is a known component of the mitochondrial permeability and transition pore (MPTP), which when formed, depolarizes the electron transport chain, leading to reactive oxygen species (ROS) production and ultimately damages the mitochondria. Of note, Bipolar Disorder (BD) has been increasingly associated with mitochondrial dysfunction. Thus, the purpose of this study is to evaluate the expression of TSPO in peripheral blood mononuclear cell (PBMCs) of BD type-I patients, and then to correlate the recorded TSPO levels with mitophagic markers and NLRP3 inflammasome activation.

Methods: The participants in our study included 31 patients with BD type-1 and 25 healthy matched controls; both groups were assessed with the Mini-International Neuropsychiatric Interview (MINI). Blood samples were collected and then processed to separate the PBMCs. Gene expression in participant PBMCs was assessed through RNA isolation followed by measurement of mRNA levels. Protein levels in participant PBMCs were assessed through immunoblotting. Differences between the two groups (patients vs. controls) were assessed by Mann–Whitney or Student's t tests when non-normally or normally distributed, respectively. All statistical tests were two tailed and used a significance level of $p<0.05$.

Conclusions: A novel finding in our study is that our results show an increase in mRNA expression and protein levels of TSPO in PBMCs of BD patients, indicating an increase in MTPT formation, and leading to increased ROS production and mitochondrial damage. Furthermore, our results show a negative correlation between TSPO levels and the protein levels of integral proteins in the mitophagy pathway (Parkin, p62/SQSTM1, LC3A), as well as a positive correlation between TSPO levels and the mRNA expression of integral proteins in NLRP3 inflammasome activation (NLRP3, ASC, Caspase-1, IL-1β, IL-18). This suggests that the increased ROS production and mitochondrial damage associated with elevated TSPO levels may have an inhibitory effect on the mitophagy pathway while also serving as an NLRP3 inflammasome activation signal, which could account for the increased number of dysfunctional mitochondria and inflammation seen in BD patients. Therefore, this study is important because it sheds light on the mechanisms of BD and highlights the mitochondria as a prime therapeutic target.

ABSTRACT

Barriers Faced by Parents of Infants Transitioning Home from the NICU: Analysis of a Group Interview

CAMERON KERL *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Mary T Austin, MD, MPH, Department of Pediatric Surgery
Supported by: The Department of Pediatric Surgery, McGovern Medical School at UTHealth
Key Words: NICU, Transition to Home, Barriers, Focus Group

Introduction: Transitioning from the Neonatal Intensive Care Unit (NICU) to home is a vulnerable time for parents of NICU infants. This transition to home is the period in which parental knowledge, skills, and resources can have tremendous impact on the infant's outcome. Uncertainty exists as to the barriers parents experience when transitioning home from the NICU. We conducted a group interview with parents of former NICU infants to understand challenges faced by parents during the discharge process when transitioning home.

Methods: A group interview was conducted November, 2017 with ten parents of former NICU infants recruited from the NICU Parent Advisory Council and by recommendations of NICU social workers/discharge coordinators. The group interview was conducted by a qualitative researcher, audio recorded and transcribed. A thematic content analysis of the coded data was performed by the research team. A base of 40 codes was created inductively and deductively by the research team to answer the research question. Codes were assigned to quotations in the transcript by members of the research team and then discussed as a group to reach consensus of the emergent themes.

Results: This group of parents identified multiple challenges in the discharge process. Major themes included lack of support, information sharing, lack of preparedness or parental education on durable medical equipment, expectations, and feelings of anxiety / overwhelming stress (see Table). Parents often lacked a robust support system on an emotional, mental, and physical level. Anxiety and stress surrounding the unknown and the information gap that existed with respect to the complex care of their child were commonly described by parents. Some parents also felt unprepared with regard to operating various forms of durable medical equipment. They stated that information regarding discharge schedule and care management changes were not always clearly communicated. Parents highlighted the use of social media to seek further information to address these barriers. To help manage the complex care of their children, parents developed their own schedules, checklists, and alarms.

Conclusion: This study identified specific barriers that parents of our NICU infants have when transitioning home. As such, this raises the need to create a program that may address these barriers in order to improve not only patient satisfaction, but also improve healthcare outcomes in our most vulnerable population.

Theme	Quotations
Lack of Support	"I wish I had somebody there. I wasn't thinking about the RSV and all that stuff because I just wanted somebody, um, to be here with me and help me out."
Information Sharing (Parents and Clinicians)	"Sometimes you want to hear it raw. It's like sometimes you want to hear what's—what's really going to happen, not what's supposed to happen."
Anxiety/Overwhelmed/Stress	"It's like you're being thrown into a fire and you just got to do it."
Lack of Preparedness	"The doctors and nurses ... are in the hospital that nobody was able to give us an idea of what happens once you walk out the door"
Expectations	"...we didn't have that [notification of discharge the day before], and I felt blindsided by that."

ABSTRACT

Molecular and Phenotypic Characterization of *Bacillus cereus* Clinical Isolates

JOHN E. KRAPF *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Theresa M. Koehler, Ph.D., Department of Microbiology and Molecular Genetics
Supported by: Herbert L. and Margaret W. DuPont Distinguished Professorship in Biomedical Science to T.M. Koehler
Key Words: *Bacillus cereus*, *Bacillus anthracis*, Clinical isolates

INTRODUCTION: *Bacillus cereus* is an opportunistic human pathogen that is a common blood culture contaminant in hospitals and a well-documented causative agent for cases of foodborne illness. Pathogenic *B. cereus* strains secrete three pore-forming enterotoxins which drive the pathogenesis of a diarrheal syndrome: nonhemolytic enterotoxin (Nhe), cytotoxin K (CytK) and hemolysin BL (Hbl). Transcription of *nhe*, *cytK* and *hbl* is controlled by the global virulence regulator, PlcR. Recently, non-type conforming *B. cereus* strains have been reported to cause life-threatening anthrax-like infections in humans. These atypical *B. cereus* isolates were found to have plasmids with high sequence similarity to the virulence plasmids of *B. anthracis*, the causative agent of anthrax. Furthermore, the plasmids contain a gene orthologous to *atxA*, the global virulence regulator of *B. anthracis*. Herein we conduct a preliminary screen for the genetic basis of atypical virulence in *B. cereus* clinical isolates through phenotypic and molecular characterization techniques.
METHODS: 50 *Bacillus* clinical isolates suspected of being *B. cereus* were obtained from the Clinical Microbiology Laboratory at Memorial Hermann Hospital. Upon further characterization, 30 of these isolates were ultimately identified by the hospital as *B. cereus*. Sources of the isolates include blood, CSF, lung tissue, pelvic fluid, and skin. We phenotypically characterized all 50 isolates by noting colony morphology, growth rate, hemolytic activity, lecithinase activity, and endospore-forming ability. Molecular characterization consisted of 16S rRNA sequencing and phylogenetic analysis. Additionally, degenerate and traditional primer sets were designed for highly conserved DNA sequences to screen for the presence of genes encoding for toxins (*cytK*, *hbl*, *nhe*) and their global virulence regulators (*plcR*, *atxA*). All positive PCR amplifications were confirmed by southern blot.
RESULTS: 28 of the 50 clinical isolates were identified by 16S rRNA sequencing as *B. cereus* group members. The clinical laboratory failed to identify two isolates as being *B. cereus* and misidentified four isolates as *B. cereus* which were shown through 16S rRNA sequencing to be *Enterobacter* or non-*B. cereus Bacillus* species. PCR-based screening with confirmatory southern blots revealed that two of the *B. cereus* isolates as well as an isolate identified as *Clostridium* were positive for the *B. anthracis* global virulence regulator gene, *atxA*. Of the 28 *B. cereus* isolates all 28 were positive for *nhe*, 27 positive for *plcR*, 27 positive for *cytK*, and 25 positive for *hbl*. Phenotypically, it was noted that all *B. cereus* isolates grew rapidly and reached a colony diameter of 3-5 mm after 24 hours at 30*C. All 28 isolates had B-hemolytic activity when cultured on blood agar, lecithinase activity when cultured on egg yolk agar, and 26 of the 28 isolates formed endospores. Altogether, the preliminary data obtained by this screening adds to

our knowledge of virulence in pathogenic *B. cereus* strains and promotes further study into the molecular mechanisms behind atypical virulence in *B. cereus*.

ABSTRACT

CT Scan Guided Sizing in TAVI: Pre-Procedural Planning and Post-Procedural Outcomes

SUNGITA KUMAR *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Angelo Nascimbene, MD, Cardiology
Supported by: Center for Advanced Heart Failure – Memorial Hermann
Key Words: Aortic valve insufficiency/diagnostic imaging; risk factors; transcatheter aortic valve replacement/methods; treatment outcome

Introduction: Transcatheter Aortic Valve Implantation (TAVI) is a minimally invasive technique to treat aortic valve stenosis in high and intermediate risk patients.
Objective: The objective of this study is to identify anatomical factors, variations in implant technique, and procedural variations that have led to intraoperative complications.
Methods: We retrospectively analyzed CT scans of 261 patients who underwent TAVI with S3-THV at our institution in 2016. TAVI patients were divided into groups based on annular anatomy and device size. Each implant was then subsequently matched with the degree of aortic insufficiency (AI) after the initial implant and the need for post dilatation due to residual AI. The degree of post implant AI was determined by echocardiography at the time of the procedure. Based on annular area, specific volumes were loaded into the initial delivery system.
Results: Out of 261 patients, 37 were implanted with the 20-mm valve, 88 with the 23-mm valve, 101 with the 26-mm valve, and 35 with the 29-mm valve. Volumes at initial deployment were nominal (i.e. based on manufacture recommendation) in 96% of cases. Of the 247 valves deployed at nominal volumes, 85% (211/247) showed no signs of aortic insufficiency (central regurgitation nor paravalvular leak) at the time of deployment. The remaining 15% (36/247) showed the following insufficiencies: 31 mild, 4 mild-moderate, and 1 significant. We collected extensive CT-guided anatomical variables, including left coronary artery calcium volume, sinotubular junction diameter, right coronary artery height, and left coronary artery height. Using these variables, several mathematical models were constructed with significant discrepancies between logistic and random forest models. This likely results from the non-linearity relationship between clinical features and outcomes. Ultimately, we used a classification and regression tree to build a non-linear model, which was able to predict the risk of paravalvular leak based on CT anatomy, with a high degree of certainty. This model re-stratified patient characteristics into 14 subgroups of varying risk of paravalvular leak based on anatomical features. Finally, our current implant strategy seems to be safe in addition to being effective, as only 5 of the 261 TAVR procedures (1.9%) suffered significant complications, including 3 emergent ECMO placements and 3 pericardiocentesis procedures. These valves were deployed at nominal volume and were within indicated ranges for their respective annular areas (three 23 mm valves and two 26 mm valves). None were post-dilated.
Conclusion: The current S3 device sizing strategy for TAVI significantly eliminates the degree of post-implant aortic regurgitation and seems to be relatively safe, as the probability of major adverse events is less than 2%. Using the current model, we can identify subsets of patients who are more likely to require post-dilatation or higher deployment volume pre-loaded in the

delivery system based on individual anatomy. Larger data sets will be needed to confirm our initial model.

ABSTRACT

Ankyrin-G Regulation of Myozenin and Calcineurin in Cardiomyocytes

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Sponsored by: Dr. Shane Cunha
Supported by: AHA Grant-in-Aid
Key Words: Ankyrin-G, Myozenin, Calcineurin, Cardiomyocytes

The goal of the project was to test the hypothesis that the protein myozenin's molecular interaction with the protein ankyrin-G plays a key role in the regulation of the protein calcineurin at the T-tubules of cardiomyocytes. We believe that if the interaction of myozenin and ankyrin-G is disrupted the net result will be an increase in calcineurin signaling. The first step was creating a dominant negative myozenin construct, that would disrupt ankyrin-G association with the endogenous myozenin. The generation of the dominant negative myozenin was unsuccessful for reasons not fully understood. However, in the process I was the first to show using a Western blot that calcineurin, myozenin, and ankyrin-G all interact. The unsuccessful generation of the dominant negative myozenin forced us to find a new method to knock down myozenin expression. The alternative method was to use RNAi to decrease the transcription of myozenin mRNA in the cells. Unfortunately, due to time limitations I was not able to complete this project. However, I performed the necessary groundwork for other researchers to advance this project in Dr. Cunha's lab.

ABSTRACT

Intraoperative Platelet Rich Plasma and Bone Marrow Aspirate Concentrate in Anterior Cruciate Ligament Reconstruction

KYLE LAUCK *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Lane Bailey, P.T., Ph.D., C.S.C.S.
Director of Research and Education
IRONMAN Sports Medicine Institute

Key Words: ACL Injury, ACL reconstruction, Biologics, Stem Cells, Platelet Rich Plasma

Introduction: Anterior cruciate ligament (ACL) injury has historically been challenging for clinicians to manage with reported failure rates of up to 29.9% documented following ligament reconstruction. In a search for novel treatment modalities research has begun to examine the application of biologics in ACL injury management to augment healing and subsequently reduce the incidence of reinjuries. Platelet Rich Plasma (PRP), blood derived product containing a high concentration of platelets, growth factors, and other molecules which promote healing and tissue anabolism has shown promising preclinical data. However clinical trials have shown more mixed results. Additionally, stem cells, which can be cultured or may be aspirated from the bone marrow often at the time of surgery, have recently grown in popularity. They are applied to the graft where they have been shown in animal models to enhance healing. However due to barriers such as cost (etc.), while the preclinical data is positive, there is a relative absence of clinical data currently available. In light of this lack of consistent and available clinical data, the purpose of this study was to assess the effectiveness of intra-operatively applied PRP and/or bone marrow aspirate concentrate (BMAC) on improving postoperative function and reinjuries in patients who received intraoperative biologics versus those who did not receive intraoperative biologics during ACL reconstruction.

Methods: A matched controlled analysis will be completed for patients undergoing ACL reconstruction using a single surgeon database with over 1,000 patients. Patients will be matched based on age, gender, BMI, surgical profile, and prior level of function using the MARX scale. Functional outcome measures will include range of motion, single leg balance, dynamic jump landing assessment, single leg hopping and agility testing assessed at the time of return to sport for participating patients. Additionally, patient subjective function [International Knee Society Committee (IKDC)] and psychological profile (ACL-Return to Sport Index) will be considered among the primary outcome measures. Group comparisons will be examined using a *one-way analysis of variance (ANOVA)* by group with a statistical level of significance set at alpha .05.

Current Status: To date we are completing data collection and transitioning into data reduction and analysis. The anticipated completion date is October 1st, 2018.

ABSTRACT

Impact of Hurricane Harvey on ESRD Mortality

Frederick LeMaistre *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dr. Donald A. Molony, M.D., Internal Medicine
Supported by: Dr. Donald A. Molony, M.D., Internal Medicine
Key Words: Hurricane Harvey, End Stage Renal Disease Mortality

Background: Hurricane Harvey caused widespread disruption to healthcare resources in Houston due to extensive flooding. During natural disasters, end stage renal disease (ESRD) patients represent a particularly vulnerable population due to interruption in care. Few studies have extensively examined the effects of natural disaster on ESRD mortality beyond 30-day intervals. We hypothesize Hurricane Harvey increased gross mortality and mortality rates significantly in affected areas compared to those unaffected.

Methods: The study examined both gross mortality and mortality rates using 2749 Death Certificates from the Centers for Medicare & Medicaid Service claims Data. The study compared gross mortality and mortality rates between the years 2016 and 2017, as well as gross mortality and mortality rates between Hurricane Harvey effected zones and non-effected zones. Zones were defined based on FEMA designation of Hurricane Harvey effected counties. 745 death certificates were included in the 2016 control group from the months August to November, and 811 deaths were included in the 2017 comparison group. In comparing between effected zones in 2017, 1630 deaths certificates were included in the effected zones, and 3434 deaths were included in the non-effected zones. Death certificates were assigned to area based on primary dialysis facility. Gross mortality was stratified by dialysis facility, zip code, and county and compared between groups. Mortality rates of counties between hurricane zones were similarly compared. Differences in mortality rates between 2016 and 2017 were also examined. An auto-regressive integrated moving average (ARIMA) model was performed to analyze the data and construct a forecasting model.

Results: The largest increase in gross mortality and mortality rate occurred 90 days post Hurricane Harvey impact in affected areas. Annualized mortality rate increased 5.84% 90 days post Hurricane Harvey while Non-Hurricane Harvey area mortality rate increased only .69% in the same time frame. In a similar timeframe, annual mortality rates for counties effected in 2016 increased 1.17% in 2016, while only increasing .44% in 2017.

Conclusion: The increase in mortality rate for Hurricane Harvey affected areas compared to non-affected areas suggests the increased mortality was attributable to events caused by the hurricane, as opposed to a seasonal event such as influenza. Increased 90-day mortality may be due to the interruption of care for dialysis patients leading to fatal complications. The smaller increase in mortality in 2017 may be due to loss of granularity between 2016 and 2017 datasets. Further, more granular study is needed to determine medical and socioeconomic characteristics that predict increased risk of mortality in patients with ESRD as well as center characteristics that predict outcomes. Once such risk factors are identified, mitigation strategies can be developed to improve outcomes in this patient population during a natural disaster.

ABSTRACT

Comparing the Effect of Lens Extraction with Endoscopic Cycloplasty and Lens Extraction Alone on Peripheral Angle in Eyes with Plateau Iris Configuration: An Anterior Segment Optical Coherence Tomography Study

MONICA LU *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Robert M. Feldman, MD, Department of Ophthalmology and Visual Science
Supported by: Robert M. Feldman, MD, Department of Ophthalmology and Visual Science
Key Words: Plateau iris, ASOCT, endocycloplasty, angle closure glaucoma

Background: Plateau iris configuration (PIC) is an anatomical abnormality with a large or anteriorly positioned pars plicata that pushes the peripheral iris root forward, causing an occludable configuration of the anterior chamber angle which appears as a steep iris insertion. This steep insertion upon dilation can obstruct the trabecular meshwork and prevent aqueous humor drainage, causing elevated intraocular pressure. Although lens extraction (LE) with phacoemulsification is often adequate to relieve primary angle closure from PIC, it is not universally effective and doesn't resolve the underlying etiology. In contrast, LE with endoscopic cylcoplasty (ECPL) directly treats the anatomical anomaly of PIC by applying laser thermal energy which shrinks and rotates the posterior ciliary processes, widening the angle. The primary objective is to quantitatively determine the effect of these two treatments for PIC, LE with ECPL versus LE alone, on angle parameters measured with anterior segment optical coherence tomography (ASOCT). The secondary objective is to compare ECPL-treated angles with non-treated angles within a PIC eye.

Methods: This is a retrospective case-control study of patients with PIC seen at Robert Cizik Eye Clinic of the Ruiz Department of Ophthalmology & Visual Science that had LE with phacoemulsification performed between January 1, 2014 and December 1, 2017. Eyes with documented PIC that underwent ASOCT prior to and post treatment were included. Demographics, clinical examination findings, and surgical data were recorded. Ultrasound biomicroscopy was used to confirm the diagnosis. ASOCT images were read by a previously validated reader to compute the following parameters: angle opening distance (AOD), trabecular iris space area (TISA), trabecular iris circumferential volume (TICV), and irido-trabecular contact (ITC). Clinical data and ASOCT parameters were compared between LE/ECPL and LE alone eyes using a 2 sample t-test. P-values were adjusted by the false discovery rate method; $P^* < 0.05$ was considered statistically significant. A paired t-test was used to compare treated (nasal) and untreated (temporal) angles in LE/ECPL treated eyes.

Results: Twenty-three eyes of 14 participants were included in the study. Ten eyes (43%) eyes of 7 participants were treated with LE/ECPL and thirteen eyes (57%) of 7 participants were treated with LE alone. After surgery, ASOCT parameters were similar between the two groups ($P^*>0.11$) and angles were significantly deepened by treatment in both groups ($P<0.001$). Change in AOD, TISA, TICV and ITC length from preoperative to postoperative showed that the magnitude of deepening in treated (nasal) quadrants was greater in LE/ECPL eyes than in

LE alone eyes (P*<0.05). In the LE/ECPL group, the ECPL treated angles were deepened more than the untreated angles by 3 out of 4 parameters: AOD, TISA, and TICV (P<0.002).
Conclusion: To our knowledge, this is the first study quantitatively comparing LE/ECPL with LE alone in eyes with plateau iris configuration. The results show that LE with ECPL is more effective than LE alone in opening the anterior chamber angle, and that endocycloplasty deepens treated angles.

ABSTRACT

Herpes simplex virus CSF PCR testing in adults and children with meningitis and encephalitis

BERT MA *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Rodrigo Hasbun, MD MPH. Department of Internal Medicine
Supported by: Rodrigo Hasbun
Key Words: Herpes simplex virus, PCR testing

Herpes simplex virus (HSV) is a common treatable cause of meningitis and encephalitis. Delayed antiviral therapy is associated with worse clinical outcomes in HSV encephalitis.
We performed a retrospective review of 1239 adults and children with community acquired meningitis and encephalitis patients and a statistical analysis of clinical characteristics, laboratory findings and adverse outcomes of patients with a positive HSV CSF PCR at 9 hospitals in Houston, TX from January 1 2003 through December 31 2017. Data was analyzed by using SPSS for MAC version 21. We did a bivariate analysis of the data and used the Chi-square and ANOVA tests. Of 1239 patients, 633 (51%) underwent CSF HSV PCR testing. Adults were more commonly tested than children (83% vs 64%, P <0.0001). Additionally, patients with more comorbidities and clinical findings of encephalitis (e.g., altered mental status, focal neurological findings, seizures) were more commonly tested for HSV (P <0.001). In total, 72 of 633 (11.4%) patients tested had a positive CSF HSV PCR. Predictors for a positive CSF HSV PCR on logistic regression analysis were nuchal rigidity (odds ratio [OR], 3.248 [1.633-6.461]; P= 0.001), lymphocytic pleocytosis >50% lymphocytes (OR, 11.491 [2.651-49.800] P= 0.001). CSF HSV PCR is underutilized in community acquired meningitis and encephalitis and is done more frequently in adults and in those with an encephalitis presentation.

ABSTRACT

Defining Group A *Streptococcal* Antibiotic Resistance in the Houston Pediatric Population

OLGA ROSALIE MACIAS *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Anthony R. Flores, MD, MPH, PhD, Division of Infectious Diseases, Department of Pediatrics, Center for Antimicrobial Resistance and Microbial Genomics
Supported by: Anthony R. Flores, MD, MPH, PhD
Key Words: Group A *Streptococcus*, antibiotic resistance, whole genome sequencing

Background: Group A *Streptococcus* (GAS) is a common pediatric pathogen that accounts for a variety of diseases including pharyngitis, skin and soft tissue infections (SSTI) and more severe invasive infections. Beta-lactam antibiotics have been the mainstay for the treatment of GAS infections with no documented resistance to date. However, treatment with second-line, non-beta-lactam antibiotics (e.g. macrolides) are used in cases of beta-lactam allergy or in the eradication of the carrier state. Resistance to these second-line agents has increased as their usage has increased in certain pediatric populations. We sought to define the frequency of GAS antibiotic resistance in the pediatric population of Houston, Texas.
Methods: We used a previously defined collection of pediatric GAS spanning a 4-year period (2013-2017) from Texas Children's Hospital in Houston, TX. GAS isolates were defined by disease type including invasive, SSTI, and pharyngitis. Susceptibility testing to individual antibiotics was performed using disk diffusion and interpreted according to published standards. Whole genome sequencing (WGS) using both long- and short-read platforms was performed with subsequent de novo assembly on a subset (*emm* types 11, 75, 77, and 92) of GAS strains to determine presence and diversity of antimicrobial resistance genes.
Results: Of the 929 GAS isolates examined, we identified 214 (23.04%) that showed resistance to at least one antibiotic. No significant difference in the overall frequency of resistance was observed between any disease type. However, the frequency of resistance was significantly greater in invasive compared to pharyngitis to clindamycin (3.80% vs 1.39%, p=0.04) and erythromycin (9.13% vs 4.41%, p=0.01). Of the 214 resistant isolates, *emm* types 11, 75, 77, 92 showed the highest intrinsic (within *emm* type) resistance and accounted for over 25% of the total resistant population. Further, as a group, *emm* types 11, 75, 77, 92 were significantly overrepresented among the invasive cases and showed a higher invasive index as compared to all other *emm* types (2.55 v 0.96, p=0.03). WGS and de novo assembly revealed that Tn*916* and Tn*916*-like elements contributed primarily to tetracycline and macrolide-lincosamide-streptogrammin B (MLS_B) resistance phenotypes in the 4 *emm* types examined. Moreover, resistance was associated with prophage and integrative conjugative elements (ICE) in *emm75* and *emm11* including recently described ICE conferring macrolide resistance in *emm12* scarlet fever-associated GAS from Southeast Asia. *Emm92* GAS isolates universally harbored a plasmid (pRW35) conferring resistance to macrolides (*ermT*) and a putatively novel ICE conferring resistance to both tetracycline (*tetM*) and aminoglycosides [*aph(3')-IIIa* and *ant(6)-Ia*].

Conclusions We observed an overall resistance rate of 23% in our pediatric population, with a small number of *emm* types contributing substantially to the overall rate. Continued surveillance and research are needed to further evaluate these trends.

ABSTRACT

Diagnostic Concordance of DSM-IV and DSM-5 Bipolar Disorder in Pediatric Populations

ROJA MANOHAR *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Cristian P. Zeni, MD, PhD, Department of Psychiatry and Behavioral Sciences
Supported by: Cristian P. Zeni, MD, PhD, Department of Psychiatry and Behavioral Sciences
Key Words: Bipolar disorder, pediatric, DSM-IV, DSM-5

Bipolar disorder (BD) is a condition characterized by cyclic changes in mood, energy, and activity levels, classified as periods of mania or hypomania and depression. DSM-IV criteria for the diagnosis of a manic or hypomanic episode required the presence of abnormal mood symptoms including elation or an irritable mood. With the switch to DSM-5, an additional requirement for a diagnosis of a manic episode was added- that of a distinct period of abnormally increased energy and activity levels in addition to the mood shifts outlined in DSM-IV. Changes in diagnostic systems, including the switch from DSM-IV to DSM-5, can cause impacts on the prevalence of certain disorders. Due to the lack of biological markers for the identification of psychiatric disorders, it is of paramount importance to fully understand how the changes in diagnostic criteria impact prevalence rates. So far, no study has addressed these changes in pediatric populations. We hypothesized that the diagnostic concordance will be high between DSM-IV and DSM-5 and that the prevalence of bipolar disorder will be decreased. Data to perform this study was available from two different samples. Sample 1 was assessed in Brazil, in the ProCAB study and Sample 2 was assessed in Houston, Texas via the Pediatric Bipolar Registry. Initial analysis of the Houston data ($n=132$) revealed that out of 132 patients who met criteria for DSM-IV bipolar disorder, 116 (87%) met the stricter DSM-5 criteria. We are performing chi-squared tests for categorical variables and t tests for continuous variables for both Houston and Brazilian populations to compare sociodemographic data, mood disorder symptoms, and comorbidities among those who met the DSM-5 criteria and those who do not. Preliminary results from the Houston population showed that there are no significant differences in this data among the two groups. The average number of hypomanic episodes among those who did not meet DSM-5 criteria was 33.53, while the average among those who did meet the criteria was 40.15 ($p = 0.531$). The average number of depressive episodes was 28.88 among the DSM-IV-only BD patients and 31.46 among the DSM-5 BD patients ($p= 0.682$). Comorbidities with ADHD were 65.72% and 67.2% respectively in the group who did not meet DSM-5 criteria and the group who did ($\chi^2= .120$, $p=0.729$). The lack of significant differences among the groups indicate that there is a high degree of concordance between DSM-IV and DSM-5 BD. The results of this study will contribute to understanding of the prevalence of BD in pediatric populations and the concordance between the two diagnostic manuals, in addition to providing opportunities for further research into how these diagnostic changes will affect clinical outcomes.

ABSTRACT

Effect of a Pill-Based, Multi-Modal Pain Regimen on Discharge Opioid Prescribing in Trauma Patients

STEPHANIE MARTINEZ *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dr. John A. Harvin, MD., Charles E. Wade, PhD, Department of Surgery
Supported by: McGovern Medical School Department of Surgery; CeTIR. Dean's Office stipend
Key Words: Opioids, multi-modal pain regimen, trauma, injury.

Introduction: The prescription of opioids has increased in the past decade and brought about many potential harms for individual patients, such as increased risk of opioid addiction. In 2013 the Red Duke Trauma Institute implemented a pill-base, multi-modal pain regimen as a means to decrease opioid usage both in the hospital and after discharge. We hypothesize that using an opioid-minimizing multi-modal pain regimen at discharge will have reduced the percent of patients who are discharged with a prescription for opioids.
Methods: We conducted a retrospective study that included all the trauma patients ≥16 years of age with ≥1 rib fracture(s) that were admitted to the Red Duke Trauma Institute from January 1, 2010 through December 31, 2017. From this population we collected: age, race, sex, Injury Severity Score (ISS) and whether or not these patients were given a prescription for opioids at discharge and which opioid they were given. To assess for significant changes, we used a Chi Square on unadjusted data by year.
Results: There was an increase in the median age of our patient population from 46 years old in 2010 to 48 years old in 2017. There was an increase in the Hispanic patient population from 18% in 2010 to 31% in 2017. There was no significant change in ISS, the percentage of patients with major trauma (ISS > 15), and the percentage of patients with severe chest trauma (AIS Chest ≥3). Overall, there was a significant decrease in the percentage of patient discharged with an opioid prescription, from 80% in 2010 to 74% in 2017. However, there were significant changes in the types of opioids prescribed at discharge (Table).

	2010 (n=818)	2011 (n=871)	2012 (n=905)	2013 (n=959)	2014 (n=886)	2015 (n=870)	2016 (n=894)	2017 (n=730)	*p*
Opioid at Discharge	656 (80%)	718 (82%)	776 (86%)	830 (87%)	720 (81%)	689 (79%)	698 (78%)	542 (74%)	<0.001
Opioid Prescribed									
Codeine	1 (0%)	1 (0%)	3 (0%)	0 (0%)	54 (8%)	84 (12%)	134 (19%)	97 (18%)	<0.001
Tramadol	53 (8%)	80 (11%)	90 (12%)	269 (32%)	371 (52%)	488 (71%)	515 (74%)	421 (78%)	<0.001
Hydrocodone	598 (91%)	657 (92%)	713 (92%)	757 (92%)	530 (74%)	277 (40%)	228 (33%)	142 (26%)	<0.001
Oxycodone	47 (7%)	55 (8%)	553 (7%)	20 (2%)	25 (3%)	96 (14%)	111 (16%)	61 (11%)	<0.001
Methadone	3 (0%)	2 (0%)	1 (0%)	0 (0%)	4 (1%)	1 (0%)	1 (0%)	4 (0%)	0.163
Tramadol or Codeine only	14 (2%)	17 (2%)	26 (3%)	58 (7%)	166 (23%)	313 (45%)	355 (51%)	337 (62%)	<0.001

Conclusion: The multi-modal pain regimen was effective at reducing the absolute percentage of patients discharged with opioids prescription by 6%. There were significant changes in the type of opioid prescribed. The specific contributions of the multi-modal regimen and concomitant regulatory changes to this change remain unclear.

ABSTRACT

Risk of Intracerebral Hemorrhage Associated with Pregnancy in Women with Cerebral Arteriovenous Malformations: A Large-Scale Controlled Cohort Study

ANNIKA MEDHUS *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Sunil A. Sheth, MD, Department of Neurology
Supported by: Sunil A. Sheth, MD
Key Words: Pregnancy, AVMs, Hemorrhage

Introduction: Prior single-center reports have suggested an increased incidence of intracerebral hemorrhage (ICH) from cerebral arteriovenous malformation (AVM) rupture during pregnancy. Unfortunately, data on this topic are limited due to small sample size as well as the aggregation of all patients with AVMs, failing to account for the well-described variability in ICH risk based on AVM size, location and morphology.

Methods: Using administrative data on all discharges from hospitals in New York (2005-2014) and Florida (2005-2015), we identified patients with first time pregnancy and delivery. The primary endpoint was first time ICH. We used a case-crossover design in which each woman and her unique AVM served as her own control, by matching the pregnancy period with an equal duration of time 1 year prior. Women were excluded for any treatment (embolization, surgery or radiosurgery) for AVM or first time ICH prior to the control period. Results are presented as OR [95% CI] or median [IQR].

Results: Among 6,273,562 women with first time pregnancy, median age was 28 [23 – 33], 49% were white, 19% were black, and 19% were Hispanic. Of these patients, 1,024 (0.02%) had an AVM and 79 were excluded for ICH or treatment prior to the control period. Women with AVMs were more likely to undergo Caesarian section than those without (58% vs. 36%, $p<0.001$). There were no major differences in vascular risk factors between the women without an AVM versus those with AVM. In unmatched analysis, the incidence of first time ICH in women with AVMs was greater than those without in the control (0.8% vs. 0.001%, $p<0.0001$), pregnancy/delivery (5.1% vs. 0.01%, $p<0.0001$), and 12-week post-partum (1.2% vs 0.01%, $p<0.0001$) periods. In matched case-crossover analysis in women with AVMs, pregnancy was associated with an increased risk (OR 3.4 [1.4 – 8.6]) relative to the control non-pregnant period.

Conclusion: In this large-scale cohort study in which women with AVMs served as their own controls, we account for the variability in ICH risk based on AVM morphology and identify a nearly 350% increased risk of ICH associated with first time pregnancy and delivery. These findings support the need for further work on mechanistic underpinnings as well as a major need for improved methods to abrogate ICH risk.

ABSTRACT

The Impact of Prehospital Whole Blood on Arrival Physiology, Shock, and Transfusion Requirements

NICHOLAS MERUTKA *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Bryan A. Cotton, M.D., Acute Care Surgery
Supported by: Charles E. Wade, PHD, Center for Translation Injury Research
Key Words: Prehospital whole blood transfusion

Introduction: Several US trauma centers have begun incorporating uncrossmatched, group O whole blood into civilian trauma resuscitation. Our hospital has recently added this product to our aeromedical transport services. We hypothesized that patients receiving whole blood in the field would arrive to the emergency department with more improved vital signs, improved lactate and base deficit, and would receive less transfusions following arrival when compared to those patients receiving pre-hospital component transfusions.

Methods: In November 2017, we added low-titer group O whole blood (WB) to each of our helicopters, alongside that of existing RBCs and plasma. We collected information on all trauma patients receiving prehospital uncrossed, emergency release blood products between 11/01/17 and 07/31/18. Patients were divided into those who received any prehospital WB and those who received only RBC and or plasma (COMP). Initial field vital signs, arrival vital signs, arrival laboratory values, and ED and post-ED blood products were captured. Statistical analysis was performed using STATA 12.1. Continuous data are presented as medians (25th-75th IQR) with comparisons performed using Wilcoxon rank-sum. Categorical data are reported as proportions and tested for significance using Fisher's exact test. Following univariate analyses, a multivariate model was created to evaluate post-arrival blood products, controlling injury severity score, field vital signs, and age.

Results: 174 patients met criteria, with 98 receiving prehospital WB and 63 receiving COMP therapy. 116 WB units were transfused in the prehospital setting. Of those receiving WB prehospital, 84 (82%) received 1 U, 14 (12%) received 2U. There was no difference in age, sex, race, or injury severity scores between the two groups. While field pulse was similar (WB: median 117 vs. COMP: 114; p=0.649), WB patients had lower field systolic pressures (median 101 vs. 125; p=0.026) and were more likely to have positive field FAST exam (37% vs. 20%; p=0.053). On arrival, however, WB patients had lower pulse and higher systolic pressures than COMP patients (WB: median 106, 102 vs. COMP: 110, 95; p=0.093, 0.048). There was no difference in arrival base excess and lactate values (WB: median -7, 4.6 vs. COMP: -6,4.0; p=0.093, 0.048). However, WB patients had less ED and post-ED blood transfusions than the COMP group. A multivariate linear regression model demonstrated that field WB was associated with a reduction in ED blood transfusions (corr. coef. -10.8, 95% C.I. -19.0 to -2.5; p=0.018).

Conclusion: Prehospital WB transfusion is associated with improved arrival physiology with

similar degrees of shock compared to COMP treated patients. More importantly, WB patients received less transfusions after arrival than their COMP counterparts.

ABSTRACT

The Morbidity of Survivorship in Congenital Diaphragmatic Hernia

Chase Miller *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Matthew T. Harting, MD, MS; Department of Pediatric Surgery
Supported by: Matthew T. Harting, MD, MS; The University of Texas Health Science Center at the Houston Medical School – Office of the Dean
Key Words: Congenital diaphragmatic hernia, Pulmonary Morbidity, Gastrointestinal Morbidity

Introduction: As advances in care re-define survivorship in congenital diaphragmatic hernia (CDH), particularly among infants with severe CDH, the onus is shifting to long-term management. CDH survivors are frequently challenged by pulmonary, gastrointestinal, neurodevelopmental, and orthopedic morbidities. Our objective was to characterize long-term morbidity in the modern era of care and the association with neonatal risk factors as defined by CDHSG Stage (A-D).

Methods: A single center, retrospective cohort study of survivors born 2011-2017 was performed. Patients with CDH clinic visits between 1-2 years of age and 4-5 years of age were included. Patient demographics, prenatal, and neonatal characteristics were reviewed. The primary outcomes were morbidities at two and five year (±12 months) follow-up. Morbidities included gastrointestinal, pulmonary, neurologic, and orthopedic.

Results: A total of 37 patients were included in the study cohort. The cohort includes 27 patients followed at 2 years and 10 patients were followed at 5 years of age. No patients were followed at both the 2 and 5 year time points. Overall morbidity was 88.9% and 90% at 2 and 5 years respectively. At two years of age, 11(41%) had pulmonary, 9(33%) neurologic, 13(48%) gastrointestinal, or 10(37%) orthopedic morbidities. At five years of age, 8(80%) had pulmonary, 2(20%) neurologic, 3(30%) gastrointestinal, or 4(40%) orthopedic morbidities. For both 2 and 5 years when stratified by defect size χ^2 indicated no difference in observed incidence of morbidity.

Conclusion: Survivors with CDH still face significant morbidity at two and five years. At two years the spectrum of morbidity resembles that of discharge, with a predilection towards gastrointestinal morbidity. Alternatively, at five years the primary source of morbidity is pulmonary. These preliminary data will inform multi-center collaboration in long-term CDH data collection.

ABSTRACT

Comparison of Whole Blood and Component Therapy Effects on Platelet Function in Trauma Patients

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Sponsored by: Charles E. Wade, PhD, Center for Translation Injury Research
Supported by: The William Stamps Farish Fund and the Howell Family Foundation
Key Words: Whole blood, component therapy, blood transfusions, trauma, platelet function

Whole blood was introduced as a transfusion option on Memorial Hermann's Life Flight helicopters in November of 2017. In comparison to component therapy, whole blood is associated with smaller total transfusion volumes in patients not suffering from traumatic brain injuries. Other benefits of whole blood over component therapy include improvements in platelet function, thrombin generation, clot strength, and procoagulant factor levels. An important distinguishing factor between whole blood and component therapy transfusions on Life Flight helicopters is the lack of platelets in component therapy due to the logistical complications of bringing platelets into the field. With this unique comparison, the effects of early administration of platelets on hemostatic potentials can be further explored. We hypothesize that the use of whole blood in place of component therapy in pre-hospital trauma patients improves platelet count and function. To test this, a retrospective analysis of prospective collected data was conducted between two populations: trauma patients on Life Flight who received whole blood and those who received component therapy. The two populations will be matched for based on factors associated with poor outcome such as ISS, base excess, GCS, and pH. The main parameters measured were platelet count and platelet function based on thromboelastography (mA) and Multiplate analyzer (ADP, RISTO, ASPI, TRAP). Current data shows that there are significantly higher hemoglobin levels in whole blood transfused patients. There was no significant difference in platelet function assessed by Multiplate or thromboelastography between the two groups, however, platelet count was notably increased. Platelet function has been shown to significantly reduce as the shelf life of the blood product is prolonged. This is an area for further investigation as the study moves forward.

ABSTRACT

Distal MCL Lesions: Improving Imaging Recognition and Patient Outcomes

WILLIAM MORRIS *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Manickam Kumaravel, MD, Department of Diagnostic & Interventional Imaging
Supported by: Manickam Kumaravel, MD, Department of Diagnostic & Interventional Imaging; McGovern Medical School at UTHealth – Office of the Dean
Key Words: Medial collateral ligament, distal, Stener lesion

Introduction: The medial collateral ligament (MCL) is one of the most frequently injured ligaments of the knee. MCL tears are typically treated nonoperatively, as there is typically no indication for surgical intervention. While most lesions are located proximally (near the femoral attachment) or at the midsubstance of the ligament, surgery is often considered for distally-situated lesions due to concern for Stener-like lesion. Stener-like MCL tears involve the displacement of the ruptured MCL fibers over the pes anserinus tendons. This displacement prevents the ligament from contacting its distal attachment point, thereby preventing proper healing.

Methods: A retrospective analysis was performed on a cohort of 32 patients who were diagnosed with a sprain of the MCL and underwent surgical repair in 2016 with the UTHealth Department of Orthopedic Surgery. Basic demographic data (age, gender, BMI) and injury information (mechanism, side, history of same-sided injuries) were collected from the patients' charts. Additional data including the injury grade, location, and associated injuries (ACL, PCL, quadriceps tendon, patellar tendon, pes anserinus, medial meniscus, lateral meniscus, chondral) were gathered from both the MRI reports and the operative reports for comparison.

Results: Of the 32 patients in the cohort, 2 were omitted as the location of the lesion was unknown. Among the remaining 30 patients, 27 (90%) were male, and 3 (10%) were female. The median age was 22.9 (14-51), and the median BMI was 27.4 (19.4-45.9). The cohort was subdivided into 2 groups: distal MCL lesions (n = 15) and non-distal MCL lesions (n = 15). ACL injuries were more highly associated with non-distal lesions (87%) than distal lesions (47%), p-value = 0.05. PCL injuries were associated with 33% of distal lesions and 20% of non-distal lesions. LCL injuries were associated with 7% of distal lesions and 20% of non-distal lesions. Medial meniscal injuries were associated with 40% of distal lesions and 20% of non-distal lesions. Lateral meniscal injuries were associated with 40% of distal lesions and 73% of non-distal lesions. Chondral injuries were associated with 13% of distal lesions and 33% of non-distal lesions. The p-value was only significant for associated ACL injury. There were no patients with associated quadriceps tendon, patellar tendon, or pes anserinus injuries.

Conclusion: This study provides a good first step toward improving our ability to diagnose distal MCL lesions. Our results indicate that there may be differences in severity as well as types of associated injuries. However, a larger population will be required to yield significant results.

ABSTRACT

Outcomes of Robotic Revisional as Opposed to Primary Roux-en-y Gastric Bypass: Evaluating a Potential Role of Robotic Assisted Laparoscopic Techniques

THOMAS NGUYEN *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Shinil K. Shah, DO, Minimally Invasive and Elective General Surgery
Supported by: Shinil K. Shah, DO, Minimally Invasive and Elective General Surgery
Key Words: Robotic-Assisted, Roux-en-Y Gastric Bypass, Revision

Background: Weight loss surgery is the most effective treatment for morbid obesity and associated comorbidities. Revisional weight loss surgery, which may be necessary to treat weight regain as well as complications of previous bariatric surgery, is traditionally associated with increased complication rates and conversion to open operations. The data regarding robotic assisted laparoscopic weight loss surgery suggests increased operative times and costs without a consistent improvement in outcomes. We hypothesize that robotic assisted techniques will allow for equivalent rate of major complications in revisional as compared to primary laparoscopic roux-en-y gastric bypass (RYGB).

Methods: We reviewed our single institution experience of all patients undergoing robotic assisted primary or revisional RYGB from 2009-2017. Specific variables analyzed included demographic data, operative time, operative conversions, hospital length of stay, as well as post operative weight loss and measures of morbidity. Statistical analysis was performed using the appropriate parametric or non-parametric analysis (continuous data) or Pearson's Chi-squared test or Fisher's exact test (categorical data).

Results: There were 710 patients identified who underwent robotic assisted RYGB (484 primary, 226 revisional). Revisions were noted from previous adjustable gastric bands (120), fixed gastric bands (11), vertical banded gastroplasty (39), mini-gastric bypass (1), gastric bypass (22), transoral gastroplasty (4), fundoplication (7), and sleeve gastrectomy (22). Patients in the revisional RYGB group were more likely to be female (87.6 vs 77.3%, $p=0.001$), were older (50.9 vs 46.5 years, $p<0.001$), had lower body mass index (BMI) (42.1 vs 46.3 kg/m^2, $p<0.001$), and had longer operative times (203.8 vs 176.1 minutes, $p<0.001$). Average duration of follow up was shorter in the revisional group (13.8 vs 19.8 months, $p<0.001$). Strictures were more common in the revisional group (9 vs 7 patients, $p=0.04$). Other major complications, including leaks and operative conversions were not significantly different.

Conclusions: Although associated with longer operative times and higher rates of anastomotic stricture, robotic assisted RYGB have similar perioperative and post-operative outcomes as compared to primary RYGB. Whether this is secondary to potential advantages afforded by the robotic platform deserves further study.

ABSTRACT

An Evaluation of Household Chemicals and Risk of Kidney Failure

TYLER NOVY *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Donald A. Molony, MD, Department of Internal Medicine
Supported by: Donald A. Molony, MD, Department of Internal Medicine; McGovern Medical School—Office of The Dean
Key Words: Kidney Failure, End Stage Renal Disease, Pesticides, Chemical Exposure

Introduction: The medical causes of End Stage Renal Disease (ESRD) (diabetes, hypertension, glomerulonephritis, etc.) have been well documented. However, there are patients living with ESRD without a known cause for their kidney failure. Occupational and environmental exposures could provide an explanation for relatively healthy people who develop idiopathic kidney failure. Animal studies have demonstrated an association between chlorinated hydrocarbon pesticides and the induction of cell injury in nephron tubular cells. Previous research conducted by Dr. Donald Molony has demonstrated that there may be an increased risk of developing kidney failure for individuals who use insecticides in the home more frequently. However, previous work on this association was limited by sample size and a lack of follow-up.

Hypothesis: We hypothesize that there will be a significant increase in the risk of developing kidney failure when an individual has been chronically exposed to insecticides in the home. The results of this study could reveal another risk factor for developing kidney failure and help guide public health interventions that work to reduce the harmful impact of ESRD.

Methods: This project is in the form of a case-control study that compares the usage of insecticides in the home between Houston residents who are living with kidney failure and those who are not living with kidney failure. Participant data was collected through a survey that queried individuals about their general health, presence or absence of kidney problems, and household use of common chemicals (including insecticides). Demographic and current zip code of residence information was also collected to reduce the level of confounding between the kidney failure and control group. One survey instrument was created specifically for patients who were currently receiving dialysis for kidney failure. This survey was designed to be distributed to and completed by at least 100 DaVita dialysis patients in the Houston area. Another survey was created to be distributed to at least 200 individuals who were not currently receiving dialysis. The 200 individuals were to be recruited through community organizations that shared similar zip codes with the patients who were on dialysis.

Results: At the time of writing this abstract, 29 individuals on dialysis have completed the survey. Recruitment of more dialysis patients has been delayed pending permission from DaVita to survey additional patients. Recruitment of our control group will commence once we have the zip codes in Houston the dialysis patients are residing in so that we can match for area of residence when conducting data analysis. From general analysis of the existing data, 16 out of the 29 dialysis patients claim to spot spray insecticides at least every week in their homes.

ABSTRACT

Characteristics of EMS intubation in the ESO cohort

TRACY NWANNE *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Henry E. Wang, MD, MPH, MS, Emergency Medicine
Supported by: Henry E. Wang, MD, MPH, MS, Emergency Medicine
Key Words: Advanced airway management, intubation, EMS

Objective: Despite its important role in care in out-of-hospital critical care, there have been few large-scale descriptions of the epidemiology of Emergency Medical Services (EMS) advanced airway management (AAM) and the variations in care with different patient subsets. We sought to characterize AAM performance in a national cohort of EMS agencies.

Methods: We used data from ESO solutions, a national EMS electronic health record system. We analyzed EMS emergency patient encounters during 2006-2015 with attempted AAM. We categorized AAM techniques as conventional endotracheal intubation (cETI - orotracheal, nasotracheal, video laryngoscopy, retrograde), drug-facilitated ETI (sedation-assisted ETI or DFI - rapid-sequence), supraglottic airway (SGA - King LT, Combitube, LMA, SALT), and cricothyroidotomy (needle and open). EMS providers reported successful AAM for all patient encounters. We analyzed the data using descriptive statistics, determining the incidence and clinical characteristics of AAM cases. We determined AAM success rates each for each AAM technique, stratifying by the subsets cardiac arrest, medical non-arrest, trauma, and pediatrics (age <18 years).

Results: Of the 7,431,450 emergency responses, AAM occurred in 61,793 patients among 552 EMS agencies representing 38 US states. AAM patients in this cohort were older (mean age 61±20 years), male (60.2%) and white (69.5%). The most common clinical conditions associated with AAM cases were cardiac arrest (63.6%), respiratory emergencies (10.7%), trauma/electrical injuries (8.4%), and altered mental status (7.9%). Overall AAM success were 89.0% (95% CI: 88.7-89.2%) across all patients. AAM success rates varied by patient subset: cardiac arrest n=38,063, 91.7% (91.4-91.9%); medical non-arrest n=19,138, 84.8% (84.3-85.3%); trauma n=7,158, 86.1% (85.32-86.93%); pediatric n=1,925, 77.6% (75.7-79.5%). When stratified by patient subset, AAM success rates varied with intubation technique: SGA n= 9,993 90.2% (89.6-90.7%); RSI n= 7,229, 89.7% (89.0-90.4%); SAI n=3,095, 79.2% (77.7-80.6%), cETI n=41,261, 77.1% (76.6-77.5%); cricothyroidotomy n=215, 18.6% (13.6-24.5%).

CONCLUSIONS: AAM success rates varied by airway technique and patient subset. These results may guide EMS AAM practices.

Medical Student

Cardiopulmonary Exercise Testing as a Risk Assessment Strategy in Cancer Patients Undergoing Intra-abdominal Surgery

COLLEEN A ONEILL *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Anh Q. Dang MD, Department of Anesthesiology and Perioperative Medicine
Supported by: University of Texas M.D. Anderson Cancer Center, Houston, Texas
Key Words: Preoperative screening, abdominal surgery, cardiopulmonary exercise testing

The intraoperative and postoperative periods of major intra-abdominal surgery require metabolic demands on cancer patients that greatly exceed those at rest. Current preoperative screening tools such as pulmonary function tests (PFTs), echocardiograms, and stress tests are limited in that they only test a single organ system. The current risk indices, including the American Society of Anesthesiologists (ASA) classification are static and based only on preoperative morbidities. Cardiopulmonary exercise testing (CPET) utilizes breath-by-breath gas exchange analysis to evaluate the integrated response of the body to physiologic stress. By measuring the intake of O2 and output of CO2 during exercise, CPET quantifies the patient's anaerobic threshold (AT) as well as peak oxygen consumption (VO2). AT and VO2 may be used to assess fitness, with lower values indicative of compromised exercise capacity. The objective of this study is to determine whether CPET is a valid and objective tool in assessing morbidity and mortality in the postoperative period for this patient population. By identifying high risk individuals, other treatment options may be presented or the course of treatment may be modified to allow for the most optimal outcome.

Forty-nine patients undergoing a major intra-abdominal procedure were identified. Each patient underwent CPET analysis prior to surgery to determine physiologic capacity. Following surgery, patients were monitored for morbidity and mortality prospectively for 30 days. A retrospective chart review scored postoperative complications over the next 30 days. Three patients were excluded due to suboptimal CPETs. Statistical analyses of the remaining 46 patients' CPET results and post-operative risk index scores were performed using an unpaired t-test. We utilized the Clavien-Dindo Classification system and the Postoperative Morbidity Survey (POMS) to rank the complications in a reproducible and objective manner. The POMS was used to measure events that occurred on postoperative day 5. Using the Clavien-Dindo, the rate of major complications was 24%. Using the POMS, the complication rate was 39%. With regards to CPET parameters, there were no significant differences between patients who experienced a major complication and those who did not. CPET analysis evaluates the integrated response of the cardiac and pulmonary systems; therefore, it is a better determinant of fitness for surgery since it simulates the hypermetabolic state experienced during the postoperative period. Because an imbalance between energy supply and demand may lead to postoperative morbidity and mortality, CPET may be a useful tool to risk stratify patients preoperatively. Limitations of this study include a small sample size and possible technical errors. Confounders of this study include the variability between patients in terms of their type of cancer, extent of disease, and exposure to neoadjuvant chemotherapy or radiation. Furthermore, the surgeries included in this study were not homogenous, differing in the level of invasiveness and length of operation. Previous studies have proven the effectiveness of CPET parameters in providing objective and reliable predictors of all-cause postoperative morbidity.

Due to our negative findings, further investigation should be made to account for the confounding factors noted in our study.

ABSTRACT

Cryo-Stent: Preventing Severe Radiation-Induced Oral Mucositis via Tongue Displacement and Cooling

STEPHEN PALASI *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dr. Eugene Koay, MD, PhD, Department of Radiation Oncology
Supported by: MD Anderson Summer Research Program
Key Words: Radiation, Mucositis, 3D Printing, Cooling

Radiation-induced oral mucositis (RIOM) is a common complication for head and neck cancer patients receiving radiation therapy. Symptoms include painful swallowing, impaired speech, increased opportunistic infections, and inability to provide oral alimentation. Multiple studies have demonstrated that intraoral stents provide reductions in mucositis severity during head and neck radiotherapy via tongue displacement and tissue immobilization. Newer techniques have improved the efficiency of this process by 3d printing customized stents using computer software modelling.

To improve upon the model of a 3d printed stent, the Cryo-Stent utilizes a hollow frame which allows for injection of cooling fluid. The Cryo-Stent aims to induce vasoconstriction via cooling the tongue and buccal mucosa to further reduce the effects of severe radiation-induced oral mucositis. Temperature analysis experiments were carried out to determine the cooling capabilities of the Cryo-Stent on the oral mucosa. Based on the analysis, the Cryo-Stent achieved an average intraoral temperature reduction of 10.0 F over 18 minutes. An analysis of covariance (ANCOVA) indicates a significant difference in oral temperature between pre-cooled stents with fluid versus without fluid. Further studies are being done for reproducibility of results. Additional experimental considerations include assessment for dentition hypersensitivity, reactionary perfusion, and altering cooling fluid composition.

The Cryo-Stent utilizes a two-pronged approach to reducing the incidence of severe mucositis. By displacing the tongue and reducing oral temperature, the Cryo-Stent has potential to reduce complications of head and neck cancer patients receiving radiation therapy.

ABSTRACT

Maternal Vaccination Rates Improve with Physician Advocacy and Patient Education

TAYLER PARKER *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Kuojen Tsao, MD
Supported by: Kuojen Tsao, MD
Key Words: Maternal Tdap Vaccinations

Background: To prevent pertussis infection among infants, the Centers of Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) recommends maternal pertussis vaccination (Tdap) between 27 and 36 weeks gestation. Women who are not vaccinated during pregnancy should receive postpartum immunization. Despite these recommendations, maternal vaccination rates in the United States remain suboptimal; Tdap rates are only 51-56%.

Methods: We interviewed 200 postpartum patients who delivered between May-July 2018 using a qualitative, semi-structured survey. Women who were less than 18 years old, delivered nonviable babies, or did not speak English or Spanish were excluded. Tdap vaccination was offered to eligible patients had not already received it. If the patient elected to receive the vaccine, the bedside nurse was notified. We then performed prospective chart review to determine if women were vaccinated prior to discharge and to audit compliance with the electronic medical record (EMR) vaccination screening tool.

Results: 200 subjects were interviewed for vaccination assessment. Most subjects were English-speaking (92.5%), non-Hispanic (64%), and married or living with their partner (65%). Level of education varied widely: 10% had a graduate or professional degree, 30% had an associate or bachelor's degree, 21% had completed some college, and 36% had a 12th grade education or lower. 62% had already received a Tdap during their pregnancy prior to time of interview on day of discharge (n = 124). Top reasons for vaccination included to protect the baby (n = 61), protect mom and baby, and doctor's recommendation. Of the patients who did not receive Tdap prior to admission, 45% said it was because the vaccine was not offered to them (n = 34). Of these patients, 60% received Tdap prior to discharge (n= 45). Of women who did not receive Tdap prior to discharge (n=31), 61% did not receive it because they declined. In 32%, the vaccine was ordered but never administered. However, most of these women had expressed reasons why they did not want the vaccine, therefore it is likely that the patient refused to let the nurse administer the vaccine. In these patients, top reason for not vaccinating was safety concerns.

Conclusions: Most women who do not receive the recommended vaccines during pregnancy were not offered the vaccine by their OB. Most vaccinated patients received the shot from their OB's office (81%) further signifying the importance of vaccine advocation and availability by physicians. In 15% of cases (n = 30) the EMR vaccination screening tool recording was

inconsistent with what the patient said, indicating that improvements in screening tool compliance and patient communication may be needed. Addressing patient's safety concerns and educating moms on the benefits for the baby could improve final immunization rates.

ABSTRACT

Potential risk factors that may determine risk of developing breast cancer-related lymphedema

KAY T. PHAM *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Melissa B. Aldrich, MBA, PhD, UT Health Center for Molecular Imaging
Supported by: Lymphatic and systemic immune changes in post-radiation lymphedema: NIH R01 CA201487
Key Words: Breast cancer-related lymphedema, NIRFLI, indocyanine green

Introduction: Breast cancer-related lymphedema (BCRL) is a disfiguring, debilitating disease afflicting up to 40% of breast cancer survivors. Cancer surgery and radiation treatment are commonly blamed for causing LE. In an ongoing study, 100 breast cancer patients at MD Anderson Cancer Center (MDACC) receiving axillary lymph node dissection (ALND) and radiation treatment are being surveilled for lymphedema (LE) appearance for two years post-cancer treatment. Presently, 25 patients have been examined, and surprisingly, many exhibit abnormal lymphatic vessel anatomy and pumping prior to surgery. These findings suggest pre-existing risk factors may cause lymphatic stasis leading to LE.
Methods: A group of 25 BCRL subjects at MDACC were studied. Prior to receiving neoadjuvant chemotherapy, the following potential risk factors were recorded: BMI, hormone status, Her2Neu status, number of lymph nodes (LNs) involved, number of LNs removed, tumor volume, tumor classification, and nodal classification. The subjects underwent near infrared fluorescence lymphatic imaging (NIRFLI) of their arms using indocyanine green dye. LE status was assigned to each subject depending on multiple characteristics indicating abnormal lymphatic vasculature including pulse frequency, tortuosity index, and extravascular dye from dermal backflow. Logistical regression and Chi squared test were performed to determine how likely the development of LE would be dependent on any of the potential risk factors listed previously. Odds ratios were calculated to quantify strength of association.
Results: None of the covariates were significant due to low sample size. However, the odds ratios described to us the following: 1) increasing BMI by 1 unit decreased the odds of development of LE by 14%, 2) increasing the number of LNs involved by 1 increased the odds of developing LE by 14%, 3) the odds of developing LE decreased by 65% if the patient was hormone positive, and increased by 50% if the patient was Her2Neu positive, and 4) the odds of developing LE increased by 52% and 200% if the cancer was classified as early (T1 or T2) and late (T3 or T4b), respectively.
Conclusion: Our results to this date are inconclusive, as no potential risk factor significantly increased the probability of developing BCRL. However, the odds ratios suggest that the following may be possible: 1) BMI is not a reliable indicator of LE development, 2) tumor presence in LNs may impair lymphatic transport capacity, 3) positive Her2Neu status, which is strongly associated with increased disease recurrence and poor prognosis, reinforces the idea that more severe cancers can adversely affect the lymphatics, and 4) primary tumor classification may be a better predictor of LE risk compared to the other variables examined. Most of the subjects we observed displayed dysfunctional lymphatics prior to surgery, and these

preliminary results imply that pre-existing variables, not cancer surgery or radiation, determine whether the subjects develop LE.

ABSTRACT

Human Bursa-Derived Mesenchymal Stem Cells as a Therapy in Arthroscopic Rotator Cuff Repair

AUSTIN PICKRELL *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Polina Matre, PhD, Department of Orthopaedic Surgery
Supported by: Johnny Huard, PhD, Department of Orthopaedic Surgery
Key Words: Human Bursa-Derived Stem Cells, Rotator Cuff Repair, Tenogenesis

BACKGROUND: Rotator cuff injuries are one of the most commonly encountered tissue pathologies within orthopaedic medicine. Despite advances in surgical techniques, rotator cuff repair failure rates are still high. Previous studies have shown that sub-acromial bursa, which is usually discarded during surgery, contains large amounts of mesenchymal stem cells. Our project seeks to develop a single-step, intra-operative technique of autologous stem cell delivery to the site of arthroscopic rotator cuff repair. To achieve this, we seek to confirm the identity, viability, and multipotency of the human bursa-derived stem cells (hBDSCs) collected.
METHODS: Sub-acromial bursa tissue was collected from 10 patients undergoing shoulder arthroscopic repair surgery. Cells were cultured in DMEM supplemented with 10% FBS. Chondrogenic (StemPro™ Chondrogenesis Differentiation Kit, Gibco), adipogenic (DMEM supplemented with 10% FBS, 0.5 mM methylisobutylxanthine, 1 µM dexamethasone and 10 µg/mL insulin) and osteogenic (DMEM, 10% FBS, 50 µg/ml ascorbic acid, 10 mM β-glycerophosphate, 10 nM dexamethasone) induction media were used for the respective differentiation assays. After 7 days, the monolayer assays were stained with Oil Red O, Alcian Blue, and Alkaline Phosphatase to visualize adipogenesis, chondrogenesis and osteogenesis respectively. TRIzol RNA Isolation Reagent was used for RNA isolation. The Bio-Rad reagents iScript and SYBR Green Supermix were used for RT-PCR. Genes were normalized to 18S ribosomal RNA and Actin B (β-actin). Four-week pellet culture was performed using chondrogenic media and stained with Alcian Blue/Nuclear Fast Red. Additionally, tenogenic assays were run using media supplemented with 100 ng/ml BMP-12 and 50 µg/ml Ascorbic Acid for 7 and 14 days for RT-PCR and tenomodulin/scleraxis immunostaining respectively.
RESULTS: Flow Cytometry showed expression of putative MSCs surface marker CD90, and negative expression of CD31, CD34, CD45, and CD146. Monolayer staining showed positive staining for adipogenesis chondrogenesis and osteogenesis. Additionally, RT-PCR showed a significant increase in gene-expression for Adipogenic (*AdipoQ*, *FABP4*, and *PPARG*), Chondrogenic (*ACAN*, *Col2A1*, and *SOX5*) and Osteogenic (*Osteocalcin*, *OSX*, and *RUNX2*) markers. Pellet culture showed significant chondrogenesis with positive Alcian Blue staining with appropriate counter stain. Tenogenic RT-PCR data showed a significant increase in the tenogenic marker *THBS4*. Immunoglobulin staining was positive for the tenogenic markers tenomodulin and scleraxis. These results together indicate the BDSCs are multipotent cells with the ability to differentiate into fat, cartilage, and bone cells and possess tenogenic potential.
CONCLUSION: Our findings suggest that the sub-acromial bursa tissue collected contains mesenchymal stem cells and that these cells can differentiate into adipocytes, chondrocytes,

osteocytes, and tenocytes. The work presented is essential to establishing novel protocols for BDSC isolation, expansion, and differentiation toward a tendon lineage for the development of novel stem cell therapies aimed at improving rotator cuff tear healing.

ABSTRACT

B-1a Cells Lose Proliferation & Self-Renewal Ability in Bmi1 KO Mice

COLTON REEH *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Momoko Yoshimoto, MD, PhD, Center for Stem Cell & Regenerative Medicine
Supported by: Momoko Yoshimoto, MD, PhD, Michihiro Kobayashi MD, PhD,
Key Words: B-1a, self-renewal, proliferation, Bmi1

Background: Research in the development of early mouse embryos has indicated that various progenitors arise before hematopoietic stem cells (HSC's). Of interest to us is the production of B-1a lymphocytes from these progenitors which develop primarily in the embryonic to neonatal period in the fetal liver and are important contributors to innate-like immunity in the body. Due to their derivation from the fetal liver, it has been established these cells possess the ability to maintain lifelong self-renewal, much like HSC's. Previous research established the importance of Bmi1 in maintaining stem cell proliferation and self-renewal ability. This, along with our preliminary data that B-1a cell number is reduced in Bmi1 KO mice, leads us to hypothesize that Bmi1 also plays an important role in the self-renewal ability of B-1a cells. Examining the effect of Bmi1 deletion on self-renewal ability of B-1a cells will allows us to resolve a long-lasting question in this field.

Methods: To test our hypothesis, we examined B-1a cell-proliferation ability upon antigen stimulation and self-renewal ability by competitive cell transfer assay using Bmi1 KO mice. The Cre-LoxP system was used in conjunction with CD19 to specifically target B-cells for Bmi1 gene deletion. 7-12 month-old mice were used in this study. The following mouse genotypes were used $CD19^{cre/WT}$:$Bmi1^{F/F}$(wildtype), $CD19cre^{KI/+}$:$Bmi1^{+/+}$(single heterozygote), $CD19cre^{KI/+}$:$Bmi1^{+/F}$(double heterozygote), and $CD19cre^{KI/+}$:$Bmi1^{F/F}$ (knockout). Peritoneal cells were collected by injecting PBS and each B cell subset was sorted using BD FACS Aria II. For the in-vitro proliferation experiment, 3×10^4 B-1a cells were cultured in IMDM with 10% FBS and 10ng/mL IL5, and with or without 5µg/ml R-848 (TLR7/8 agonist) (Resiquimod). After 48 hours incubation at 37°C, cells were counted with trypan blue as well as performing an apoptosis & cell death assay by incorporating the use of PI-Annexin V staining. For the self-renewal experiment, an in-vivo competitive cell transplant study was performed in which 1×10^5 donor B-1a cells from each mouse genotype were injected with 1×10^5 competitor B-1a cells from BoyJ mice into the peritoneal cavity of immunodeficient NSG mice. After 1-month, peritoneal cells were collected from each of the NSG recipient mice and flow cytometry was performed to measure the repopulating ability of each of the four B-cell genotypes against BoyJ.

Results & Conclusion: We first confirmed that the deletion of Bmi1 in B cell lineage led to significant cell count reduction of peritoneal B-1a ($p<0.01$), B-1b ($p<0.01$), and B2 ($p<0.01$) cells**.** Bmi1 KO B-1a cells showed decreased proliferation upon stimulation with R-848 ($p=0.0483$). Cell apoptosis and cell death assays revealed increased apoptosis and cell death in KO B-1a cells compared to controls ($p<0.05$ and $p<0.01$, respectively). Competitive cell transfer assay demonstrated reduced self-renewal ability in KO B-1a cells. Taken together, these results

suggest that Bmi1 is required for cell proliferation and self-renewal ability in peritoneal B-1a cells.

Future Studies: Future studies will focus on RNA sequencing to determine specific Bmi1 targets involved in the self-renewal mechanism.

ABSTRACT

The Comparison of Gram-Positive and Gram-Negative Bacterial Infections in Nosocomial Meningitis

THOMAS ALEX ROGERS *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Rodrigo Hasbun, MD MPH, Department of Internal Medicine
Supported by: Grant A Starr Foundation
Key Words: Nosocomial meningitis, gram stain, cerebrospinal fluid, outcome, lumbar puncture

Nosocomial illness is a well-recognized source of significant morbidity and mortality, especially in the neurosurgical setting. There is, however, limited information comparing the classes of bacterial nosocomial meningitis (NM) to one another in diagnostic and outcome statistical analysis. Our study is a retrospective analysis of patient charts from December 2003 until January 2016 from patients within the Memorial Hermann Hospital system in Houston, Texas. We found that among 272 cases of meningitis using the NHSN/CDC definition of NM in adults, only 91 of them grew out at least one bacterium on a cerebrospinal fluid (CSF) culture. Of these culture positive cases, 42 (45.1%) of the cultures grew out a gram-positive organism and 50 (54.9%) grew out a gram-negative organism. A statistically significant difference was noted most commonly in the differences between the CSF chemistries of the patients of gram-positive and gram-negative NM. There was no statistically significant difference in adverse outcomes for the patients of either group.

ABSTRACT

Assessing the Quality of Life in Infants with Deformational Plagiocephaly

JACOB RYALL *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Matthew R. Greives, MD, Department of Pediatric Surgery
Key Words: Deformational Plagiocephaly, Quality of Life

Background: With the advent of the Back-To-Sleep campaign, the incidence of sudden infant death syndrome has drastically decreased. However, this prolonged supine positioning has increased the incidence of posterior deformational plagiocephaly in the infant population. The mainstay of treatment for this is helmet therapy to reshape the infant's skull. Very little is known about the quality of life for the parents and infants before and after the therapy. Our study focused on evaluating the impact of helmet therapy on the quality of life of infants and caregivers.

Methods: An IRB approved prospective analysis was performed for patients with deformational plagiocephaly entering helmet therapy. The Infant Toddler Quality of Life Short Form 47 (ITQOL-SF47) questionnaire was administered to caregivers in clinic to evaluate the baseline level of impairment in the daily functioning in infants with posterior deformational plagiocephaly (pre-helmet). Patients were identified and consented during their initial consult in the clinic. Following completion of helmet therapy (3-6 months later), a second ITQOL-SF47 was administered to assess the changes in impairment of daily functioning in the infants (post-helmet). Normative data was obtained from a prior study in order obtain a data sample from a healthy population for which we could compare to our population. Results were compiled into a database, converted into raw scores, and compared using unpaired t-tests to evaluate the impact of deformational plagiocephaly on infant and caregiver quality of life across seven variables.

Results: The pre-helmet plagiocephaly group scored significantly lower than their healthy peers in the following categories: Physical Functioning, Bodily Pain, General Health Perceptions, Parental Emotional Impact, and Parental Time Impact. There was no significant difference between pre-helmet plagiocephaly children and healthy children with respect to Growth and Development. Interestingly, the pre-helmet plagiocephaly group scored significantly better than healthy children with respect to Temperament and Moods. The scores from the pre-helmet evaluations were then compared to post-helmet evaluations to assess changes in quality of life brought about through helmet therapy. Across eight categories there was no significant difference detected between pre and post-helmet therapy quality of life scores. Average quality of life scores increased in all but one category (Growth and Development).

Conclusion: Deformational plagiocephaly has been long considered to have a purely aesthetic impact on affected individuals. Our results demonstrate that this understanding is inaccurate as infants with plagiocephaly and their caregivers were found to have significantly decreased quality of life when compared to their healthy counterparts. This finding is critical as it reframes our understanding of deformational plagiocephaly and changes the conversation regarding the accessibility and need for appropriate therapies in these individuals. In addition, helmet therapy

was shown to have no negative impact on infant quality of life underscoring this as an appropriate therapeutic option for this condition.

ABSTRACT

Sex Differences in BAV Surgeries and Outcomes

TAHA A. SAHRAPOUR *McGovern Medical School at UTHealth* *Class of 2021*

Sponsor: Siddharth K. Prakash, M.D, Ph.D., Department of Internal Medicine
Key Words: Bicuspid Aortic Valve, Sex, Surgery

Background: Bicuspid aortic valve (BAV) is the most common adult congenital heart defect, with an estimated prevalence of 1-2% in the general population. BAV is also 3 times more prevalent in males than females. Surgical interventions for valvular and aortic disease are frequent in patients with BAV. We hypothesize that sex is a major predictor of BAV presentation and outcomes. Thus, the purpose of my study was to compare the demographic characteristics and surgical outcomes of males and females with BAV.

Methods: I identified eligible cases from the UTHealth Bicuspid Aortic Valve Research Registry at McGovern Medical school. The principal inclusion criteria were confirmation of BAV diagnosis in operative or echocardiogram reports and at least one documented cardiothoracic surgery. I distinguished early onset BAV (EBAV) by the development of significant BAV-related complications (valve or aortic surgery, enlarging aneurysm or aortic valve stenosis or regurgitation) prior to age 30. 126 registry participants (96 male, 30 female) met the inclusion criteria and were included in my analysis. Of these, I identified 28 (20 male, 8 female) as EBAV cases. I abstracted relevant clinical data from medical records, including medical history, operative reports, discharge summaries and echocardiograms, into a customized REDCap database. Between sex comparisons were analyzed using t-tests or their non-parametric equivalents as appropriate.

Results: The mean age of males (48±16 years) and females (46±18 years) at first cardiac surgery was not significantly different. The principal indications for surgery (aortic valve regurgitation and thoracic aortic aneurysm) were evenly distributed between males and females. I discovered that the mean length of hospitalization after the index operation was significantly longer for males than for females in both the BAV (11.8 days vs 9.4 days) and EBAV (12.2 days vs 7.8 days) cohorts. I did not identify significant differences in major adverse post-operative events (renal failure, stroke, atrial fibrillation, infection, pleural/pericardial effusion, DVT/PE, respiratory failure and death) between males and females. EBAV females were more likely to undergo a second cardiothoracic procedure than males (OR=1.4, 95%CI 1.1-1.8). The primary indication for second procedures was elective ascending aortic intervention. The prevalence of coarctation repair in the primary surgical intervention was higher in EBAV females than in males (OR=3.1, 95% CI 2.8-3.4).

Conclusion: I found that females with BAV present with a greater burden of congenital cardiac defects, such as coarctation, and require more frequent follow-up cardiothoracic procedures. In contrast, the average length of hospitalization after the first operation was significantly longer in males. These observations may have important implications for clinical management of BAV patients and merit additional investigation in larger cohorts.

ABSTRACT

Characteristics of Patient with less than 20% TBSA Admitted to the Burn Unit for Under a Day

JOAQUIN SANTOY IV *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Charles E. Wade, PhD, Department of Surgery
Supported by: Dunn Foundation and the James H. "Red" Duke Distinguish Professor Chair
Key Words: Burns, length of stay

Introduction: Patients with burns less than 20% total body surface area (TBSA) make up the majority of burn admissions. Yet there is minimal data in the literature pertaining to the characteristics of these patients and their individual contributions to length of hospital stay (LOS). The purpose of this study was to analyze and identify the characteristics of patients with small burns with a hospital length of stay of one day.
Methods: This was a retrospective cohort study of patients (> 15 years) with less than 20% TBSA burns admitted to Memorial Hermann Dunn Burn Center over three years (2015-2017). Patients were stratified into three cohorts by LOS = 1, LOS ≥ 2 who did not undergo an operative (OR) procedure, and LOS ≥ 2 days who underwent OR procedure(s) after the exclusion of patients with road rash, sun burns, Steven-Johnson syndrome, and expired patients that had LOS of 1 day. The following variables were recorded and analyzed: age, TBSA, gender, race, etiology of injury, mechanism of injury, burn location, length of hospital stay, mortality, incidence of work-related injury and inhalation injury, comorbidities such as hypertension, diabetes mellitus, seizure disorders, and psychiatric problems. The main outcome under study was length of stay. Wilcoxon rank sum tests, Fishers' exact test, and multivariate logistic regression using a cumulative logit model for ordinal responses were used to analyze the association of covariates and LOS.
Results: During the study period, 917 of 1003 (91.4%) patients had small burns with less than 20% TBSA. Patients were typically male (n=665, 73%), non-Hispanic whites (n=363, 40%) and had a median age of 41 years (IQR 18, 98). Out of 917 patients, 255 (28%) had a LOS of 1 day, 338 (37%) had a LOS ≥ 2 days without an OR procedure, and 324 (35%) had a LOS ≥ 2 days with OR procedure. The median length of stay for LOS ≥ 2 days without and with OR procedure was 4 days (IQR 2, 7) and 11 days (IQR 8, 17), respectively. There were no differences in gender, BMI, or race between cohorts. Patients with LOS = 1 had a smaller percent TBSA (2.5 (0, 15.5) vs. 5.0 (0.1, 19.0) and 5.0 (0.05, 19.0), p <0.001), as well as lower incidences of inhalation injury (1.5 vs 5% and 3%, p=0.007) and psychiatric illness (14 % vs. 25% and 29%, p <0.001). Mechanism of injury was different, with thermal injuries being lower in LOS = 1 (86% vs. 94% and 84%, p<0.001). Several locations of burn injury (p<0.001) by length of hospital stay and mechanism of injury were different (Flame vs. other ratio = 2.01, CI 95% [1.43 -2.82], p=0.011) between the three cohorts. Comorbidities with the strongest relationship for length of hospital stay were diabetes mellitus (Yes vs. no ratio = 0.62, CI 95% [0.44-0.88], p=0.007) and psychiatric illness (Yes vs. no ratio = 0.59, CI 95% [0.44-0.80], p<0.001).
Conclusion: Our study presents the opportunity to reduce the health care burden and improve resource utilization by highlighting the potential to treat small burn patients with less than 20% TBSA burns as outpatients.

ABSTRACT

Using a Standardized Script and Process Further Improves Pediatric OR to ICU Handoffs

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Sponsored by: Akemi L Kawaguchi, MD, Department of Pediatric Surgery
Supported by: McGovern Medical School at UTHealth, Department of Pediatric Surgery
Key Words: handoff, protocol, surgery, ICU, medical error

Introduction: Medical errors are one of the leading causes of death in the United States and lapses in communication during patient handoffs have been identified as a significant contributor to medicals errors nationwide. We hypothesized that a scripted, standardized handoff protocol for all pediatric surgical patients transferred from the operating room to an intensive care unit will improve team member presence, information exchange, and communication.

Methods: A three-staged pre/post intervention observational study was conducted for the handoffs of pediatric patients from the operating room (OR) to the neonatal (NICU) and pediatric (PICU) intensive care units. The pre-intervention group (Group A) did not have a standardized handoff process. The first post-intervention group (Group B) used a standardized handwritten handoff form, while the second post-intervention group (Group C) used a standardized handoff process that included scripted questions developed by a multidisciplinary team of physicians. Team member presence at handoff, length of the handoff, number of distractions, and the transfer of essential patient and procedural information were measured through direct observation.

Results: Direct observation was done for 24, 36, and 45 handoffs in groups A, B, and C respectively. While the anesthesia team was nearly always present at the handoffs (96, 100, 100%), the surgical (4, 64, 73%) and ICU (38, 86,100%) teams vastly improved their attendance at handoffs. The time required for handoffs did not change significantly in the three groups (3.1 ± 2.8, 4.1 ± 3.0, and 3.5 ± 1.9 minutes, respectively). Patient care distractions during handoffs decreased over the three intervention periods (54%, 22%, and 11% of handoffs, respectively). The transfer of essential patient and procedural information improved with each intervention for the surgical teams (see chart). Anesthesiologists had stable reporting of airway concerns and opioid administration (88, 94, 88% and 87, 97, 95% for groups A, B, and C, respectively). Anesthesiologists showed modest improvements in relaying information about opioid and paralytic administration and dosage (50, 58, 75%, and 58, 86, 95% for groups A, B, and C, respectively). Antibiotic name and dosage were improved, but still missed almost half of the time (21, 44, 59% and 21, 36, 45% for groups A, B, and C, respectively).

Conclusion: Implementation of a scripted, rather than a written, standardized handoff process improved team member presence, decreased distractions, and further improved the transfer of

information during handoffs. Future efforts will focus on improving adherence to the scripted handoff protocol and examining the relationship between handoffs and patient outcomes.

ABSTRACT

Prevalence of frailty in homebound older adults in Harris County

SARA SHIRAI *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Jessica Lee, MD, MS, Department of Internal Medicine, Division of Geriatric and Palliative Medicine
Supported by: Consortium on Aging, McGovern Medical School Office of the Dean
Key Words: Frailty, Homebound older adults, Fried Frailty Phenotype

Background: The United States Census Bureau estimates that by year 2050, the number of people aged 65 and older will be 83.7 million. In order to effectively adjust to the aging population, it is essential to be aware of the factors affecting the health of older adults, such as frailty. Frailty is a distinct clinical syndrome characterized by the body's failure to correct itself from homeostatic imbalance. It is caused by age-related decline in physiological systems and it increases the risk of falls, delirium, disability, hospitalizations, and mortality.
Objectives: Measure frailty using the Fried Frailty Phenotype (FFP) in homebound patients residing in Harris County and identify factors that correlate with frailty status.
Methods: We performed a cross-sectional study in which we measured frailty status in homebound older adults age 50 years and older. Demographic data including age, gender, ethnicity, number of medications, and number of diagnoses were obtained during visits to the participants' homes. Frailty was measured using the FFP criteria of unintentional weight loss, weakness, poor endurance, slowness, and low physical activity. Participants who met three or more criteria were considered frail, those who met one or two criteria were considered prefrail, and those who met no criteria were considered robust.
Results: We visited 25 homebound patients (average age 73) in the Harris Health-UTHealth LBJ Bridge House Call Program and screened for frailty using the FFP as part of their clinical exam. Of the 25 patients we screened for frailty, 14 (56%) were considered frail, 11 (44%) were considered prefrail, and none (0%) were considered robust. The patient population consisted of 12 (48%) females and 13 (52%) males with 17 (68%) African Americans, 5 (20%) Hispanics, 2 (8%) Caucasians, and 1 (4%) Asian. 53% of African American patients were frail and 47% were prefrail, 60% of Hispanic patients were frail and 40% were prefrail, 50% of Caucasian patients were frail and 50% were prefrail, and the one Asian patient was considered frail. Those who took 5 or more medications (polypharmacy) were 63% frail and 37% prefrail, while those who took less than 5 medications were 33% frail and 67% prefrail. Those who had more than 10 diagnoses were 57% frail and 43% prefrail, while those who had less than 10 diagnoses were 50% frail and 50% prefrail (average number of diagnoses = 17).
Conclusion: As we had anticipated there was a greater prevalence of frail and prefrail homebound older adults when compared to the prevalence found in community-dwelling older adults (10% and 40%, respectively). Across our ethnically diverse patient population, the distribution of frailty and prefrailty was similar (about 50/50 distribution). Participants who were prescribed more than 5 medications were more likely to be frail when compared to those who were prescribed less than 5 medications. We also saw a trend where the more diagnoses the patients had the more likely they were to be frail. We would like to continue on this study

to increase the sample size of this study. We would also like to closely examine each of the FFP criteria in correlation with our data to develop interventions that could mitigate frailty.

ABSTRACT

The Increasing Incidence of Stroke in Trauma Patients: Is it BCVI or age related? A collaborative review between the Departments of Surgery and Neurology at UT McGovern Medical School.

CEDAR SLOVACEK *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Dr. Michelle K. McNutt, M.D., Trauma Surgery
Supported by: Dr. Hari Indupuru, PhD, Dr. Erin Fox, PhD, Dr. Sean Savitz, M.D.
Key Words: Stroke, BCVI, Trauma, Aging

Introduction: While evidence-based medicine guides early diagnosis and treatment of blunt cerebrovascular injury (BCVI) to decrease stroke rates, there is a paucity of trauma research addressing other etiologies of stroke including atherosclerotic disease and atrial fibrillation. Both are age-related diseases that should contribute to a rising stroke rate with the increasing age of the trauma population. The purpose of this study is to evaluate the incidence, treatment, and etiology of strokes in our trauma population, and for those related to BCVI to evaluate the impact that screening and treatment guidelines have on the incidence of BCVI-related strokes.

Methods: This study was a retrospective review of all adult trauma patients admitted to a level 1 hospital who suffered a stroke during trauma admission from 2010 to 2017. Data was collected from two prospectively maintained databases by the UTHealth Trauma and Stroke services. Chi-squared test was performed for trends in proportions. Mann-Whitney U test was used to compare continuous variables.

Results: Of the 43,674 adult blunt trauma patients admitted during the study period, 97 (0.2%) were diagnosed with a stroke during the index admission, of which 22% were caused by BCVI. The age and volume of trauma patients increased during the study period as did the incidence of BCVI ($p<0.001$). While the incidence of all strokes increased over time ($p<0.001$), this was associated with a decrease in BCVI strokes and an increase in non-BCVI strokes. Of our patients with BCVI-related strokes, 79% received appropriate anti-thrombotic therapy at a median of 6 hours and 59 minutes from time of arrival. Patients with non-BCVI strokes (78% of the stroke population) had a higher median age (71 vs 44, $p<0.001$), lower median ISS (12 vs 26, $p<0.001$) and similar length of stay (12 vs 14 days, $p=0.986$) compared to patients with stroke secondary to BCVI. The mortality rate for BCVI strokes and non-BCVI strokes were 38% and 22% respectively, and patients with BCVI strokes were 1.7 times more likely to die than non-BCVI strokes (RR: 1.70, 95%CI: 0.86-3.39, $p=0.14$).

Conclusion: Strokes are rare in the trauma population but are increasing as the trauma population ages. Despite a large volume of evidence for BCVI treatment and stroke prevention, the majority of strokes are secondary to advanced age and comorbidities. Medical optimization of comorbid conditions during trauma hospitalization will become increasingly important for stroke prevention as the population ages.

ABSTRACT

Implementation of 3D Printing in Anatomical Education

ANTHONY SOTO *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Leonard Cleary, Ph.D. Department of Neurobiology and Anatomy
Supported by: Human Structure Facility, Department of Neurobiology and Anatomy
Key Words: 3D Printing, Education, STL, DICOM

Introduction: Three-Dimensional (3D) printing is a relatively new, rapidly expanding method of manufacturing that has found numerous applications including medical education. One application is the creation of anatomical structures from radiographic images. Human models of various structures can be manufactured that were once only able to be appreciated in situ, such as arterial systems. This technique could also supplement dissections by capturing the 3D relationships in situ and by giving a better idea of organ involvement in the human body.

Methods: A MakerBot Replicator Z18 was used with MakerBot PLA Filament (biodegradable plastic) to print various anatomical structures. The printer settings were optimized based on the structure being printed. For the majority, the density of the interior was increased to create more solid structures. The MakerBot Print interface was used to print STL files. Models from Thingiverse were initially used for proof of concept and for testing the limitations of the MakerBot Replicator Z18. The process of rendering structures from CT/MRI datasets was more challenging. 3D Slicer was used to extract data from CT/MRI datasets (DICOM format). The models were exported to STL format for printing. Many models required further editing to produce acceptable prints. MeshLab was used to remove any unnecessary digital information that was left in the image after rendering. It was also used to isolate and smooth the 3D models. The most useful features were those for removing isolated faces, selecting individual faces for removal, Poisson Mesh, and merging mesh layers. The Laplacian Smooth feature was the final step.

Results: The first objective of this project was to compile an instruction manual for future users. The second objective was to print a number of different structures to explore the capabilities of the printer. The following structures were created directly from open source models: inner ear, ossicles, mandible and heart with valves. The following were created from digital datasets: coronary arteries, heart with aorta, cranial venous sinuses with a tumor, mandible, abdominal aortic aneurysm, knee joint, and circle of Willis.

Conclusion: The protocol developed can be used for making models to supplement anatomical education. For example, while you may be able to see the bifurcation of the abdominal aorta into the iliac arteries, a 3D print represents the path the arteries take without destruction of the surrounding structures. 3D printing has its share of limitations such as the time it takes to print a single model, reliability of the printer and the time it takes to clean the model after printing. However, with the correct protocol in place all these factors can be minimized. The project also shows specific promise for closely examining models both of classic and atypical pathologies such as tumors and aneurysms without risk to patients.

ABSTRACT

Training Residents to place IP LARC: An Update among U.S. Residency Programs

CAROLINE STARLING *McGovern Medical School at UTHealth* *Class of 2018*

Sponsored by: Cristina M. Wallace Huff, MD, Department of Obstetrics, Gynecology and Reproductive Sciences
Supported by: Department of Obstetrics, Gynecology and Reproductive Sciences; Dean's Office Award
Key Words: Immediate Postpartum, Long-acting Reversible Contraception, Training

Purpose: To survey U.S. Obstetrics and Gynecology (Ob/Gyn) Residency Programs on immediate postpartum (IP) long-acting reversible contraception (LARC) training and challenges.

Background: In 2016, the American College of Obstetricians and Gynecologists (ACOG) released a committee opinion supporting IP LARC. Growing evidence describes provider/hospital barriers which hinder IP LARC provision. We hypothesize similar difficulties have prevented programs from implementing training.

Methods: We distributed an electronic survey addressing IP LARC training to 273 U.S. Accredited Council for Graduate Medical Education (ACGME) Ob/Gyn Residency Program Directors from the 2017-2018 Academic Year. Data analysis was performed with chi-square and Fisher's exact tests.

Results: Of 94 programs that participated, residents were trained in the immediate postpartum period to place implants in 58 programs (62%) and to place intrauterine devices (IUDs) in 55 programs (59%).

Prior to 2015, only 18% of the programs were training their residents to place IP IUDs. Twenty-eight percent of eligible programs initiated training in 2017. The majority of programs focused training interns (96%). Patient/provider convenience motivated 47% of programs to offer IP LARC and compliance motivated 27%.

The two barriers most frequently encountered, regardless of program training status, were problems with billing and compensation for services (63%) and the pharmacy (32%).

Programs that reported primarily seeing patients with insurance, either private or Medicaid, were more likely to have IP IUD training compared to programs seeing mostly indigent/uninsured populations ($p<0.05$).

Conclusion: IP LARC training has increased since the ACOG Committee opinion was published, however many programs are still facing challenges with implementation, affecting resident training.

ABSTRACT

Analysis of Survival in Pediatric Brain Tumor Patients: A Single-Center Study

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Sponsored by: Manish N. Shah, MD, Department of Pediatric Neurosurgery
Supported by: Manish N. Shah, MD
Key Words: Pediatric Brain Tumor, Survival

Background: Brain tumors are the most common solid neoplasms in children. They also represent the leading cause of pediatric cancer-related mortality. While significant advances have been made to improve our understanding of the origin and complex biology of these tumors, the heterogeneity of tumor types and anatomic locations in which they present continue to complicate diagnosis and management. This study aimed to broadly assess clinical outcomes in a large population of pediatric brain tumor patients.

Methods: We retrospectively reviewed 350 patients treated for a brain tumor at Children's Memorial Hermann Hospital between 1995 and 2017. Patients with a diagnosis of a brain tumor between the ages of 0 and 18 were included. Data on race, gender, age at diagnosis, histopathology/pathogenomics, presence of disseminated disease along the neuroaxis, treatment and disease progression were collected. A one-way analysis of variance (ANOVA) test was used to determine the statistical significance of these factors within tumor types. Kaplan-Meier analysis was used to determine progression-free survival (PFS) and overall survival (OS). Survival estimates were compared to published data on mean OS in the United States (SEER 1995-2012).

Results: The study population (n = 350) had a mean age at diagnosis of 8.2 years (range 0.1-18 years). Of the 350 patients, 160 had surgery, 110 had surgery and adjuvant therapy, 10 had biopsy, 14 had biopsy and adjuvant therapy, 24 had adjuvant therapy only and 32 had no therapy. Median follow-up was 3.1 months. There were 232 patients (62.2%) lost to follow-up. PFS at one-year was 66.7% and OS was 90.8%. Tumors were stratified into four broad classes for statistical analysis that included medulloblastoma (n = 19), glioma (n = 98), germ cell tumors (n = 4) and choroid plexus tumors (n = 6). Mean age at diagnosis was significantly different for these classes (medulloblastoma mean age is 6.5 years; glioma mean age is 8.6 years; germ cell tumor mean age is 10.9 years; choroid plexus tumor mean age is 4.3 years; p = 0.006).

Conclusion: Our results indicate that overall survival at one-year in the study population compares favorably to estimates of the national average, 90.8% vs. 86.6% respectively. Further work is needed to strengthen the study by obtaining treatment information, follow-up and disease status for patients lost to follow-up.

ABSTRACT

Surveying Caregivers of NICU Infants after Transitioning Home

Brian Tang *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Mary T Austin, MD, MPH, Department of Pediatric Surgery
Supported by: The Department of Pediatric Surgery, McGovern Medical School at UTHealth
McGovern Medical School at UTHealth – Office of the Dean
Key Words: NICU, Transition to Home, Barriers, Survey

Introduction: The transition from the neonatal intensive care unit (NICU) to home can be a period of high parental stress, which may lead to a negative impact on the healthcare outcome of the infant. There are many factors that influence this discharge process, as well as the immediate period at home after discharge. Our aim was to evaluate potential barriers to a successful discharge and identify opportunities to improve the transition to home by surveying parents of recent NICU graduates.

Methods: A cross-sectional survey was developed in English and Spanish and included the following categories: pregnancy course, pre-discharge education, post-discharge needs, and general demographics. The survey was revised based on stakeholder feedback and then administered to parents of infants discharged from our NICU between January 1, 2018 and July 30, 2018. The surveys were conducted in our institution's high-risk infant and pediatric surgery clinics.

Results: A total of 45 parents of recent NICU graduates were surveyed. Of the 45 survey responses, 37 were in English and 8 in Spanish. About 1/2 of the infants were discharged with durable medical equipment (DMEs). The most common DMEs were feeding tubes and supplementary oxygen. Of the families discharged with DMEs, all reported that they felt comfortable with the instructions given prior to discharge. However, after discharge, 25% reported it took longer than one week to feel comfortable using their DMEs. About 1/3 of all parents reported never referring to the discharge paperwork provided to them by the NICU. Of the 10 respondents who referred to the discharge paperwork daily, 6 completed the survey in Spanish. When asking about the use of technology, 75% of families reported that they own either a smartphone or a tablet. Of these, about ½ already use their smartphone in the care of their child, and 3/4 strongly agree or agree that they would utilize a telehealth application to help with the care of their child.

Conclusion: Although most parents of NICU graduates reported feeling comfortable with the discharge process, they often did not feel comfortable in caring for their infants at home. In addition, a large percentage of families do not refer to discharge paperwork for information following discharge. However, many already use mobile health tools to help care for their child and the majority are in favor of a telehealth application specifically designed to support parents in caring for NICU graduates.

ABSTRACT

The Association of Leptin Concentrations with Obesity and Metabolic Health in a Mexican – American Border Population

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Sponsored by: Absalon D. Gutierrez, MD, Department of Internal Medicine
Supported by: NIH (Grant # R01DP000210-01) and Centers for Disease Control and Prevention (Grant #MD000170P20)
Key Words: Metabolic health, leptin, diabetes

Background: Leptin is a hormone which suppresses hunger, inhibits lipogenesis and increases energy utilization. Leptin is involved in the pathogenesis of obesity and the metabolic syndrome, which includes hypertension, dyslipidemia, and insulin resistance. However, the mechanisms of leptin in these diseases require further investigation. Prior studies in multiple human populations have yielded contradictory results. The present study examines associations between leptin levels, obesity, and metabolic health in a Mexican-American border population.
Significance: 1) In a Mexican-American border population, the association of plasma leptin levels with obesity status and metabolic health status is unknown.
Hypotheses: 1) Obese subjects display higher leptin levels, regardless of metabolic health. 2) Metabolically healthy subjects display higher leptin levels, regardless of obesity status**.**
Experimental Design: We performed a cross-sectional, retrospective study using patient data collected by the Cameron County Hispanic Cohort in Brownsville, Texas. We classified obesity as BMI ≥ 30 kg/m^2. We determined metabolic health status by assessing the presence of the following four criteria: elevated blood pressure (SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg), triglycerides ≥ 150 mg/dL, HDL cholesterol decreased (males < 40 mg/dL; females < 50 mg/dL), and fasting glucose ≥ 100 mg/dL (or use of hypoglycemic medications). The presence of < 2 of these criteria defined a subject as "metabolically healthy." We categorized the patients into four groups: metabolically healthy non-obese (MHNW, n = 245), metabolically healthy obese (MHO, n = 107), metabolically unhealthy non-obese (MUHNW, n = 97), and metabolically unhealthy obese (MUHO, n = 187). We excluded patients less than 18 years of age, current smokers, patients with major cardiovascular events or active malignancy, and patients using confounding medications.
Results: Obese subjects (MHO μ = 30.9, sd = 19.4; MUHO μ = 29.3, sd = 22.1) displayed higher levels of leptin compared to non-obese patients (MHNW μ = 11.1, sd = 9.3; MUHNW μ = 13.5, sd = 10.7) regardless of metabolic health status.
Conclusion: In this Mexican-American population, the results showed that leptin levels were influenced by obesity but not by overall metabolic health status. These findings confirm Hypothesis #1 and run contrary to Hypothesis #2. These findings support more research on the mechanisms of leptin's role in obesity in Mexican-Americans.

ABSTRACT

Role of Hydroxurea in Ascorbate Cycling (via CYBRD1)

NICOLE THOMASON *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Richard Kulmacz, PhD, Department of Internal Medicine - Hematology
Supported by: McGovern Medical School at UTHealth-Office of the Dean; American Heart Assn Grant # 16GRNT29170013
Key Words: Sickle Cell Disease, Hydroxyurea, CYBRD1

Hypothesis: Adult sickle cell disease (SCD) patients who are on effective hydroxyurea (HU) treatment will have higher levels of cytochrome b reductase 1 (CYBRD1) protein in their red blood cell (RBC) membranes than patients who are not on effective HU treatment.
Background: Due to the wide-ranging roles of ascorbate in humans, chronic ascorbate insufficiency could lead to a risk of pathology over long term. Processes that deplete plasma ascorbate, such as oxidants generated in chronic ischemia/reperfusion cycles in SCD patients, may lead to dysregulation and pathology. CYBRD1 is a RBC membrane protein that is important in maintaining plasma ascorbate levels. SCD patients tend to have low plasma ascorbate levels but normal levels inside RBC. This suggests there are more circulating oxidants and/or less RBC CYBRD1. Hydroxyurea (HU), the current primary therapy for SCD, alters expression of many RBC proteins, notably HbF and it would be useful to know if RBC CYBRD1 levels are affected.
Methods: RBC membrane suspensions were prepared from blood samples drawn from consented adult SCD patients (homozygous HbSS) from the UT Health sickle cell clinic. Patients were assigned as "on" or "not on" effective HU treatment based on health records and standard study criteria. Membrane suspensions were dissolved in DMSO/TFA/water and serial dilutions were prepared. Each sample and dilution was dotted onto a PVDF filter. Filters were probed with primary CYBRD1 antibody, and visualized with alkaline phosphatase secondary conjugate and chromogenic substrate. Images were analyzed in ImageJ to quantitate the CYBRD1 protein with reference to a recombinant CYBRD1 standard.
Results: SCD patients not on effective HU treatment (n=5) averaged 0.98 ± 0.25 ng CYBRD1/ug membrane protein, whereas patients on effective HU treatment (n=4) averaged 1.76 ± 0.45 ng CYBRD1/ug membrane protein; $p < 0.013$ by t-test.
Conclusion: Although the sample size was small and needs to be expanded, the results suggest that HU therapy increases the CYBRD1 content of SS patients' RBC membranes. If increased levels of RBC CYBRD1 are confirmed, it would be a new mechanism for benefit from HU therapy.

ABSTRACT

Restoration of Dystrophin Expression in Muscle Progenitor Cells using CRISPR/Cas9 in Mouse Models of Muscular Dystrophy

ANDREW THOMSON *McGovern Medical School at UTHealth* *Class of 2021*

Sponsored by: Polina Matre, PhD, Johnny Huard, PhD, Department of Orthopedic Surgery
Supported by: Department of Orthopedic Surgery
Key Words: CRISPR/Cas9, Duchene Muscular Dystrophy, Muscle Progenitor Cells

Background: Duchenne Muscular Dystrophy (DMD) is an X linked mutation that ceases expression of dystrophin, an important protein for muscle cell integrity, leading to progressive muscle wasting and early death. Despite lack of dystrophin from birth, clinical and histological signs of DMD appear around the ages of 4-8. A possible explanation for this is that the number of Muscle Progenitor Cells (MPCs) which fuse with and repair damaged muscle cells are concurrently depleted around this age. A common murine model for the study of DMD is *mdx* which has a mutated exon leading to a lack of dystrophin expression, but a more recent model, *mdx/mTR*, possess a dystrophin as well as telomerase mutation leading to MPC depletion with age not observed in previous models and more severe clinical manifestations of DMD as seen in humans.
Hypothesis: MPC depletion plays a pivotal role in DMD, so Ex vivo CRISPER/Cas9 restoration of dystrophin in MPCs may improve the cells' ability to proliferate, differentiate, and survive the hostile microenvironments found in dystrophic muscle.
Methods: Plasmids encoding the sgRNAs, Cas9, and GFP were used for cloning, and after cell sorting using flow cytometry, deletions of mutated exons in MPCs were confirmed with PCR. A Proliferation Assay comparing edited and unedited *mdx/mTR* MPCs was done in 12 well plates monitored over several days using Celltiter-Blue Cell Viability Assay. Edited and unedited LacZ labeled *mdx/mTR* MPCs were injected into *mdx* mice hind-legs, and engraftment efficiency of frozen sections was measured after several weeks using X-Gal staining. Differentiation potential of edited and unedited *mdx* cells after 4 weeks in pellet culture with osteogenic or chondrogenic media was measured using Alcian Blue for chondrogenic and Von Kossa for osteogenic staining of frozen sections.
Results: PCR revealed successful excision of the mutated exon in *mdx/mTR* MPCs. Restoration of dystrophin greatly improved the proliferation of *mdx/mTR* cells. After 4 days, edited *mdx/mTR* cells increased in cell number over four fold while unedited cells increased 1.6 fold ($p<0.0005$). Engraftment efficiency and differentiation potential are awaiting quantification, but qualitative analysis suggests that edited *mdx/mTR* and *mdx* MPCs are improved compared to unedited MPCs.
Conclusion: This evidence suggests that dystrophin expression in MPCs plays an important role in maintaining the stim cell pool in muscles as its restoration improved the MPCs' proliferation, differentiation, and engraftment efficiency. Restoration of MPCs may also prove to be superior to previous therapeutic approaches such as exon skipping in RNA using oligonucleotides or viral introduction of CRISPER/Cas9 to restore dystrophin in muscle cells because restoring MPCs may improve both young and old DMD patients who have a depleted stim cell pool.

ABSTRACT

Comparing Endoscopic Visualization Between Topical 0.05% Oxymetazoline and 1:1000 Epinephrine During Endoscopic Sinus Surgery

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Supported by: The Department of Otorhinolaryngology- Head & Neck Surgery; McGovern Medical School at UTHealth- Office of the Dean
Key Words: Chronic rhinosinusitis, endoscopic sinus surgery, topical vasoconstrictors

Background: Topical 1:1000 Epinephrine (EPI) and 0.05% Oxymetazoline (OXY) are topical vasoconstrictors commonly used during endoscopic sinus surgery (ESS) to improve surgical field visualization. Visibility of the surgical field is critical for patient safety as bleeding can increase the risk of intraoperative complications and lengthens operating time. Research has indicated EPI is safe to use in ESS; however, there are reports of inadvertent injection leading to cardiovascular changes; therefore, some physicians favor OXY. The choice of topical vasoconstrictor varies on physician preference.

Objective: We sought to compare OXY to EPI in the visualization of surgical fields and blood loss in patients undergoing bilateral ESS for chronic rhinosinusitis (CRS).

Methods: A paired-control, randomized double-blinded prospective study in 10 adult patients (>18yrs) with CRS undergoing ESS was performed at a tertiary rhinology practice. Inclusion criteria included Lund-Mackay scores ≥ 14 and ≤ 2 point variability between sides. The laterality of the vasoconstrictor was randomized in a block fashion. The surgical field visualization score was assessed intraoperatively via the Boezaart scale at the basal lamella, sphenoid sinus, and frontal recess and at 20-minute intervals.

Results: Both vasoconstrictors had similar effectiveness in controlling bleeding and surgical field visualization. The mean Boezaart scale scores for EPI and OXY at the ethmoid sinus were 2.55±0.15 and 3.0±0.19 ($p= 0.07$) respectively. Although insignificant, EPI shows a slight predilection for improved visualization at the ethmoid sinuses. The average Boezaart scale scores did not differ between the two groups at the other sinuses and at 20 mins, 40 mins, and 60 mins.

Conclusions: No significant differences exist between EPI and OXY based on the Boezaart scale during ESS. Oxymetazoline serves as a comparable alternative to topical Epinephrine in providing hemostasis.

ABSTRACT

Therapeutic Use of Anti-Cancer Sphingosine Kinase-2 inhibitor on the progression of Huntington's Disease in vivo Transgenic mice

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Sponsored by: Andrey S. Tsvetkov PhD, Department of Neurobiology and Anatomy
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Key Words: Potential Drug Target for Huntington's Disease

Without developing a preventative treatment within the next thirty years, twelve million Americans will be diagnosed with a neurodegenerative disease. Huntington's, Parkinson's, and Alzheimer's are neurodegenerative diseases that lead to patient dyskinesia, disability and death. One hallmark of neurodegeneration is DNA damage in diseased neurons. DNA damage repair mechanisms become faulty due to age, stress, or genetic predisposition. Huntington disease affected (HD) neurons have a propensity towards DNA damage accumulation.

The protein signaling cascades in cells are multifactorial and can influence DNA damage repair mechanisms. One such messaging system is the sphingosine-1-phosphate (S1P). S1P is an important signaling phospholipid involved in cell survival. Sphingosine is phosphorylated to S1P by sphingosine kinases 1 and 2 (SK1 and SK2). S1P has a dual role as both an extracellular signaling messenger, and intracellular secondary messenger. When in the cytosol of neurons, S1P regulates autophagy. In the nucleus of non-neuronal cells, the complex SK2/S1P binds to and inhibits histone deacetylates 1 and 2 (HDAC1, HDAC 2). Studies have shown inhibition of histone deacetylates to be beneficial in treating DNA damage. However, due to the multifaceted nature of SKs, SK2 in the nuclei of neurons is cytotoxic. Overexpressed SK2 increases DNA damage.

In a clinical trial for bile duct cancer, ABC294640 acts as an oral selective SK2 inhibitor. ABC294640 has shown to be protective in two neuronal models of HD in rodents. The next task at hand was to see if ABC294640 could be therapeutic for a HD mouse model. The most commonly used animal model of HD transgenic R6/2 mouse was tested with. Two groups of mice were given either the placebo or drug (20 mg/Kg) in water starting at age of 4 weeks. The mice's locomotion, spatial awareness, and activity levels were tested by rotarod and open field assays. Rotarod is a platform that spins incrementally, testing the balance of mice. Open field assay is a maze that tests mice activity and spatial awareness. Mice were trained on a rotarod for 3 trials, and then tested on the accelerated rotarod from 0 to 40 rpm. The mice started showing motor deficits at 8 weeks. Male transgenic mice treated with the drug performed better in rotarod assessment than the non-treatment mice, however did not achieve a statistically significant improvement ($p=0.13$). In the open field assay, mice were significantly more active ($p=0.017$). Mice treated with the drug visited the center of the open-field more often ($p=0.0001$) t-test; N=4 per group. Immunohistochemistry of the transgenic treated had lower astroglosis; suggesting that there is reduced inflammation and reduction in pathology. These initial tests suggest that ABC294640 might be neuroprotective in HD, and further more diverse in vivo experiments with biochemical analysis might be warranted to evaluate if ABC294640 might be a potential drug or drug target pathway for new HD medications.

ABSTRACT

Retrospective Analysis of Focused Assessment with Sonography for Trauma in Predicting Exploratory Laparotomy and Angiography in Lieu of CT Scan in Children

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Sponsored by: Hannah E. Smith, MD, Department of Emergency Medicine
Supported by: Department of Emergency Medicine
Key Words: Pediatric, FAST, Hemodynamic Stability

Introduction:
The role of focused assessment with sonography for trauma (FAST) in pediatric blunt abdominal trauma is uncertain. This study investigated the utility of FAST in determining the need for emergent intervention (EI) in hemodynamically (HD) unstable patients presenting to the emergency department (ED).

Methods:
Using the trauma registry, all pediatric level 1 patients ages 0 – 15 y with blunt abdominal trauma at the Memorial Hermann Texas Medical Center ED from January 1, 2009 through June 30, 2018 were retrospectively reviewed. Descriptive statistics and univariate analyses, where a 2-sided p-value <.05 is considered statistically significant, was used. EI is defined as either operative management (laparotomy or thoracotomy) or angiography within 4 hours of arrival to the ED. Hemodynamic instability was determined in accordance with parameters set forth by the pediatric basic and advanced life support guidelines from the U.S. Department of Health and Human Services.

Results:
One thousand fifty-six children were included in this study. One hundred seventy (170/1056, 16.1%) had a positive FAST, and of these 44 (44/170, 25.9%) were HD unstable. Of the FAST positive and HD unstable patients, 14 (14/44, 31.8%) had EI, compared to 20 (20/126, 15.9%) of the FAST positive and HD stable patients (p=0.02). Sixty-six (66/1056, 6.25%) patients had EI, of which 32 (32/66, 48.5%) were FAST negative and 34 (34/66, 51.5%) were FAST positive. Of the FAST positive with EI patients, 14 (14/34, 41.2%) were HD unstable, compared to 4 (4/32, 12.5%) of the FAST negative with EI patients (p=.01).

Conclusion:
The FAST exam may be a valuable tool in predicting EI in the HD unstable child with blunt abdominal trauma.

ABSTRACT

To Close or Not to Close – Skin Management after Trauma Laparotomy

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Sponsored by: Center for Translational Injury Research
Supported by: Dr. Lillian Kao
Key Words: Superficial SSI, Trauma Laparotomy, Skin Management, Wound Closure

Introduction: Skin management after fascial closure may influence the risk of superficial surgical site infection (SSSI) development, which occurs in up to 25% of patients after emergent trauma laparotomy. Leaving skin open is thought to decrease SSSI risk, but increases wound care burden and results in poor cosmesis. Given the lack of high-quality evidence guiding skin management after trauma laparotomy, it is unknown whether skin incisions are being closed or left open appropriately. We aimed to characterize skin management in adult trauma laparotomy patients and to determine whether skin closure strategy is associated with SSSIs.

Methods: We performed a retrospective cohort study of a trauma laparotomy database between 2011 and 2017 at a high-volume, level-1 trauma center. SSSI diagnoses were determined by chart review according to the Center for Disease Control definition. Patients who never achieved fascial closure and those who died prior to the first recorded SSSI (on postoperative day 2) were excluded. Open versus closed skin management was determined by reviewing operative reports. Open skin entailed use of gauze packing or wound VAC, and closed skin entailed closured with staples (with or without wicks) or sutures. Univariate and multivariable analyses were performed. The multivariable model included variables that generated the best area under the curve (AUC). Inverse probability weighted propensity scores (IPWPS) were used to compare patients' predicted probability for open versus closed skin management with the skin management strategy they received.

Results: Of 1322 patients, 309 (23%) received open skin management, while 1013 (77%) had skin closure. The overall SSSI rate was 6%. On univariate analysis, there were no significant differences in development of SSSIs in open versus closed skin groups (8% versus 6%, $p = 0.12$). On adjusted analysis, damage control laparotomy, wound class 2, skin closure, large bowel resection, and higher body mass index were significantly associated with SSSIs. Skin closure has 3-times higher odds of SSSI development. IPWPS assignment showed that 75% of patients with closed skin had a propensity score of >0.9 for skin closure. In contrast, 11% of patients with open skin had a propensity score of <0.1 for skin closure.

Conclusion: Even though the rate of SSSI was only 6%, almost 25% of trauma patients had initial open skin management. Although there was consistency in the use of skin closure based on patient and wound characteristics, skin closure was associated with higher odds of SSSIs. Better predictive models are needed to accurately stratify patients' risk for SSSI after emergent trauma laparotomy to determine optimal skin management strategy.

ABSTRACT

Predictors of Enteral Autonomy in Pediatric Intestinal Failure

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Key Words: Intestinal failure, enteral autonomy, parenteral nutrition, pediatric

Introduction: Although achievement of enteral autonomy (EA) after pediatric intestinal failure (IF) is known to improve survival, the reported rates of and contributing factors to EA are highly variable in the literature. The aim of our study was to determine the incidence and predictors of EA in pediatric IF patients treated in a tertiary referral intestinal rehabilitation program.

Methods: We conducted a single-center retrospective cohort study of pediatric (<18 years) IF patients (2013-2018). IF was defined as either a bowel resection or gastrointestinal motility disorder diagnosed at <1 year old requiring parenteral nutrition (PN) for ≥60 of 74 consecutive days. EA was defined as discontinuation of PN for >3 consecutive months with maintenance of growth variables. Demographics, clinical characteristics, and operative details were collected. Descriptive statistics, Wilcoxon-rank sum, chi^2, and multiple logistic regression were used for analysis.

Results: Forty-one patients met inclusion criteria. The majority were male (56%), other race (51%), non-Hispanic (58%), and Medicaid funded (90%). Median age at study inclusion was 85 days (IQR 76-102). Median gestational age was 30 weeks (IQR 25-34) and birth weight was 1170 grams (IQR 725-2140). The most common cause of IF was necrotizing enterocolitis (63%). EA was achieved in 27 patients (66%) at a median of 123 days (IQR 101-184). Of the 14 (34%) that did not achieve EA, 8 (20%) remained PN dependent, 4 (10%) died, and 2 (5%) weaned off PN but did not meet EA criteria. No patient underwent intestinal transplant. The median follow-up was 20 months (IQR 11-30). On univariate analysis, EA was associated with preserved ileocecal valves (ICV) (85 vs 36%, p=0.00), longer residual small bowel length (SBL) (60 vs 33 cm, p=0.01), and higher percent of expected SBL (42 vs 17%, p=0.01). Additionally, the following variables were identified as potential contributing factors to EA and used in our multiple logistic regression model: lower direct bilirubin (2.6 vs 3.9, p=0.14), lower aspartate aminotransferase to platelet ratio index (1.0 vs 1.7, p=0.08), decreased cholestasis (59 vs 86%, p=0.08) and increased restoration of intestinal continuity (91 vs 71%, p=0.14). Residual SBL and percent of expected SBL was omitted on multiple logistic regression analysis, due to incomplete data (n=21, 51%). Only a preserved ICV predicted achievement of EA (OR 5.65, CI 1.06-30.21).

Conclusion: An EA rate of 66% was comparable to prior studies and was best predicted by ICV preservation. Efforts to preserve the ICV and SBL are paramount to the achievement of EA and, ultimately, to the survival of this vulnerable patient population.

ABSTRACT

The role of cyclooxygenase 2 signaling pathway in the development of heterotopic bone formation in muscular dystrophy mice

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Key Words: Duchenne's Muscular Dystrophy

Duchenne Muscular Dystrophy (DMD) is a genetic disorder characterized by muscle degeneration attributed to abnormal or absent expression of functional dystrophin protein and is often fatal in early adulthood. However, a dystrophin-deficient mouse (Mdx) remains largely asymptomatic despite underlying muscle and bone pathology. Dystrophin-/-/utrophin-/- double knockout mouse (Hom) is a mouse model that closely mimics the clinical manifestation of DMD patients. They develop severe muscle histopathologies including heterotopic bone formation (HO) and exhibit very short life span. In this study, we harvested bone tissues and associated muscles (e.g. gastrocnemius) from 4 weeks mdx, Het and Hom mice and C57BL/10J control mice for microCT scanning and histology and thigh muscle for measuring prostaglandins E4 and Q-PCR. MicroCT results showed HO in all groups of muscle. Von Kossa staining detected HO in the muscle tissue of Mdx, Het and Hom mice in comparison to no HO in control. Immunofluorescent staining for prostaglandin E2 (PGE2) receptors E2 and E4(EP2 and EP4) expression and colocalization with CD68 macrophage marker (M1 macrophage) showed significant increase of these two PGE2 receptors in the muscle of Mdx, Het and Hom mice compared to control mice accompanied by high number of macrophage infiltration. Furthermore, Q-PCR results showed cyclooxygenase 2 (Cox2), EP2, EP4 and 15-prostaglandins dehydrogenase (15-Pgdh) are significantly increased in Mdx, Het and Hom mice compared to B10 control mice. Tissue ELISA results showed PGE2 is significantly increased in Mdx, Het, and Hom mice compared to control mice. Moreover, the PGE2 is also significantly higher in Hom mice muscles than in Mdx, Het mice. Since PGE2 is important for endochondral bone formation, therefore elevated PGE2 most likely are one of the reason of HO formation, we conclude the upregulation of PGE2 and down-stream receptors EP2 and EP4 is likely responsible for the activation of COX-2/PGE2 pathways and subsequently resulted HO in the muscle tissues of muscular dystrophic mice.