THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
AT DALLAS

FIFTY-THIRD ANNUAL
MEDICAL STUDENT RESEARCH FORUM

MONDAY, JANUARY 26th, 2015
Oral Presentations 2-4:00 pm
Poster Presentation 4-5:00 pm

PROGRAM DIRECTOR: Rene Galindo, M.D., Ph.D.

PROGRAM COORDINATOR: Amanda Arista, M.A.Ed.

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53rd ANNUAL MEDICAL STUDENT RESEARCH FORUM

LIST OF ORAL PRESENTATIONS

Barbara Burton
"High-throughput chemical screen for EWS-FLI1 inhibitors using a transgenic zebrafish model of Ewing Sarcoma"
Mentor: James Amatruda, MD, PhD, Department of Pediatrics

Scott Carlson
"Hippocampal Volume Changes in Patients with Asthma"
Mentor: Sherwood Brown, MD, PhD, Department of Psychiatry

Erik Contreras
"microRNAs and Related Tissue Remodeling Genes in Rotator Cuff Repair in a Rat model"
Mentor: Chris Chen, PhD, Department of Orthopaedic Surgery

Zehra Farzal
"Masqueraders of Appendicitis"
Mentor: Anne Fischer, MD, PhD, Department of Pediatric Surgery

PRESENTATION OF GUEST SPEAKER

Michael A. Choti, MD, MBA

Chair of the Department of Surgery
Surgeon-in-Chief for William P. Clements Jr. University Hospital
University of Texas Southwestern Medical Center

RECEPTION AND POSTER SESSION IMMEDIATELY FOLLOWING
S.C. Cafeteria

53rd Medical Student Research Forum

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KEY
Ω Oral Presenter - UT Southwestern Medical Student Research Forum
† NIDDK Medical Student Research Trainee
¥ R25 NHLBI Research Program Trainee
Û Funded by UT Summer Research Program

In Cell Stress Conditions, VEGFR2 Exerts Pronounced Effects on Cell Growth in Dysplastic Barrett's Epithelial Cells

Olivia Belli

Mentor and Collaborators: Rhonda F. Souza, MD, & Qiuyang Zhang, PhD.
Department of Internal Medicine

Background & Aims: Vascular endothelial growth factor (VEGF), a potent inducer of angiogenesis, recently has been shown to exert direct pro-proliferative and pro-survival effects on cancer cells through binding to its receptors, VEGFR1 and VEGFR2. In earlier studies, we showed that VEGF/VEGFR2 signaling exerts direct pro-proliferative effects on transformed Barrett's and adenocarcinoma cells in an autocrine fashion, with no significant effects on apoptosis. To explore the potential contribution of VEGFR signaling to cell growth of dysplastic Barrett's cells, we knocked down the VEGFR1 or VEGFR2 and studied the effects on cell morphology, cell number, proliferation, and apoptosis.
Methods: We used 3 high-grade dysplastic Barrett's epithelial cell lines (CP-B, CP-C, and CP-D). VEGFR1 and VEGFR2 were knocked down through stable infection with retroviral shRNA vectors. Knockdown was assessed through qRT-PCR for VEGFR1 and Western blot for VEGFR2. Cell morphology was assessed by optic microscopy. Cell numbers were assessed by cell counts at 48 hours in full growth media (FM) and under cell stress conditions (1% FM); proliferation was assessed by BrdU incorporation and apoptosis was assessed by a cell death Elisa in 1%FM.
Results: Knockdown of VEGFR1 was seen in 34% of CP-C, 22% of CP-D, and 0% of CP-B. Thus, we used CP-C only to assess effects of VEGFR1 knockdown. By Western blotting, we observed knockdown of VEGFR2 in CP-B and in CP-D, but not in CP-C. Thus, we used CP-B and CP-D to assess effects of VEGFR2 knockdown. We did not observed any morphology changes in the VEGFR knockdown cell lines compared to controls. In FM, dysplastic cells containing either VEGFR1 or VEGFR2 knockdown had higher cell numbers compared to control cells. In 1%FM, there was no significant difference in cell number between CP-C cells containing VEGFR1 knockdown and controls. In contrast, at 48 hours in 1%FM, CP-B and CP-D containing VEGFR2 knockdown had lower cell numbers ($19.9 \pm 1.3 \times 10^4$ and 10.5 ± 1.4 cells, respectively) compared to controls (41.4 ± 4.4 and 16.9 ± 1.6 cells). Compared to controls, VEGFR2 knockdown significantly increased BrdU incorporation in CP-B cells, even though overall cell number was decreased, whereas in CP-D, BrdU incorporation was decreased ($p=0.059$) along with overall cell number. Compared to controls, VEGFR2 knockdown increased apoptosis in CP-B and CP-D cells.
Conclusions: VEGFR2, but not VEGFR1, contributes to cell growth of dysplastic Barrett's cells, but only under conditions of cell stress, with both pro-survival and pro-proliferative effects. These findings support a potential role for anti-VEGFR2 therapies in the treatment of high grade dysplasia in Barrett's esophagus.

High-throughput chemical screen for EWS-FLI1 inhibitors using a transgenic zebrafish model of Ewing Sarcoma

Barbara Burton

Mentors and Collaborators: James Amatruda,MD, PhD, Joanie Neumann, PhD & Christie He
Department of Molecular Biology

Ewing Sarcoma is the second most common primary bone tumor of children and adolescents. With a lack of targeted therapies, survival remains poor despite remarkably intense chemotherapeutic regimens. 85% of Ewing cases are caused by a translocation between the EWS gene on chromosome 22 and the FLI1 gene on chromosome 11 [t(11;22)(q24;q12)]. The fusion EWS-FLI1 gene codes for a chimeric transcription factor which activates and suppresses expression of a diverse array of target genes, and is an enticing candidate for therapeutic investigation. EWS-FLI1 activity can be readily observed in a homozygous transgenic zebrafish model, in which the fusion gene is inserted downstream of the Microphthalmia-Associated Transcription Factor promoter, localizing EWS-FLI1 expression to melanocytes derived from the neural crest. These fish present with an increased melanocyte count on the dorsum of the head compared to wild type. We hypothesized that compounds which suppress EWS-FLI1 activity will prevent the formation of this phenotype in homozygous zebrafish larvae. A high-throughput chemical screen was performed using two libraries of FDA approved compounds. One compound was found to significantly reduce melanocyte count in EWS-FLI1 homozygous zebrafish compared to unexposed homozygous controls ($p < 0.0001$) in a dose-dependent manner. Furthermore, treated homozygous larvae displayed melanocyte phenotype similar to that of untreated wild type controls. From these results, we conclude that this compound interferes with EWS-FLI1 activity in the mitf:EWS-FLI1 homozygous zebrafish model. Further testing on Ewing Sarcoma cell lines will determine the potential significance of this compound as a specific inhibitor of tumor growth.

Inducible Nitric Oxide Synthase Inhibitors to Treat Diabetic Retinopathy: Assessment of Intravitreal Toxicity in an Animal Model

Caitlyn Emigh and Cameron Carr

Mentor: Chan Nguyen, MD, Phd, Department of Ophthalmology

Introduction: Diabetic retinopathy is the leading cause of blindness in the working adult population. This disease is characterized by damage to retinal vessels and abnormal vitreal neovascularization. Current treatments for diabetic retinopathy are not always effective. Nitric oxide (NO) is a signal for vitreal neovascularization, and inducible nitric oxide synthase (iNOS) inhibitors aminoguanidine (AG) and 1400W have been shown to prevent diabetic retinopathy in rats and dogs. Oral aminoguanidine has proven beneficial for human diabetic retinopathy as a secondary outcome in phase 3 clinical trials for diabetic kidney disease. The inhibition of iNOS by intravitreal injection is a treatment strategy that has not yet been investigated. Before this therapy can be tested in clinical trials, lack of toxicity must first be demonstrated in an animal model.

Methods: Four rabbits were used to test all doses of both AG and 1400W. Baseline ocular examination, pachymetry, tonometry, fundus photos, and electroretinography (ERG) were performed on each animal. The drug was then administered to each animal by intravitreal injection into the left eye. An equal volume of balanced salt solution was injected into the right eye to serve as a control. Lower concentrations were chosen for subsequent experiments on different animals until a non-toxic dose was achieved. Toxicity was determined by ocular examination, pachymetry, tonometry, fundus photos performed 1 day and 6 days after injection, ERG performed 7 days after injection, and histology performed after the animals were sacrificed on day 13.

Results: At high doses of both AG (5 mg) and 1400W (2 mg), toxicity was demonstrated by vascular attenuation with associated ischemia followed by complete infarction and/or hemorrhage. Decreased ERG response of the rods and cones, abnormal retinal histological findings, and a transient or sustained decrease in intraocular pressure were observed. The highest non-toxic dose was 0.25 mg for AG and 0.4 mg for 1400W, neither of which showed abnormalities in ocular exam, ERG, or histological exam.

Discussion: This project has identified the highest non-toxic dose of AG and 1400W in an animal model. With this information, phase 1 clinical trials can be designed to determine the safety of the use of these drugs in humans. Further studies will be needed to evaluate this treatment method in comparison to and in combination with current treatment strategies for diabetic retinopathy.

microRNAs and Related Tissue Remodeling Genes in Rotator Cuff Repair in a Rat model

Erik Contreras

Mentor and Collaborators: Christopher Chen, PhD, Fuxin Wei, & Michael Khazzam, MD, Department of Orthopaedic Surgery

The majority of rotator cuff tears seen clinically are atraumatic and chronic in nature, which can contribute to joint inflammation and tendon degeneration. Although some inflammation is vital to the healing process, excessive inflammation and high levels of matrix-degrading enzymes have been associated with impaired healing of the rotator cuff. The underlying factors regulating the level of inflammation in the injured rotator cuff still remain unclear. The purpose of this study was to investigate the expression of miRNAs in the setting of acute and delayed repair of a torn rotator cuff in a rat model. We hypothesized that the expression of miRNAs related to the inflammatory process would be altered in the injured rotator cuff compared to the control. Fourteen rats were randomized to either acute or delayed rotator cuff repair. Seven animals underwent detachment of the supraspinatus and infraspinatus tendons followed by immediate repair, while the remaining seven underwent delayed repair 2 weeks later. Sham surgery on the contralateral shoulder was used as a control. mRNA expression for COL1A1, COL3A1, TGF-β1, MMP-9, MMP-13 and IL-6 was determined and select samples were analyzed for miRNA profiles. Upon analysis, 57 miRNAs showed significant differences between groups, including 14 miRNAs with significant differences between acute and delayed repair groups ($p<0.05$). miRNA correlation analysis with mRNAs expression revealed two distinct groupings. The first grouping includes IL-6, MMP-13, and MMP-9, genes that are traditionally associated with inflammation and matrix degradation. The second grouping contains TGFβ1 and COL1A1, genes that are traditionally associated with the repair process. These findings suggest that groups of miRNA expression may play a more global role in regulating the balance between the inflammatory and repair processes, although any specific interactions have yet to be determined. Interestingly, IL-6 has been shown to promote increased levels of miR-18a* expression in hepatocytes, where it then acts in a positive feedback loop of the IL-6 signaling pathway. Our data, which shows a positive correlation between IL-6 and miR-18a* ($R2=0.63$), is consistent with these findings. We speculate that there may be a similar interaction between IL-6, miR-18a*, and the expression of downstream targets involved in rotator cuff inflammation and repair. These findings support our hypothesis that the expression of miRNAs related to the inflammatory process is significantly altered in the injured rotator cuff compared to the control tendon. Of particular interest is miR-18a*, which has been shown to increase levels of matrix-degrading enzymes, pro-inflammatory cytokines, and chemokines in arthritis synovial fibroblasts. This will require further experimentation in order to determine the precise gene targets and whether or not down-regulation of miR-18a* could lead to a mechanism by which one could decrease

A Role for POU3F3 in Myocyte Differentiation:
Exploring New Frontier in Alveolar Rhabdomyosarcoma Development

Amelia Denegre

Mentor and Collaborators: Rene Galindo MD, PhD, Valerie Granados PhD Candidate; Usha Avirneni PhD
Departments of Pathology, Molecular Biology, and Pediatrics

Summary: Children who are diagnosed with pediatric rhabdomyosarcoma (RMS), a mesenchymal-derived soft tissue cancer that comprises 3.5% of childhood cancers, are often delivered a bleak prognosis with little hope of a future. Despite significant advances illuminating transcription factor signaling in RMS onset and progression, research is still needed to precisely understand RMS pathogenesis on a molecular level in order to develop targeted treatment options.

Objective: The goal of this project is to explore the role of POU3F3 in myogenesis, particularly in relation to cell fusion and myocyte differentiation.

Methods: ***Immunofluorescence:*** POU3F3 knockdown cells were differentiated in 2% horse serum. On day 2 of differentiation, cells were probed with POU3F3 primary and red immunofluorescent secondary antibody, allowing for imaging of POU3F3 localization during myoblast differentiation. ***Western Blot:*** Three knock-down shPOU3F3 C2C12 cell-line constructs were tested. Western blots were performed that compared C2C12 control, POU3F3 overexpression, and POU3F3 knockdown cells. ***Crystal Violet:*** After differentiation, POU3F3 knock-down and control cell lines were stained with crystal violet stain to visualize the effect of POU3F3 knockdown on differentiation.

Results: ***Immunofluorescence:*** We confirmed that in knockdown C2C12 cells, POU3F3 localizes like control C2C12, in the periphery. Previous research has shown that in overexpressed POU3F3 C2C12 cell lines, POU3F3 localizes to the nucleus. The implication of the disconnect between POU3F3 location in controls and knock-downs versus overexpressed cell lines is an area that is an opportunity for further research. ***Western Blot:*** Western Blot analysis confirmed that POU3F3 knockdown was successful, and provides a platform for further POU3F3 interrogation. ***Crystal Violet:*** Crystal violet staining suggests that POU3F3 participates in a myoblast differentiation, as the control cells fuse into myotubes, while POU3F3-silenced cells do not.

Conclusion: These initial results suggest that POU3F3 participates in muscle differentiation. Next, the Galindo lab will be probing POU3F3 function in myogenesis in greater depth, insights they will next apply to RMS.

Efficacy of Contact Lens Care Solutions Against Neutrophil Enhanced Biofilms

Jorge A. Hinojosa

Mentors and Collaborators: Danielle M. Robertson, OD, PhD, Naiya Patel, & Meifang Zhu, Department of Ophthalmology

Purpose: To evaluate currently available chemically preserved and peroxide-based lens care products (LCPs) antimicrobial efficacies against neutrophil enhanced biofilms in reference strains of *S.auerus*(SA), *S. marcescens* (SM), *S. maltophilia*(ST), *and P.aeruginosa*(PA).
Methods: Lotrafilcon B lenses were inoculated with 2.5 x 107 CFUs of American Type Culture Collection (ATCC) reference strains of either SA, SM, ST, or PA and 8.3x106 cells of human neutrophils harvested by whole blood centrifugation. Lenses were then incubated over night under conditions that facilitate biofilm formation. Lenses were then disinfected with either multipurpose contact lens solutions (MPS): Biotrue (BT), PureMoist (PM) or hydrogen peroxide-based lens care systems (HPB): ClearCare (CC), PeroxiClear (PC) according to specific manufacture guidelines. Antimicrobial activity was then quantified by quantitative culturing (colony-forming units) and by fluorescence confocal microscopy (FCM) using LIVE/DEAD BacLight Bacterial Viability Kit (Molecular Probes, Eugene, OR).
Results: Mean colony growth counts for each bacterial strain + neutrophils were: SA= 1.44 x 107 (CFU/ml), SM= 2.56x109 (CFU/ml), ST= 1.17x1010 (CFU/ml), PA= 3.43x109 (CFU/ml). After treatment, SA exhibited a 7-log reduction with all LCPs (P=0.609); SM exhibited 9-log reduction for all LCPs except BT, which showed a 7-log reduction ($P < 0.001$); ST exhibited a 9-log to 10-log reduction for all LCPs (P=0.040); PA showed a 9-log reduction for all LCPs (P=1.000). FCM with viability staining revealed the presence many unviable bacteria still adhered to the lens surface after treatment with LCPs.
Conclusions: Although all LCPs meet FDA criterion of a 3-log reduction minimum even against neutrophil enhanced biofilms, FCM revealed that many remnants still remain adhered on the lens surface after just one use. Further deposition of bacterial products from continued used could enhance biofilm formation and promote a host inflammatory response, both of which could precipitate into a corneal infiltrative event (CIE). In addition, mean colony growth counts showed that SA exhibited the lowest growth on lens surfaces, which may explain why SA is more commonly associated with sterile CIEs.

Characterization of Receptor Protein Tyrosine Phosphatase epsilon (PTPRE) gene promoter

Thomas Isaacs

Mentors and Collaborators: James Amatruda, MD, PhD, Dinesh Rakheja, MD, & Abhay A Shukla, PhD, Department of Pediatrics and Pathology

Background: Receptor protein tyrosine phosphatase epsilon (PTPRE) is a receptor bound phosphatase that has been shown to be downregulated in Wilms' tumors compared to normal tissue, and could potentially be a target for future therapy. Our objective is to identify and characterize the promoter of the PTPRE gene and define the critical role of Wt1 transcription factor (commonly downregulated in Wilm's tumor) in PTPRE gene expression and in Wilms' tumor progression.
Methods: Our first step involved cloning and sequence analysis of the upstream region of the human PTPRE gene followed by PCR primer design and PCR amplification. The amplified fragment was then cloned into a promoterless reporter vector (pGl3 Basic) and transfected in Hek293 cells. Promoter DNA was used for deletion analysis where multiple PCRs were performed using a single forward primer and multiple reverse primers with nucleotides sequentially deleted from the 3' end. The different size PCR products were then cloned into pGL3 Basic vector DNA, transfected into HEK cells and had reporter assay (luciferase assay) performed to calculate fold change in PTPRE expression over promoterless vector. After the critical transcription factor binding motif was identified, PCR was performed to amplify full length promoter lacking 76 bases. The role of the deleted nucleotides was confirmed via luciferase assay. The sequence of deleted nucleotides was then analyzed for the presence of transcription factor binding motifs. Next, a predicted Wt1 transcription factor binding motif was mutated using site directed mutagenesis. Mutated fragment was cloned into pGl3Basic vector. Both wild type and mutated vector were transfected and luciferase assay was performed to confirm role of Wt1 binding motif for PTPRE promoter activity. Chromatin immunoprecipitation assay was then performed for further evidence. Promoter activity was also compared in two cells lines having differential expression of Wt1. Western blot and semi-quantitative PCR are used to confirm the expression levels of Wt1.
Results: Promoter deletion analysis confirmed that the Wt1 binding motif present at -16 position is critical for PTPRE expression and mutation of this site results in 95% loss in promoter activity in Hek293 cells. PTPRE promoter activity was shown to be high in Hek293 cells and low in Hela cells (high and low WT1 expression respectively), suggesting WT1 driving promoter activity. ChiP using WT1 antibody confirmed WT1 binding of the critical transcription factor binding motif.
Conclusion: These results shed light on why PTPRE expression is lower in Wilms' tumors and reveals potential future targeted therapy.

The Role of Ascl1 in NG2 Cells in the Spinal Cord

Demetra Kelenis

Mentor and Collaborator: Jane Johnson, PhD, & Tou Yia Vue, PhD
Department of Neuroscience

NG2 cells, one of the major glial cell populations within the central nervous system (CNS), are highly proliferative cells identified by the expression of the NG2 proteoglycan. Throughout life, NG2 cells can differentiate into oligodendrocytes to myelinate axon fibers, or they can be maintained in a proliferative or quiescent state as NG2 cells indefinitely. A recent study showed that deletion of tumor suppressor genes specifically within NG2 cells was sufficient to produce brain tumors in a mouse model, indicating that NG2 cells may serve as a potential cell of origin for gliomas. At present, however, understanding of how NG2 cells are regulated to proliferate or differentiate in the CNS remains incomplete. Interestingly, Ascl1, a proneural basic-helix-loop-helix (bHLH) transcription factor that is highly expressed in neural progenitor cells, is also expressed in NG2 cells. Although previous studies have shown that the loss of Ascl1 affects the initial specification and differentiation of NG2 cells, the specific role of Ascl1 in NG2 cells during embryonic and postnatal development remains unknown.

In this study, we investigated the direct requirement of Ascl1 in NG2 cells during embryonic and postnatal development in the grey matter (GM) and white matter (WM) of the spinal cord. More specifically, we conditionally deleted Ascl1 specifically within NG2 cells (Ascl1-CKO) at E14.5 or at P30 using an NG2-CreERT2 mouse strain in which the tdTomato (tdTom) fluorescence reporter was also incorporated to allow direct visualization of the development of NG2-labeled (tdTom+) cells. We found that Ascl1-CKO at E14.5 resulted in a decrease in the number of tdTom+ cells in the GM, but an increased number of tdTom+ cells in the WM. In contrast, Ascl1-CKO at P30 resulted in a significant reduction in the number of tdTom+ cells in both the GM and WM. Quantification of the percentage of tdTOM-labeled cells that had differentiated to mature oligodendrocytes revealed that Ascl1-CKO at E14.5 does not affect NG2 cell differentiation, while Ascl1-CKO at P30 accelerated NG2 cell differentiation.

Taken together, these findings indicate that Ascl1 is differentially required to regulate the number of NG2 cells in the GM and WM during embryonic development, whereas Ascl1 is essential for regulating both the differentiation and number of NG2 cells in the adult CNS.

Inhibition of corneal scarring in animal models of refractive surgery

Grayson Koval

Mentor: Matthew Petroll, PhD, Department of Ophthalmology

Background: Corneal keratocytes are transformed into myofibroblasts following wound infliction to the cornea, which results in development of scar tissue during healing and a resultant decrease in visual acuity. Evidence suggests that the Rho kinase signaling pathway is essential for this transformation to take place. Thus, Rho kinase inhibition might decrease scar tissue formation during corneal wound healing.
Objective: The purpose of this experiment was to use *in vivo* confocal microscopy (IVCM) to quantify the amount of light scattering (backscattering), which correlates with keratocyte transformation and scar tissue formation, following lamellar keratectomy (LK) and to see if Rho kinase inhibition modulates these responses.
Methods: In part one of the study, the corneas of six rabbits were scanned using IVCM to establish a baseline for corneal light backscatter, followed by LK on the left eye of each rabbit. Following surgery, the rabbits were scanned at 7, 14, and 21 days. Two rabbits were sacrificed at each time point and the corneas were extracted for the purpose of imaging by immunocytochemistry. In part two of the study, pre-scans were done on ten rabbits followed by LK. Five rabbits were treated and five were used as a control group. Starting immediately after surgery, the treated group received eye drops (in both eyes) containing Rho kinase inhibitor Y-27632 four times a day for the following 7 days, and the control group received eye drops containing PBS for the same time period. The rabbits were scanned using IVCM at 7, 14, and 21 days post-surgery and sacrificed after the 21 day scans.
Results: As expected, we observed a significant increase in backscatter from baseline at 7, 14, and 21 days upon examination with IVCM following surgery in the first six rabbits. In the second part of our experiment, we observed a significant difference in backscatter between the treated and control group at 7 days (average treated = 7,712, average control = 17,085, p-value = .008), and trends at 14 days (average treated = 14,910, average control = 19,891, p-value = .09), and 21 days (average treated = 10,354, average control = 17,591, p-value = .09). It is possible that after discontinuing treatment with Y-27632 the rabbits experienced a “rebound” effect and thus an increase in backscatter.
Conclusions: Rho kinase inhibition shows promise in helping to prevent corneal scarring following injury. In particular, this inhibition might help healing following vision correction procedures such as photorefractive keratectomy (PRK).

Page 11 (16 within the PDF) of this booklet is not publicly-available online. It has been removed at the request of the author's mentor.

Reciprocal Interactions of STIM1 with Orai1 and L-type Ca^{2+} Channels in Cardiac Myocytes

Derek Nguyen

Mentor: Xiang Luo, MD, PhD, Joseph Hill, MD, PhD
Department of Internal Medicine (Cardiology) and Molecular Biology

Background: Pathological cardiac hypertrophy can be triggered by abnormal Ca^{2+} levels. It has been shown that the mechanisms governing context-dependent changes in Ca^{2+} influx are linked to stromal interaction molecule 1 (STIM1). STIM1 is a sarcoplasmic reticulum Ca^{2+} sensor that regulates Ca^{2+} influx by directly activating store operated calcium channels such as Orai1 in response to stress such as intracellular Ca^{2+} depletion. STIM1 is also known to regulate L-type Ca^{2+} channels in cardiomyocytes, though the mechanism has not been elucidated.
Hypothesis: The Ca^{2+}-sensing protein, STIM1, molecularly interacts with Orai1 and L-type Ca^{2+} channels in cardiomyocytes to facilitate Ca^{2+} influx as a master regulator of Ca^{2+} channels.
Methods: To address this, we monitored STIM1 interactions with either Orai1 or L-type Ca^{2+} channels in neonatal rat ventricular cardiomyocytes (NRVMs) and adult rat ventricular cardiomyocytes (ARVMs) using the Duolink in situ fluorescence assay. This technique utilizes proximity ligation assay technology to directly monitor interactions between proteins within 40nm. These channel interactions were observed under endogenous culture conditions as well as thapsigargin-mediated calcium store depleted conditions. Differences in STIM1 interactions between control (untreated) and thapsigargin-treated NRVM and ARVM cells were observed.
Results: In NRVM cells, STIM1 interactions with Orai1 increased by 44.79 ± 2.68% when treated with thapsigargin as compared to the control population (n=73-83). Conversely, STIM1 interactions with L-type Ca^{2+} channels decreased by 52.31 ± 3.45% compared to the control (n=64-69). In ARVM cells, STIM1 interactions with Orai1 decreased by 59.19 ± 2.39% when treated with thapsigargin as compared to the control population (n=11-16). STIM1 interactions with L-type Ca^{2+} channels on the other hand increased by 74.13 ± 0.21% compared to the control (n=11-19).
Conclusions: We observed an opposite trend in STIM1 interactions with Orai1 and L-type Ca^{2+} channels in NRVM and ARVM cells. When treated with thapsigargin, their degree of interaction changed significantly. This would suggest that STIM1 undergoes dynamic changes in response to calcium conditions in order to regulate Ca^{2+} influx. At a molecular level, it would seem that STIM1 is a versatile Ca^{2+} channel regulator as it can alternately interact with both channels. Further studies will aid in the development of novel therapeutic strategies for the treatment of cardiac hypertrophy and disease.

Acetabular Changes Following the Induction of Ischemic Osteonecrosis of the Femoral Head in Immature Pigs

David Padilla

Mentor and Collaborators: Harry K.W. Kim, MD, Olumide O. Aruwajoye, MS,& Karen D. Standefer, BS
Department of Orthopaedics (TSRH)

Introduction: Acetabular development is significantly dependent on the shape of the femoral head. Legg-Calvé-Perthes disease (LCPD) is a femoral head deforming condition that affects children. As the femoral head deforms, the acetabulum does not form correctly and its anatomic orientation is altered. The piglet model of femoral head ischemic osteonecrosis is a well-established model of LCPD. The purpose of this study was to study the structural changes that a deformed femoral head will have on the acetabula in a large animal model. We used a 3-D CT reconstruction method to determine changes in the acetabulum following the induction of ischemic osteonecrosis.
Methods: Ischemic osteonecrosis of the right femoral head was induced in 6 -8 week old domestic pigs by placing a ligature tightly around the femoral neck and transecting the ligamentum teres. The left, unoperated side served as a control. The animals were sacrificed at 8 weeks post-ischemia and the proximal femora and pelvis were retrieved. Five isolated pelvises were scanned using a CT. These scans were imported into 3D visualizing software, Mimics, to measure the acetabular curvature, acetabular volume, anteversion angle, and acetabular offset. Anterior-posterior x-rays of the corresponding proximal femurs were obtained and the femoral head deformity was quantified using the epiphyseal index (ratio of femoral head height/diameter). .
Results: Epiphyseal index for the nonoperated side averaged 0.48 (std dev 0.03) while the operated side averaged 0.23 (std dev 0.03). Acetabular curvature was increased in 5 of 5 specimens on the operated side. Average acetabular volume increased by 20% on the operated-side. The anteversion angle increased on the operated side in 4 of 5 specimens. The center of the right best-fit sphere compared to the left showed the right sphere is more anterior (4 out of 5 specimens), more inferior (4 out of 5 specimens), and more lateral (4 out of 5 specimens).
Conclusion: We observed alteration of the acetabular volume and orientation following ischemic osteonecrosis of the femoral head. This study is the first of its kind to assess the 3-D structural changes in the acetabulum following ischemic osteonecrosis. This animal model will help shed light on the acetabular changes that occur in children with deformed femoral heads. Furthermore, this animal model provides a tool in which to study how treatment on the femoral head or acetabulum will alter the structure of the other and help to correct deformities.

Polymorphonuclear leukocyte enhancement of bacterial biofilms on contact lens surfaces

Naiya Patel

Mentor and Collaborators: Danielle Robertson, OD, PhD, Jorge Hinojosa, & Meifang Zhu
Department of Ophthalmology

Contact lens-wear represents a leading risk factor for the development of infectious keratitis, which can result in significant vision loss. It is well established that bacterial colonization of the posterior lens surface represents the initial event in the pathogenesis of lens-related infection. Using an invasive clinical isolate, our prior work has shown that *Pseudomonas aeruginosa* biofilm formation on contact lens surfaces is dramatically accelerated in the presence of dying neutrophils. The goal of this study was to investigate the capacity of five FDA test strains, all commonly associated with contact lens-related infiltrative events, to form biofilms on contact lens surfaces in the presence of neutrophil-derived cellular debris.

Neutrophils were obtained from healthy, human volunteers by venipuncture and isolated using Ficoll gradient separation. Unworn Lotrafilcon B silicone hydrogel contact lenses were incubated overnight in one of five reference strains from the American Type Culture Collection with or without neutrophils at a 1:1 bacteria:neutrophil ratio. Test strains included: *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Staphylococcus auerus*, *Stenotrophomonas maltophilia*, and *Serratia marcescens.* Adherent bacteria were visualized using scanning electron microscopy (SEM) or stained using a BacLight live/dead assay followed by laser scanning confocal microscopy. The number of viable bacteria adherent to the lens surface was also quantified by standard colony counts.

Live/dead staining showed greater numbers of viable bacteria adherent to lens surfaces when cultured in the presence of neutrophils. Colony counts confirmed a higher number of viable bacteria for four of the five test strains: *S. auerus* ($p<0.001$)*, S. maltophilia* ($p<0.001$)*, P. aeruginosa* ($p=0.030$)*, and S. marcescens* ($p<0.001$). This effect was not evident with *S. epidermidis* ($p=0.659$). SEM showed similar findings.

This is the first study to demonstrate the ability of these reference strains to form biofilms on contact lens surfaces in the presence of neutrophils. These findings suggest that, in the setting of intense inflammation under the lens, common contact lens-related pathogens possess the capacity to colonize and resist clearance by the innate immune system. Further studies are needed to correlate these findings with disease in an animal model.

Neuronal maintenance via a neuron-specific degradation pathway

Taylor Schmidt

Mentor and Collaborators: Robin Hiesinger, PhD, Eugene Jennifer Jin, Mehmet Neset Ozel, Daniel Epstein, Corey Marchant, Department of Physiology

Background: Neurons can survive for decades via cell maintenance and protein degradation. This process includes the general protein endolysosomal degradation pathway, an integral part of which is the Rab GTPase proteins. Recently, components of a neuron-specific protein degradation pathway were discovered, which include the neuronal vesicle ATPase component V100 and the synaptic vesicle protein neuronal Synaptobrevin (n-Syb). While this neuron-specific degradation pathway has been shown as necessary for neuronal maintenance in adult *Drosophila melanogaster* fruit flies, it is not known what this neuron-specific degradation pathway does, nor how it interacts with the general protein degradation pathway. Our research aimed to fill this gap in knowledge. Such research may be salient because the misregulation of protein degradation in neurons leads to neurodegenerative diseases like dementia.
Objective: We hypothesized that neurons either have an increased or a specialized need for protein degradation in comparison to other cells.
Methods:
1. The lab chose a myristoylated protein (myr) to represent general proteins found in every cell, and Synaptotagmin1 (Syt1) to represent neuron-specific proteins. The acidification-sensitive tag mCherry-pHluorin, which changes color with a decrease in pH, was placed on Syt1 and myr to visualize acidification and degradation of the two proteins.
2. The lab generated *Drosophila* lines to compare acidification and degradation of Syt1 and myr in wild-type versus the following three mutants: *rab7* mutants to disrupt general protein degradation, *v100* to disrupt the neuron-specific protein degradation, and *synaptobrevin* also to disrupt neuron-specific degradation.
3. We performed live imaging to visualize acidification and protein degradation at synaptic terminals. Brains of *Drosophila* pupae from each cross were dissected, mounted onto Petri dishes, and surrounded with a culture medium to be kept alive. A resonant confocal microscope was used to observe the brain's lamina, a layer of neurons between the eye and the brain. At the lamina, we recorded 30-minute videos showing changes in fluorescence representing protein degradation.
Results and Conclusion: Preliminary data show that *nsyb* and *v100* mutations may cause defects in the degradation of neuron-specific cargo. Such evidence suggests that the neuron-specific endolysosomal degradation pathway specifically degrades the synaptic vesicle protein Synaptotagmin1. Also, the experiments indicate that disruption of either the neuron-specific or the general endolysosomal degradation pathway has no effect on the acidification of the myristoylated protein. Such evidence implies that the general pathway of protein degradation occurs at synapses, but has no specificity for protein cargo. A greater sample size is needed for future experiments, as well as quantitative analysis.

Synthesis and Comparative study of a Library of Small Molecules Capable of Disrupting HIF2α Dimerization

Daniel Stroud

Mentor and Collaborators: Uttam Tambar, PhD & Richard Bruick PhD, Department of Biochemistry

The concept of fighting cancer growth with anti-angiogenesis treatment is not new. Currently, Bevacizumab, anti-VEGF antibody, is used in some chemotherapeutic regiments. However, this is limited in that it is specific for only those cells that rely on VEGF. Thus, a need for treatments targeting different angiogenesis pathways has grown. In the past, it has been shown that tetrazolamine derivatives are capable of inhibiting the dimerization of HIF-2α, an important molecular target in the pathway of neovascularization both aberrantly and overly expressed in different cancer cell lines such as certain neuroendocrine tumors. Using the molecular scaffolding of tetrazolamine ring as a base, 24 different derivatives were synthesized and tested to determine an efficacious inhibitor of HIF-2α in terms of Kd and IC50 using Alphascreen and isothermal calorimetry techniques, respectively, after enantiomeric separation. In addition, molecular specificity was demonstrated in vitro for a pair of enantiomers by exposing cells in hypoxic environments to this drug and monitoring its effects on HIF1α and HIF2α pathway regulation. This study, firstly, is a stepping stone for the determination of higher potency compounds targeting HIF2α transcription factor with high selectively, and, secondly, more clearly defines the shape of the molecular binding site in the HIF2α transcription factor and, finally, opens up areas of further research in this family of compounds for biologic studies.

In Vivo Sensory Cortex Dysfunction in Pyruvate Dehydrogenase Deficient Mice

Tyler A. Terrill

Mentors and Collaborators: Vikram Jakkamsetti, PhD, Levi Good PhD,& Juan M. Pascual, MD, PhD
Department of Pediatrics and Neuroscience

Background: Pyruvate Dehydrogenase (PDH) is a critical enzyme in all organisms, providing pyruvate for the Krebs cycle to generate ATP. As a result, PDH-deficient patients develop lactic acidosis and intellectual disability. Processing of sensory information in the cerebral cortex is crucial for intellectual function. We hypothesize that cortical thinning in these patients contributes to aberrant sensory processing and resulting intellectual disability. Specifically, we hypothesize that there exists a deficit in neurotransmission between cortical layers of the primary somatosensory cortex that can be tested in a novel mouse model of PDH deficiency that replicates the cardinal features of the human disorder.
Methods: Wild-type (WT, n=11), GFAP-CrePDHflox/+ heterozygous (GFAPhet, n=7), GFAP-CrePDHflox/flox knockout (GFAPKO, n=10), and Nestin-CrePDHflox/+ heterozygous mice (NChet, n=14) were anesthetized and their cortex exposed. A vertical linear electrode array was modified to stimulate in layer IV and record in layers IV and II. Synaptic activation and neuronal output were reflected on the recorded local field potentials (LFP) and action potentials. In each mouse, we examined spontaneous activity in layer II and IV, evoked response in layer II from stimulation in layer IV, and synchronized spontaneous activity between the two layers.
Results: Spontaneous oscillations of synaptic activation in layer II were significantly reduced in amplitude in both the GFAPKO and NChet mice ($p=.02$, $p=.01$). Thus, spontaneous synaptic input into a processing unit of the sensory cortex is severely impaired. Evoked LFPs in layer II were decreased in the GFAPhet, GFAPKO, and NChet mice ($p<.001$, $p=.002$, $p=.02$). Hence, neurotransmission from layer IV to layer II is significantly decreased. Synaptic oscillations in layer IV and II were less synchronized in NChet mice ($p<.001$) indicating a lack of normal cortical network activity. Additionally, there was electrophysiological evidence of paroxysmal, seizure-like activity in layer 2 of the GFAPKO mice (42% of animals, similar to the EEG of human patients.
Conclusion: We have observed a significant loss of spontaneous electrophysiological activity, evoked response, and synchronization of LFP oscillations in the PDH mutant mice. This implies cortical dysfunction in sensory processing that could contribute to intellectual disability. Treatments targeting this aspect of the phenotype could be beneficial to PDH-deficient patients.

Optimization and Characterization of Poly(lactic-co-glycolic acid)/Poly(propylene fumarate) Nanoparticles For Pediatric Tracheomalacia

Candace Wu

Mentor and Collaborators: Joseph Forbess, MD, Amy Goodfriend, & Tré Welch, PhD
Department of Cardiovascular Thoracic Surgery

Nanoparticles can be utilized for diagnosing, monitoring, and treating diseases. The formulation of polymeric nanoparticles allows for the controlled release of therapeutic agents such as dexamethasone to treat inflammation associated with pediatric tracheomalacia. The ratio of two different polymers was varied to assess the effect of polymer composition on nanoparticle characteristics. Poly(lactic-co-glycolic acid)/Poly(propylene fumarate) (PLGA/PPF) nanoparticles loaded with dexamethasone were synthesized using a solvent displacement method. PLGA 50:50 (50% lactic acid, 50% glycolic acid), PPF, and dexamethasone were dissolved in tetrahydrofuran (solvent) and an aqueous surfactant was added. The mixture was sonicated and solvent was removed via evaporation. Nanoparticles were then washed and passed through a centrifuge filter with a pore size of 0.45 μm. Scanning Electron Microscopy was used to observe nanoparticle morphology. Dynamic light scattering was used to determine nanoparticle size distribution and zeta potential, which is a measure of nanoparticle stability. High performance liquid chromatography was used to determine dexamethasone loading efficiency. Quantitative nanoparticle characteristics were statistically analyzed using a One-way ANOVA ($\alpha < 0.05$) where the 1:1 PLGA:PPF nanoparticles served as the control. The other ratios of PLGA:PPF nanoparticles analyzed were 3:4, 1:2, and 1:4. Control nanoparticles had smoother surfaces, while those with a 1:2 ratio had uneven surfaces, likely due to excess PPF. There was no statistically significant difference in effective diameter between nanoparticles synthesized from the four different polymer ratios ($n = 3$ per group). The effective diameter of the nanoparticles was around 200 nm. There was, however, a significant difference in zeta potential between control nanoparticles and nanoparticles with a ratio of 1:2 and 1:4 ($n = 30$ per group). Control nanoparticles and the 3:4 ratio appeared to be more stable. Finally, the dexamethasone loading efficiencies of 3:4, 1:2, and 1:4 nanoparticles were significantly different from that of the control ($n = 5$ per group). Nanoparticles with a 3:4 ratio had the highest drug loading efficiency (6.66±0.35%), while those with a 1:4 ratio had the lowest (4.01±0.06%). These results suggest that varying the ratio of PLGA:PPF has an impact on nanoparticle morphology, stability, and dexamethasone loading efficiency. Therefore, further investigation of the effect of polymer composition on drug release over time may have important implications in optimizing treatment with dexamethasone-loaded nanoparticles.

Macrophage Involvement in the MRL-lpr Mouse Model of SLE

Diana Yang

Mentor and Collaborators: Benjamin Chong, MD, Lin-chiang Tseng, Jennifer Pham, & Sydney Pedigo
Department of Dermatology

Systemic Lupus Erythematosus (SLE) is an autoimmune disease affecting multiple organs, such as the skin and kidney. Macrophage involvement in lupus has been investigated in some organs, such as the kidney, but has yet to be fully characterized in the skin. This research project is aimed at exploring gene expression of macrophages in the skin of lupus-prone MRL-lpr mice. This project compared the gene expression in the skin of irradiated lupus-prone MRL-lpr mice and Balb-c mice. We postulated that genes associated with M1 pro-inflammatory macrophages were up-regulated in irradiated MRL-lpr skin vs. Balb-c skin.

Skin microarray analysis of MRL-lpr (N=5) and Balb-c (N=5) irradiated with UVB three times per week for 9 weeks showed that irradiated MRL-lpr skin had up-regulated 547 genes and down-regulated 413 genes compared with irradiated Balb-c skin ($q<0.05$, fold change > 1.5). Gene set enrichment analysis showed that up-regulated and down-regulated genes in irradiated MRL-lpr skin did not show significant overlap with those in M1, M2, M2b, or M2c macrophages ($p>0.05$).

Confirmatory qRT-PCR was run for a select set of macrophage-related genes in irradiated Balb-c skin (N=5), irradiated MRL-lpr skin (N=5), and non-irradiated MRL-lpr skin (N=5). The genes studied were the following: AIF1, CCR5 and F4/80 (general macrophage markers); Cxcl9, Stat1, Cxcl10 (M1 macrophage-related genes); Retnla, Csf1R, MMP12, Mrc1 (M2 macrophage-related genes); F13a1 (M2a macrophage-related genes). Irradiated MRL-lpr skin up-regulated M1-associated markers (Cxcl10, Cxcl9 and Stat1) versus irradiated Balb-c skin. Irradiated MRL-lpr skin down-regulated M2 associated markers (Retnla, Csf1R, F13a1) compared with control Balb-c mice. Non-irradiated MRL-lpr skin trended towards up-regulating M2-associated markers (Retnla, Csf1R, F13a1) both in comparison with irradiated MRL-lpr and control Balb-c skin. However, all comparisons did not reach statistical significance.

Overall there is a trend of irradiated MRL-lpr skin upregulating M1-related genes and non-irradiated MRL-lpr skin upregulating M2-related genes compared to Balb-c skin. However, further testing will need to be done as comparisons did not reach statistical significance.

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KEY
Ω Oral Presenter - UT Southwestern Medical Student Research Forum
† NIDDK Medical Student Research Trainee
Û Funded by UT Summer Research Program

Short Messaging Service (SMS) Immunization Reminder Effectiveness at Taybeh Refugee Camp in Amman, Jordan

Seja Abudiab

Mentor: Abier Abdelnaby, MD
Department of Surgery

Introduction: UNRWA refugee camps currently host 1.5 million refugees in five regions of the Middle East. With recent outbreaks of polio and mumps surfacing in refugee camps, the infectious disease burden among refugees highlights the importance of immunizations. While immunization rates in the general region are high, missed immunization appointments increase among displaced groups. With over 75% of the world's population having cell-phone access, the use of Mobile-health and SMS messages to maintain proper immunization schedules provides an opportunity for improvement. This mixed-method study in Taybeh Refugee Camp in Amman, Jordan will focus on delay time in returning for appointments for patients before receiving an SMS-reminder and delay time after receiving a reminder. A relevant issue to the Jordanian telecommunications landscape is the presence of three telecommunication providers: Zain, Umniah, and Orange. The providers have no-contract plans, allowing customers to change their phone numbers regularly. Fluidity in phone numbers causes inconsistency in health clinic records. This prompted the need for a preliminary study on the general effectiveness of mobile health in a no-contract setting.
Method: A preliminary observational retrospective study quantified the influence of changing phone lines on the effectiveness of contacting patients through their mobile devices. After the immunization reminders were sent, individual lines were called in an attempt to verify lines that were closed, wrong numbers, non-responders, and non-defaulters (false positive defaulters). After the preliminary study was conducted, the next round of defaulters with accurate phone numbers recorded in the system received reminders as part of the mixed-method study. Messages were sent to numbers registered with the clinic and with UNRWA databases through *Clickatell*, a mass-texting system; messages were sent after the patient missed an immunization appointment. The message sent to patients who defaulted on appointments read,

> "Your child is overdue for a vaccination. Please call [clinic number] for a new appointment"
> (in Arabic: لقد فات موعد طفلك للتطعيم نرجو الاتصال ب 064127545 لتحديد موعد جديد).

Results: After sending defaulter messages, 170 phone lines were called and of those numbers, 105 were "closed", 9 were "not defaulters", 17 "did not answer" the follow-up phone call, 19 were "wrong numbers", and 20 patients were stated to have received the SMS. Results of the mixed-method study demonstrated that without a reminder, patient delay time averaged 30.7 days. With an immunization reminder, patient delay time averaged 12.2 days.

The Role of Routine Hearing Screening in Children with Cystic Fibrosis Treated with Aminoglycosides: A Systematic Review

Zainab Farzal

Mentors and Collaborators: Gopi B. Shah, MD, Ron B. Mitchell, MD, FACS, Yann-Fuu Kou, MD, & Rachel St. John, MD
Department of Pediatric Otolaryngology

Introduction: Patients with cystic fibrosis (CF) are often subject to pulmonary infections treated with antibiotics such as aminoglycosides which have the side effect of sensorineural hearing loss (SNHL). Since children with CF are often on prolonged courses and/or higher doses, they are particularly at risk.
Objective: To review the role of routine hearing screening for SNHL in children with CF who have been on aminoglycoside therapy.
Data Sources: PubMed, Cochrane, SCOPUS, and OVID databases
Review Methods: A systematic review of the literature was performed in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A comprehensive PubMed MeSH search of the English language literature with human subjects only was performed to include all indexed years and the search strategy was adapted to the additional databases.
Results: Twelve studies (1979-2014) were included in the review. Three of the 12 articles also studied adult CF patients. The study population included 762 children (age range, 5 months–20 years). Objective hearing screening measures included pure tone audiometry (PTA) at standard ± high frequency threshold (12/12), distortion product otoacoustic emissions (DPOAE) (4/12), transient-evoked otoacoustic emissions (1/12), and automated auditory brainstem response (AABR) (1/12). The overall prevalence of SNHL ranged from 0% to 29%. In a subset of children with high levels of exposure, up to 44% had SNHL. Eight studies recommended hearing screening in CF children on aminoglycosides of which 2 studies recommended screening regardless of aminoglycoside exposure. Four studies made no recommendations and in three of these, the children had a short course of aminoglycosides. HFPTA was the most commonly recommended screening measure followed by DPOAEs.
Conclusion: Hearing screenings are quick and inexpensive measures leading to interventions that can prevent significant cognitive and linguistic developmental difficulties in children secondary to hearing loss. Routine hearing screening in children with CF exposed to aminoglycosides is supported by the current literature based on the high prevalence of SNHL in this population. Future studies should define the optimal timing for hearing screening during and after aminoglycoside therapy.

Development and Evaluation of DCE-MRI of the Prostate Using Principal Component Analysis

Alexander Liu

Mentor: Neil Rofsky, MD, Department of Radiology

Purpose: (**a**) To develop an open access image viewer plugin for principal component analysis (PCA) of DCE-MRI; (**b**) To demonstrate the feasibility of using PCA for interpretation of DCE in prostate MRI.

Methods: A free and open-source image-processing software (Osirix, OsiriX Foundation, Switzerland) was used for software development, image visualization and post-processing. Projection maps generated by the PCA method were overlaid on the anatomical images in patients with prostate cancer who underwent 3T MRI of the prostate (Achieva TX, Philips, Netherlands) using a 5-channel cardiac phased array and an endorectal coil.

Discussion: Challenges in prostate cancer include limited sensitivity for early diagnosis of aggressive tumors, poor pre-treatment risk stratification, and over-diagnosis and over-treatment of indolent cancers. DCE-MRI is an important component of the mpMRI of the prostate. Enhancement trajectories are often used as surrogates for angiogenesis (suspicious for cancer), but many approaches do not fully utilize the acquired data, which often involves as many as 30 time points. PCA is a statistical way of examining the main directions of data variation that is easy to implement in clinical practice; the method relies on a region of interest and a rotation angle for rotating the three largest components. Its results are sensitive to ROI placement. However, it offers a quantitative measurement of belonging to a given component, potentially allowing for more precise characterization of the features of a determined region. The stratified projection maps of our variant PCA method also show promise – membership into more than one component is not surprising, so determining strength of membership is also important. Previous techniques considered all nonzero coefficients, but ours allows users to select pixels with significantly large coefficients or classify pixels based on strongest component membership. Potential applications include disease identification, characterization, and evaluation of response to nonsurgical management.

Conclusion: The simplicity, flexibility and robustness of PCA allow users to assess contrast kinetics on DCE-MRI independent from a particular model. This can be achieved using a plugin developed by our group for a free, open-source image viewer. Future efforts exploring PCA's role in the detection of suspected and characterization of known prostate cancer are needed. Finally, investigators can apply this technique to other datasets beyond the scope of prostate cancer.

Is Heated High Flow Nasal Cannula in the Emergency Department Safe?

Tyler Youngman

Mentor and Collaborator: Robert Suter, DO & Genine Siciliano, MD
Department of Emergency Medicine

Background: Heated High Flow Nasal Cannula (HHFNC) provides a relatively new alternative to conventional oxygen therapy in the emergency department setting.
Methods: Patients in Parkland Hospital's Emergency Department were screened for an O2 saturation of <93%. If a subject met the criteria, the student researcher then consulted the respiratory therapist to set up the HHFNC device. After gaining approval from the attending that the subject would be an appropriate candidate for the study, the subject was consented for the study. The respiratory therapist then administered the HHFNC and set the rate and temperature via their own standard protocol for the device. Once the HHFNC was ready, the student researcher measured respiratory rate, pulse oximetry, and dyspnea score at time zero. These values were then recorded at 15 min, 30 min, and 60 min of use. Adverse events were determined by the physician, nurse, respiratory therapist, or subject and documented in the data collection form. Reasons a subject would be withdrawn from the study include non-compliance, withdrawal of consent, a serious adverse event, admitted to the hospital, or a subject requiring higher level of care (bipap or intubation). After competition of the study, the subject was asked if they were comfortable with the device
Results: During the two-month study, we were able to collect data on 15 patients. Out of the 15 patients, 10 patients completed the study with 9 patients feeling comfortable with the device. Two of the patients did not complete the study due to being admitted to Parkland, three ended the study early due to feeling uncomfortable with high heated airflow, and one completed the study but did not like the device. Out of the subjects that completed the study all of their O2 saturations remained above 93 the entire duration of the study, and there were no adverse events.
Discussion: While performing this study, we ran into unexpected difficulties with the initial approval and consent for each patient. As the study required the special assistance of a respiratory therapist, the study was often delayed, as there were no dedicated clinical respiratory research personnel. In a few of the patients who qualified with an O2 saturation of <93, the heated high flow oxygen provided by the machine, often was found to be uncomfortable for patients with mild hypoxia but asymptomatic. HHFNC would likely be more beneficial in patients with acute dyspnea rather than screening by mild hypoxia or oxygen saturation alone. The initial phase of the study was intended to ensure the safety of the device, as it is not yet commonly used in the ED.

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KEY

Ω Oral Presenter Research Forum
† NIDDK Medical Student Research Trainee
¥ R25 NHLBI Research Program Trainee
Û Funded by UT Summer Research Program

Neuroforaminal Bone Growth following Minimally Invasive Transforaminal Lumbar Interbody Fusion with BMP: A Computed Tomographic Analysis

Jonny (Junyoung) Ahn

Mentor and Collaborators: Kern Singh, MD Anton Jorgensen, MD, Abbas Naqvi, BS, Islam Elboghdady, & Khaled Aboushaala, MD
Department of Orthopaedic, Rush University Medical Center
Chicago, IL

Study Design: Computed Tomographic analysis of patients collected in a prospective registry.
Objective: To identify radiographic patterns of symptomatic neuroforaminal bone growth in patients who underwent single-level minimally invasive transforaminal lumbar interbody fusion (MIS TLIF) with bone morphogenetic protein (BMP) utilizing computed tomography (CT).
Summary of Background Data: BMP induces osteoblast differentiation leading to new bone formation. Computed tomographic scans were utilized to characterize BMP-associated heterotopic bone formation with radiculopathy following an MIS TLIF.
Methods: Radiographic analysis of patients who underwent an MIS TLIF with an intervertebral cage and BMP performed by a single surgeon between 2008 and 2012 was performed. Patients who developed recalcitrant post-operative radiculopathy were identified via chart review. Post-operative CT images (axial and sagittal sections) were analyzed to identify patterns of neuroforaminal bone growth. Independent t-test was utilized to compare the area of neuroforaminal bone growth between cohorts.
Results: Post-operative CT images were compared between 16 symptomatic and 12 asymptomatic patients. The mean area of bone growth at the disc level on axial imaging (164.0±94.5 vs 83.4±106.8 mm^2) and at the lateral recess (78.6±69.8 vs 6.4±12.9 mm^2) as well as in total cross-sectional area (286.2±168.9 vs 118.3±120.7 mm^2) was greater in symptomatic patients ($p<0.05$)**.** On sagittal imaging, the mean bone growth at the foraminal level (123.4±115.2 vs 45.6±52.3 mm^2) and the total bone growth (310.9±341.6 vs 97.2±75.7 mm^2) were greater in symptomatic patients ($p<0.05$). The mean amount of BMP utilized was similar between symptomatic and asymptomatic patients.
Conclusions: In patients who undergo MIS TLIF with BMP, there is an association between recalcitrant post-operative radiculopathy and neuroforaminal bone growth as measured on computed tomographic imaging. Increased total neuroforaminal bone growth was associated with post-operative radiculopathy. The association between the extension of bone growth toward the traversing nerve root and radiculopathy following BMP application was most significant.

Pre-operative Narcotic Utilization: Accuracy of Patient Self-Reporting and its Association with Post-operative Narcotic Consumption

Jonny (Junyoung) Ahn

Mentor and Collaborators: Kern Singh, MD, Abbas Naqvi, BS, Daniel D. Bohl, MPH, Islam Elboghdady, & Khaled Aboushaala, MD

Objective: To compare post-operative narcotic consumption between pre-operative narcotic users who do and do not self-report pre-operative utilization.
Summary of Background Data: Post-operative pain management following spine surgery can be difficult; however, little is known regarding the accuracy of reporting pre-operative narcotic utilization.
Methods: Patients who underwent anterior cervical discectomy and fusion (ACDF), minimally invasive (MIS) lumbar decompression (LD), or MIS transforaminal lumbar interbody fusion (TLIF) between 2013-2014 were prospectively identified. Accuracy of self-reporting of pre-operative narcotic consumption was determined utilizing the Illinois Prescription Monitoring Program (ILPMP). Total post-operative narcotic consumption during post-operative days 0 and 1 were converted to oral morphine equivalents (OME) and analyzed.
Results: A total of 197 patients met inclusion criteria. Of these, 25% did not utilize narcotics pre-operatively, while 47% and 28% did do so with accurate and inaccurate reporting, respectively. Patients who utilized narcotics pre-operatively were more likely to demonstrate elevated post-operative narcotic consumption (adjusted RR=5.4, 95% CI 1.3-20.5, $p<0.001$). Among patients who utilized narcotics pre-operatively, no difference was demonstrated in post-operative narcotic consumption between those who inaccurately and accurately reported their pre-operative utilization ($p=0.151$). The only pre-operative factors that were independently associated with elevated post-operative narcotic consumption were Worker's compensation status and procedure type.
Conclusion: These findings highlight the significant proportion of patients who utilize narcotics pre-operatively, who inaccurately disclose this information to their treatment team, and who require increased post-operative narcotics. These findings also suggest that patients who utilize narcotics pre-operatively, but do not report this to their treatment team, demonstrate similar post-operative narcotic consumption to those who accurately report pre-operative narcotic utilization. Taken together, these data suggest that in order to anticipate post-operative narcotic consumption, it is important to determine whether patients utilize narcotics pre-operatively, and that because patients often report this inaccurately, corroborating information is critical.

Do More Choices Provide Better Treatment: Flow Diversion of Proximal Carotid Aneurysms at a Comprehensive Cerebrovascular Center

Jake Alford

Mentors: Babu Welch, MD, & James Botros, MD
Department of Neurological Surgery

Introduction: The evolution of endovascular techniques has vastly increased the treatment options available for repair of complex intracranial aneurysms of the proximal internal carotid artery. However, more treatment options result in more complex treatment decisions. The recent addition of flow diversion has the potential to challenge results of traditional microsurgical treatments. In order to analyze trends in patient management decisions and outcomes, the treatment of unruptured proximal carotid aneurysms by neurosurgeons at a single comprehensive cerebrovascular center was compared before and after the availability of an endovascular flow diversion device. We hypothesize that more treatment options will lead to better patient outcomes.
Methods: From 2008 to 2013, 259 unruptured proximal carotid aneurysms were treated in 213 patients at a single comprehensive center. Patients with similar age, aneurysm size, and pre-operative severity (SASI) were categorized according to the presence of a flow diversion device (PED) at the time of their treatment. Treatment modality, lesion occlusion, retreatment rates, stenosis, and neurological symptoms were retrospectively reviewed.
Results: For all patients in which PED was a potential treatment option, retreatment rates decreased from 10% to 5%, occlusion rates remained similar (81% to 79%), while the presence of treatment related vessel stenosis increased from 10% to 12%. Overall rates of improvement in neurological symptoms remained similar (94% to 95%). For patients specifically treated with PED, 80% had complete occlusion, 13% showed stenosis, 0% underwent retreatment, and 87% showed improvement in neurological symptoms. The percentage of patients treated by microsurgery decreased from 40% to 26%.
Conclusions: The positive outcomes of patients treated with PED and lack of predicted complications suggest that PED is a viable treatment option for proximal carotid aneurysms. The overall decrease in retreatment rates, shift in treatment type, and evidence of improved treatment in other modalities suggest that patients are better matched to specific treatments.

Pediatric evaluation of hypoglycemia in pediatric seizures: Necessity of Nuisance

Vincent Au

Mentors: Scott Golberg, MD & Phillip Ewing, MD
Department of Emergency Medicine

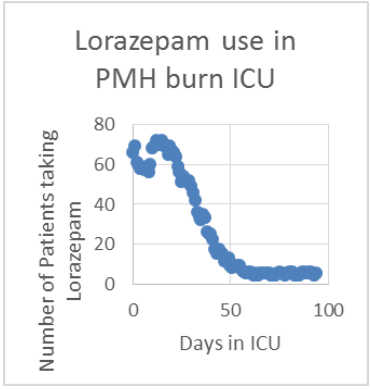
Background: While febrile seizure is the most common cause of pediatric seizure, hypoglycemia is an important and potentially correctable etiology. Current guidelines recommend a blood glucose analysis for all seizure patients regardless of age, including those occurring out of hospital. Previous studies have demonstrated a low rate of paramedic glucose analysis in the pediatric population but have not evaluated patient outcomes. The purpose of this study was to evaluate paramedic capillary blood glucose (CBG) analysis of pediatric seizure patients and to identify the rate of missed hypoglycemic seizures.
Methods: The call database of a large metropolitan, all-ALS, firebased EMS service was queried for chief concern or paramedic impression of seizure over a 1 year period. Patients 13 years old or younger transported to a tertiary care pediatric hospital were included and cases matched to hospital records. Prehospital CBG, ED CBG, ED diagnosis, and disposition were recorded. Hypoglycemia was defined as a CBG of <60 mg/dL.
Results: From April 2013 through March 2014, 429 cases were identified. 33 cases with missing data were excluded. Prehospital CBG analysis was performed in 195 cases (49%). 8 cases (2.0%) of hypoglycemia were identified in the field. 2 cases (0.51%) of hypoglycemia found on ED arrival were not identified by EMS, although seizure in neither case was felt to be a result of hypoglycemia. In two cases hypoglycemia was felt to be the cause of seizure, and both (100%) were identified in the field. All cases of hypoglycemia identified by paramedics were treated.
Discussion: Despite guidelines, paramedics are hesitant to evaluate blood glucose in pediatric patients for a variety of reasons including perceived lack of need and fear of patient discomfort. Our study confirms a low rate of paramedic glucose evaluation, in line with previous literature. However, few pediatric seizures are the result of hypoglycemia and protocolized CBG analysis in pediatric seizure patients may not be necessary in the absence of persistent symptoms. In our evaluation no cases of hypoglycemia resulting in seizure were missed. However, given the low rate of hypoglycemic seizure in our population larger studies are necessary prior to definitive recommendations.

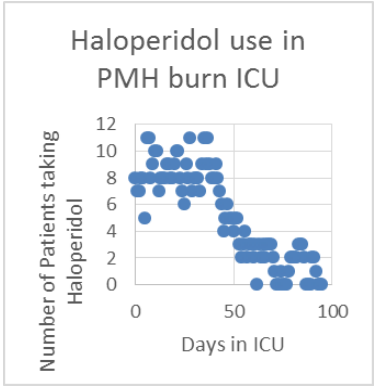
The Use of Non-Opioids for Anxiety and Delirium in the Severely Burned

Shawn Banon

Mentor and Collaborators: Steven Wolf, MD & Eunjin Jang
Department of General Surgery

Severe pain is one of the hallmarks of treatment and recovery after a significant burn. Previous analyses have not yet assessed some of the other common problems and complaints of the severely burned that are associated with pain, namely anxiety, delirium, and depression. These have all been closely related to recovery from injury, but screening and treatment are generally not standardized. In an effort to assess prevalence of these conditions, we chose to use a non-standardized approach to perform an empiric analysis of these problems through assessment of the use of non-opioid psychotropic medications. The population of interest includes all patients admitted to the burn intensive care unit between January 2011 and March 2014 with a total body surface area (TBSA) burn of greater than 20% (190 patients); the population has an average age of 36.47, an average TBSA burn of 35.22%, and an average ICU length of stay of 28.74 days. The two most common non-opioid psychotropic medications administered to this population were lorazepam (78.42%) and haloperidol (24.74%). The next most common were citalopram (5.79%), sertraline and diazepam (both 4.74%). Significant correlations were found between ICU length of stay and lorazepam treatment length (.8258) as well as ICU length of stay and haloperidol treatment length (.482). In addition, significant correlations were found between ICU length of stay and lorazepam use/nonuse ($P < .0001$), ICU length of stay and haloperidol use/nonuse ($P < .0001$), as well as TBSA burn size and haloperidol use/nonuse (P - .0053). 20.53% of the population was prescribed a non-opioid psychotropic medication upon discharge from the ICU.





Comparison of Pre-Transplant Criteria and Outcomes for Living Donor Kidney transplant Programs in India and the United States

Sukriti Bansal

Mentor and Collaborators: Hari Raja, MD, Vijay Kher, MD, & Nilum Rajora, MD
Department of Internal Medicine- Nephrology
UT Southwestern Medical Center & Medanta the Medicity Hospital
Gurgaon, India

Background: One of the greatest obstacles to treatment of end stage renal disease globally is organ donor shortage. While some nations (i.e. the US), have primarily cadaveric organ donors, developing nations rely heavily on living donors. This project is a comparison of two kidney transplants programs– one in the US & one in India – looking at the pre-transplant criteria of each & assessing the patient outcomes.
Methods: This is a cohort study of living donor kidney transplant patients from St. Paul University Hospital in Dallas, TX & kidney transplant patients from Medanta the Medicity in Gurgaon, India. Data for India was collected from a database of all patients who underwent a kidney transplant at Medanta, selected for patients who fit the following criteria: one cohort of patients had been transplanted the previous month (N=29), one cohort had been transplanted one year prior the date of the study (N=29), & one cohort had been transplanted 3 years prior (N=13). Information from the database was used to calculate patient & graft survival rates for the relevant time periods. Data for St. Paul was obtained from the Scientific Registry of Transplant Recipients, which already had the calculated 1 month, 1 year, & 3 year patient and graft survival rates. Information on pre-transplant criteria was obtained from the transplant teams at each respective institution.
Results: The majority of medical pre-operative criteria between the two programs are identical. One significant difference is ABO-incompatible transplants are performed at Medanta, while at St. Paul ABO-incompatible donor/recipient pairs are referred for paired donation. Medanta requires all living donors to be related, while St. Paul will accept unrelated donors. The patient survival rates for St. Paul are 100% (1 mo, N=32), 95.23% (1 yr, N=32) and 85.71 % (3 yr, N=21). Graft survival rates are 100% (1 mo, N=32), 95.24% (1 yr, N=32), and 81.82% (3 yr, N=22). The patient survival rates for Medanta are 100% (1 mo., N=29), 100% (1 yr, N=29), and 100% (3 yr, N=13). Graft survival rates are 100% (1 mo. N=29), 100% (1 yr, N=29), and 100% (3 yr, N=13). For all patients transplanted at Medanta, the overall patient survival rate was 98.40% (N=874) and the overall graft survival rate was 98.51% (N=874). Corresponding data wasn't available for St. Paul.
Conclusion: While it appears that the 3 year survival rates are better for Medanta than for St. Paul, there is a limitation on making conclusions because this data does not encompass the entire program at Medanta. Further study is needed to truly assess if there is a significant difference. The overall conclusion is that transplant programs in both settings have successful outcomes.

Traumatic skull base injuries – A retrospective study of incidence, management, complications and outcomes

Agnelio S. Cardentey

Mentor: Samuel Barnett, M.D.
Department of Neurological Surgery

Background: A subset of patients that have sustained head and maxillofacial trauma will also present with injuries to the skull base. Basilar skull fractures (BSF) are associated with a high risk of morbidity and mortality due to predisposition to cerebrospinal fluid leaks (CSF) and possible meningitis. Currently, studies of the incidence and treatment of these fractures are limited to small case series.

Objective: Conduct a large retrospective chart review of the treatment and outcomes for patients with skull base injuries.

Methods: The medical records of all patients with skull fractures who presented to a single level 1 trauma center, from 2007-2012 are being reviewed. Patients diagnosed with skull base fractures will be identified and information including age, sex, mechanism of injury, associated injuries, treatments, Lumbar Drain (LD)/External Ventricular Drain (EVD) placement, complications, and outcomes were collected. Correlations between mechanism of injury, treatments, complications, and outcomes will be analyzed.

Results: Currently 109 patients with a basilar skull fracture have been included in the study. 20 (18.3%) patients were dead upon arrival or died from their injuries. Of the 14 (12.8%) patients diagnosed with CSF leaks, 1 (7.1%) was subsequently diagnosed with meningitis and recovered, and an EVD or LD was placed in 10 (71.45%) of the patients, 4 (28.6%) underwent surgical repair, 1 (7.1%) died as result of their injuries and the remaining patients recovered and eventually discharged from the hospital. Most common mechanism of action is MVC at 35.7%. Most common BSF associated with CSF leaks include Temporal (57.1%), Sphenoid (57.1%) and Ethmoid (50%) with all traumatic CSF leaks involving either/or Temporal, Sphenoid, Ethmoid fractures.

Conclusion: The study is pending further data collection, chart review, and analysis.

Hippocampal Volume Changes in Patients with Asthma

Scott Carlson

Mentor: Sherwood Brown, MD, PhD
Department of Psychiatry

Background: Prior research suggests a possible association between asthma and decreased hippocampal volumes.
Objective: This study examines the association between asthma and hippocampal volume.
Methods: We conducted an analysis of participants in the Dallas Heart Study (DHS). The DHS collected an epidemiological sample of Dallas County residents to explore risk factors for heart disease. Included were 1,287 adults with complete data on study variables and without history of stroke, emphysema, or more than 5 drinks per day. Study variables included gender, age, race, and education as demographic characteristics, cognitive ability measured by the Montreal Cognitive Assessment (MoCA), and brain segment volumes measured by FreeSurfer. Study outcome variables were total, right, and left hippocampal volumes measured using FreeSurfer. General Linear Models (GLM) were conducted to examine the association of asthma diagnosis with hippocampal volumes after controlling for demographic characteristics, total MoCA score, and brain segment volume. Analysis of Variance (ANOVA) was used to examine the effect of gender on hippocampal volumes.
Results: The prevalence of lifetime asthma diagnosis among our study samples was 10.8% with 9.6% in males and 11.7% in females. Our study participants with a self-reported asthma diagnosis had significantly smaller estimated total, right, and left hippocampal volumes (95% CI 0.13%-2.9%; p = 0.03) than those without an asthma diagnosis. Asthma was significantly associated with total, right, and left hippocampal volumes in males, while not significantly associated in females after controlling for demographic characteristics, total MoCA score, and brain segment volume. Total, right, and left hippocampal volumes of males with asthma diagnoses, respectively, were 3.0% smaller (95% CI 0.77%-5.2%; p = 0.008), 2.9% smaller (95% CI 0.58%-5.2%; p = 0.014), and 3.1% smaller (95% CI 0.70%-5.6%; p =0.012) than males without asthma.
Conclusion: Hippocampal volume in a large and diverse sample of adults was significantly smaller in people with asthma as compared to those without asthma. This difference in volume was limited to males. These findings suggest that asthma may be associated with structural brain differences as well as respiratory effects. Because the hippocampus is a brain region involved in memory formation these findings may have implications for treatment adherence.

Real World Outcomes of Prasugrel and Ticagrelor versus Clopidogrel in Acute Coronary Syndrome Patients undergoing Percutaneous Coronary Intervention

Howard Chao

Mentor and Collaborators: Andres Guerra, Henry Han, Alan Sosa, Georgios Christopoulos, Muhammad Nauman Tarar, Kevin Kelly, Rick Weideman, Michele Roesle, Bavana V. Rangan, Subhash Banerjee, Emmanouil S. Brilakis, MD, PhD
Department of Internal Medicine- Cardiology, University of Texas Southwestern Medical Center & VA North Texas Healthcare System

Background: ADP P2Y12 inhibitors are routinely administered after percutaneous coronary intervention (PCI) to prevent stent thrombosis. The newer P2Y12 inhibitors, prasugrel and ticagrelor, reduced the incidence of major adverse cardiac events (MACE) compared with clopidogrel in clinical trials of acute coronary syndrome (ACS) patients, but have received limited study in routine clinical practice.
Objective: To compare the outcomes of prasugrel and ticagrelor with clopidogrel in real world ACS patients undergoing PCI.
Methods: The medical records of all patients who underwent PCI at our institution between January 2011 and November 2013 were reviewed. The 12-month incidence of MACE (death, myocardial infarction, and repeat coronary revascularization) and bleeding was compared between patients who received a novel P2Y12 inhibitor (prasugrel or ticagrelor) and a random sample of those who received clopidogrel.
Results : Two hundred and one patients who underwent PCI for ACS were included: 80 received either prasugrel or ticagrelor and 121 received clopidogrel. Mean age was 63.7 ± 9.3 years and 99% of the patients were men. The two study groups had similar baseline characteristics. The 12-month incidence of MACE in the novel P2Y12 inhibitor subgroup was 23% versus 33% in the clopidogrel subgroup ($p = 0.25$). Patients receiving prasugrel or ticagrelor had lower incidence of all cause ($p < 0.01$) and cardiac ($p = 0.05$) death, and similar incidence of bleeding.
Conclusion: In a non-selected ACS population use of a novel P2Y12 inhibitor was associated with lower incidence of death and similar incidence of bleeding as compared with clopidogrel.

Comparison of Video-Assisted Thoracoscopic (VATS) Lung Biopsy vs. Bronchopulmonary Alveolar Lavage (BAL) for Diagnosis of Fungal Disease in Pediatric Oncology Patients

Jeffrey Compton

Mentor and Collaborators: Joseph T. Murphy, MD, Lorrie Burkhalter; Shannon Cohn, MD
Department of Pediatric Surgery

Background: Pulmonary fungal infection is a known complication of the treatment of pediatric malignancy. Accurate diagnosis has relied on culture of fungi from either pulmonary lavage fluid or open biopsy of lung parenchyma. Minimally invasive lung biopsy techniques have decreased the morbidity and mortality of diagnostic lung biopsy procedures, however little data exists comparing diagnostic yields (DY) of bronchopulmonary lavage (BAL) lung washings versus video-assisted thoracoscopic surgery (VATS) tissue biopsy.

Methods: With IRB approval, the Oncology Registry and Electronic Medical Records at our institution were queried for pediatric oncology patients (age<18yrs) who have had either BAL and/or VATS for assessment of possible pulmonary fungal infection as suggested by CT imaging during treatment for various malignancies from March 2005 to May 2014 for a retrospective analysis.

Results: 106 pediatric oncology patients were identified to have undergone 146 procedures (116 BAL; 30 VATS) resulting in overall yield of 39 pulmonary fungal infections (30 BAL; 9 VATS). Overall DY was 27%, (BAL 26%; VATS 30%). While 25 patients had multiple procedures; 14 patients had sequential evaluations within 4 weeks to assess for persistent infection: 7 had multiple BAL; 1 had multiple VATS; 8 had BAL and VATS. Of the 8 who had sequential BAL and VATS procedures; in 50% the results were consistent (3 cases BAL/VATS both negative; 1 case BAL/VATS both positive); and 50% were discordant (2 had positive BAL / negative VATS; 2 had negative BAL / positive VATS). The combined use of both procedures within 4 weeks resulted in a 63% DY when all positive findings are considered.

Conclusion: BAL and VATS procedures individually resulted in comparably low diagnostic yields for detection of pulmonary fungal infection in pediatric oncology patients; however when these procedures are employed sequentially within 4 weeks of each other, the diagnostic yield increased substantially.

Geographical Mapping of Malnutrition from EMR Data

Alec Coston

Mentor: Franklin Jostin, MD & Michial Mularoni
Department of Pediatrics

Background: In Haiti, the problem of malnutrition is especially severe, exacerbated by the 2010 earthquake and a brutal rainy season. Local mapping of malnutrition with geographical information systems (GIS) makes it possible to analyze underlying geospatial risk factors of a region. In Port Salut, Klinik Timoun Nou Yo (KTNY) runs a nutrition program for affected children, and needs a tool for tracking their patient population.

Objective: A GIS tool is needed that is flexible and easy for clinical staff to operate. The tool will allow visualization of the geographical distribution of patients treated for malnutrition at KTNY. This information will aid in the analysis of malnutrition hotspots and seasonal admission trends, allowing the clinic to anticipate patient load and prepare resources effectively.

Methods: The GIS tool, called "KTNY Tracker" is written in python as a plug-in for the free software QGIS. As a proof of concept, patient data from 2013 and 2014 was uploaded and processed by the software, in order to qualitatively compare the yearly change in patient burden of the relatively new clinic, as well as assess the absolute patient distribution.

Results: The maps output by the software show a noticeable increase in patient load as well as catchment area from 2013 to 2014. This is most likely due to increased awareness about the clinic and its growing reputation, as well as extended efforts of patient pickup from remote areas. The map of overall patient load from 2013 to 2014 showed an expected high density of patients along the coastline, as well as low-density zones that may correlate with mountainous terrain, a lack of population, or other factors. These preliminary finding could be analyzed to elicit its true cause.

Discussions: KTNY Tracker in combination with QGIS's native functionality will prove to be a useful tool in visualizing clinical data and requires minimal training and experience to operate. Maps generated by this tool can serve as a visual advocate for more funding and resources for the clinic's malnutrition program. In the future, functionality will be added to assess follow-up success and failure rates, among other statistical tools for quantifying the visual data. The software is still in development, but it has promising potential as a clinical aid and as a launch pad for further studies.

Determination of Respiratory Depression measured by Capnography of Acutely Intoxicated Patients presenting to an Urban Emergency Department

Colin Danko

Mentors: Nancy Onisko, DO, & Kurt Kleinschmidt, MD
Department of Emergency Medicine

Introduction: The standard of care for monitoring the respiratory status of patients with altered sensorium until recently has been pulse oximetry and observation. While pulse oximetry measures peripheral arterial oxygen saturation, it does not adequately detect hypoventilatory status. We hypothesized that intoxicated patients would demonstrate clinically significant signs of hypoventilation and that ETCO2 monitoring may detect these changes earlier than pulse oximetry.
Methods: This was a pilot observational data collection study of intoxicated patients presenting to a single urban emergency department between June 6, 2014 and August 1, 2014. Research assistants (RA's) monitored the ED tracking board for patients presenting with chief complaints suggesting possible intoxication with drugs or alcohol. Patients eligible for enrollment were between age 18-80 years, had a baseline Rikers Sedation Agitation Scale Score of ≤ 3 and the treating ED physician believed that the patient's altered mental status was "possibly" or "probably" related to use of an intoxicant. Vital sign data and end-tidal CO2 readings were collected at Baseline, 30, 60, 90 and 120 minutes then hourly there after. End points for data collection were: 1) demonstration of alertness for at least 60 consecutive minutes 2) disposition to home or another hospital department or 3) decompensating respiratory status requiring bi-pap, c-pap or intubation.
Results: Seven hundred ninety four patients were screened. Thirty-five met all enrollment criteria and were assigned a de-identified patient number. Six patients were excluded from the final data analysis (5 for critical errors in ETCO2 data collection and 1 had AMS of non-intoxication etiology). Of the remaining 29 patients, 20 were male, 9 female. Ages ranged from 19-54 yrs. Alcohol was one of the intoxicants in almost half of patients. Other intoxicants included benzodiazepines, synthetic cannabinoids, cocaine, heroin and diet pills. Some patients had exposure to more than one intoxicant. ETCO2 values of > 45 mmHg were considered indicators of hypoventilatory state. There were a total of 19 episodes of hypoventilatory status as indicated by ETCO2 > 45 mmHg. Of the patients with multiple episodes (> 2) of hypoventilatory status, two had used heroin, one 62 mg lorazepam. Pulse oximetry reflected a normal oxygen saturation during at least 6 of the episodes.
Conclusion: ETCO2 may detect hypoventilatory status before pulse oximetry and should be standard of care in patients presenting with intoxication associated with CNS depression.

Prevalence of Prescription Medication Misuse in Patients presenting to Emergency Department in Dallas County

Jennifer Davis and Thomas Schaeffer

Mentors and Collaborators: Jakub Furmaga, MD, Kurt Kleinschmidt MD, Paul Wax MD, Amy Young MD, & Kelsey Drake MD
Department of Emergency Medicine

In the early 1990s multiple studies displayed the inadequate treatment of acute pain for patients presenting to Emergency Departments across the U.S. As a result, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) modified the standard of care in regards to acute pain management, which required more consistent assessments and diligent treatments. Subsequently, the average number of prescribed opioid analgesics in the U.S. increased from 96 mg of morphine equivalents per person in 1997 to approximately 700 mg per person in 2007. Furthermore, the number of unintentional opioid drug overdose deaths increased from 3,000 to 12,000 per year. Clinicians and policy makers are now working to reduce the effects of this new prescription drug epidemic.

Data for this study was collected from patients presenting to the ED of Parkland Memorial Hospital (PMH) with a chief complaint of 'back pain' or 'back injury' via a confidential, self-reporting survey designed to obtain demographic information, a brief medical history, and pain and anxiety medication use habits. Statistical analysis of 132 patients revealed that 71 (53.8%) patients have used prescription pain or anxiety drugs in the past 3 months, with 30 (22.7%) utilizing them on a daily or near daily basis. Although only 6 (4.6%) patients admitted to struggling with pain or anxiety medication misuse and 0 (0%) admitted to utilizing current prescription medications for recreational purposes, 12 (9.1%) reported personal troubles, 12 (9.1%) reported a failure to do what was normally expected of them at some point in the past 3 months, and 9 (6.8%) reported a friend or relative expressing concern about substance use. 24 patients reported having a current prescription for pain or anxiety medication. Of these, 17 (70.8%) were obtained from either ED or primary care physicians.

A number of relationships were also analyzed in order to determine at-risk individuals. Education level showed a statistically significant association with pain or anxiety medication use in the past 3 months ($p=0.003$), while a history of chemical dependence therapy was correlated with the expression of concern from friends or family in regard to substance use ($p=0.02$).

This data may be used to determine the prevalence and cause of prescription drug misuse among patients presenting to EDs, providing clinicians with promising areas of intervention. Understanding the scope of the issue, coupled with the ability to prevent habitual drug misuse prior to its initiation, may serve to alleviate some of the negative effects associated with this new epidemic.

Timeline of Glaucoma

David Eng

Mentors and Collaborators: Karanjit Kooner, MD, Andrew Plummer, David Seamont, Xilong Li, Beverley Huet
Department of Ophthalmology

Purpose: To established a timeline of risk factors and comorbidities in patients with primary open angle glaucoma (POAG).

Methods: In an IRB-approved cross-sectional study, patients with POAG in at least one eye were interviewed. Patients with secondary or congenital glaucoma were excluded. Patients were selected from a university-based clinic, a county hospital, and a VA hospital. Data were collected for the following variables: sex, age, race, family history, date of POAG diagnosis, comorbidities, severity of comorbidities, and date of comorbidity diagnosis. A descriptive analysis was done to determine the mean age at diagnosis and percent of patients with each comorbidity.

Results: Of the 304 patients interviewed, 51.4% had a family history of POAG, 32.7% had myopia, 81.2% had cardiovascular disease (CVD), 39.6% had rheumatoid or immune disease (RID), 43.2% had endocrine or metabolic disease (EMD), 23% had a history of cancer (ONC), and 3.3% had a history of breast cancer (BC). The average age at diagnosis for each disease were as follows: CVD, 52.78±15.2; RID, 52.92±18.4; EMD, 55.49±13.32; POAG, 56.51±14.26; ONC, 62.50±12.36; BC, 63.60±9.65.

Discussion: In this study, CVD, EMD, and RID were diagnosed before POAG, and ONC and BC were diagnosed after POAG. Although the standard deviations for age at diagnosis were high, the general sequence of disease presentation appeared as listed previously. Because this was a descriptive study, no controls were recruited. Bias based on patient population cannot be ruled out.

Conclusions: This timeline provides a snapshot of the global associations of POAG and encourages us to be aware of the potential role of comorbidities in the progression of POAG. A longitudinal study may help further elucidate the sequence of events before and after a diagnosis of POAG.

Occult Malignancies of the Facial Nerve

Tyler Enos

Mentor and Collaborators: Brandon Isaacson, MD, FACS Sachin Gupta, MD
Paul Friedman, MD, & J. Walter Kutz Jr., MD, FACS
Department of Otolaryngology

Facial nerve paralysis is a debilitating condition that has a number of etiologies. The most common cause of facial paralysis is Bell's palsy, which generally has an excellent prognosis. For this reason, patients with facial nerve malignancies presenting with facial paralysis are often misdiagnosed and appropriate treatment is delayed. The characteristics of occult facial nerve malignancies are inconsistent with those of Bell's palsy. Careful evaluation is paramount in uncovering the underlying etiology, as the consequences due to delayed treatment are detrimental. We describe the clinical presentation, operative findings, and postoperative course of five patients with occult malignancies involving the facial nerve initially diagnosed as Bell's palsy. A retrospective chart review of patients who presented with prolonged facial paralysis to the UT-Southwestern Department of Otolaryngology from January 2006 to June 2014 was undertaken. Five cases remained after excluding those with facial paralysis secondary to causes other than malignancy, incomplete records, or whom were lost to follow-up. The five patients included one female and four males, with ages ranging from 50 to 71 years. The delay from their initial presentation to surgical intervention ranged from seven to 26 months, and all received treatment for Bell's palsy upon initial evaluation. Four of the five patients had a history of cutaneous facial skin lesions with prior excisions of those lesions ranging from four days to five years prior to facial paralysis symptoms. Each patient was further evaluated after their paralysis did not improve after treatment for Bell's palsy, and initial imaging studies did not demonstrate a lesion of the facial nerve. Upon presenting to the senior authors, repeat review of the radiologic images revealed pathology in each case, and surgical intervention was undertaken. Additionally, each patient completed either radiation therapy or combination radiation and chemotherapy. Three patients continue close follow-up to evaluate for disease recurrence, one patient is being treat for lung metastases, and one patient has expired due to metastasis to the brain. Clinicians must remain vigilant in the evaluation of patients presenting with facial paralysis. Often there is information from a careful history and physical exam that can discern a true Bell's palsy from a more serious condition. Patients with persistent facial paralysis, slow onset of paralysis, and previous regional skin cancer should undergo a thorough evaluation for a facial nerve neoplasm. Despite a history of previous unremarkable radiologic studies, clinicians must closely review and evaluate these images for occult neoplasms.

Patterns of propranolol use in severely burned patients

Melanie Evans

Mentor and Collaborators: Steven Wolf, MD, Melody Seaman, Shea Finch, Anges Burris

Department of General Surgery

Introduction: Severely burned patients are affected by hypermetabolism associated with a hypercatecholamine state. The use of beta blockade with propranolol has been previously employed in children, effectively decreasing adrenergic stimulation and improving energy expenditure. However, the effects of propranolol in adult burn patients has not been well explained and can be associated with episodes of mild hypotension not observed in children. It was our focus to describe the pattern of propranolol use in severely burned adults and evaluate the resulting effects on the cardiovascular system.

Methods: We retrospectively reviewed the electronic medical records of burned adults admitted to the regional burn center ICU between January 2011 and February 2012. We included patients with a total burn surface area (TBSA) burn greater than 20% who received propranolol orally. We recorded the initial propranolol dose, any dose changes or holds, and patient hemodynamics. Statistical analysis was performed with Sigma Plot.

Results: Thirty patients out of 344 met our criteria. The mean age was 39 years (± 3 SEM) and the median TBSA burn was 31% (27, 60 [IQR]). Hospital stay was a median of 24 days (20, 51 [IQR]) with 9 (4, 27 [IQR]) median ICU days. The median propranolol start day was on day 3 (2, 4 [IQR]). Propranolol was held at least once in 23 patients with a median of 4 holds (1, 7 [IQR]). One patient had a maximum of 18 holds. Medication holds due to hypotension were documented in 13%, the remaining holds were undocumented. The dose was changed a median of 1 time (0, 3 [IQR]) and up to 5 times in one patient. Starting doses ranged from 10 to 80mg with the majority of patients, 37%, starting at 20mg. Dose was increased in 32% , and 8% of patients had a decrease in dose. The final doses ranged from 10 to 120mg of propranolol with the majority, 27%, still at 20mg. There was a statistically significant decrease in mean heart rate from 120 (± 2 SEM) prior to propranolol use to 107 beats per minute (± 2 SEM) at 2 weeks after injury ($p<0.001$). No patients were prescribed propranolol at discharge.

Conclusions: Propranolol in severely burned adults appears to be tolerated in this retrospective review. However, there were medication holds and we infer doses were lowered due to hypotension. Overall we found that propranolol did significantly decrease heart rate in severely burned adults. Further clinical trials are required to evaluate outcomes with propranolol use in adult burn.

Volumetric Analysis of the Nasal Cavity in Pediatric Patients with Unilateral and Bilateral Cleft Lip and Palate

Zainab Farzal

Mentors and Collaborators: Julia S. Kimbell, PhD, Amelia F. Drake MD, FACS, Jonathan Walsh, MD, Carlton J. Zdanski, MD, FACS, Luiz A. Pimenta, DDS, MS, PhD

Department of Otolaryngology/Head and Neck Surgery, University of North Carolina at Chapel Hill

Objective: Pediatric patients with cleft lip and palate (CLP) often suffer from nasal obstruction which may be related to alterations in nasal volume due to the anatomic and physiological changes associated with clefts. The objective of this study is to compare nasal volume and side:side volume ratios in patients with unilateral and bilateral CLP with age-matched controls.
Study Design: Retrospective case-control study with three-dimensional nasal airway reconstructions
Methods: We analyzed 20 pediatric subjects (age range: 7-12 years; 14 males, 6 females) with unilateral or bilateral CLP from a regional craniofacial center who underwent cone beam CT (CBCT) prior to alveolar grafting. Age-matched controls (5 males, 5 females) who had undergone standard head and neck CT imaging were also analyzed. The CT scans were loaded into Mimics™ software (Materialise, Inc.) which was used to create 3-dimensional reconstructions of the main nasal cavity and compute total and side-specific nasal volumes. Only those with symmetrically patent airways were included to control for active nasal cycling, the alternating congestion and decongestion of nasal veins between the nasal airway sides.
Results: There was no statistically significant difference in affected:unaffected side volume ratios in unilateral CLP ($p=0.28$) or left:right ratios in bilateral CLP ($p=0.76$) when compared to left:right ratios in controls. Mean overall nasal volumes (mm^3) were 9932±1807, 6954±2577, and 6626±2135 for control, unilateral, and bilateral CLP patients, respectively. Statistically significant decreases in volume for both unilateral and bilateral cleft subjects were noted when compared to controls ($p<0.001$).
Conclusion: This is the first study to analyze nasal volumes in patients with bilateral CLP. Overall nasal volume is compromised in unilateral and bilateral CLP patients by approximately 30%. This finding may correlate with the high prevalence of oral breathers among patients with CLP which is particularly of concern since oral breathing has been associated with slowed facial growth. Additionally, our finding of no major difference in side:side ratios in unilateral CLP compared to controls suggests that variances in our study differed from others due to exclusion of CT scans with active cycling and inclusion of the entire nasal cavity.

The Reverse-Flow Facial Artery Buccinator Flap for Skull Base Reconstruction: Key Anatomic and Technical Considerations

Zainab Farzal

Mentors and Collaborators: Adam M. Zanation, MD, FACS, Ana M. Lemos, MD
Lewis J. Overton, MD, Rounak B. Rawal, MD, Satyan B. Sreenath, BS
Department of Otolaryngology/Head and Neck Surgery
University of North Carolina at Chapel Hill

Background: The reverse-flow Facial Artery Buccinator (FAB) flap has been utilized successfully in head and neck reconstruction. Few cadaver studies have highlighted its potential as an alternative flap for coverage of skull base defects. Its advantages include the lack of external facial incisions, low necrosis rate, and minor donor site morbidity. The surgeon also has the freedom to harvest the flap following resection of the lesion and tailor it precisely to the defect.
Objective: The objective of this study is to provide an in-depth explanation of the anatomic and technical considerations for facial artery identification, harvest and transposition of the FAB flap to facilitate its future use in anterior skull base reconstruction.
Study Design: Cadaveric feasibility study with descriptive anatomic data
Methods: Eight FAB flaps were raised in four, fresh cadaveric heads and transposed via a Caldwell-Luc and medial maxillectomy approach. The flaps, herein, were divided into thirds, and the course of the facial artery at the superior and inferior borders of the flap was measured noting in which incisional third of the flap it laid. Flap length and area as well as its ability to cover defects of the anterior cranial fossa, sella turcica, clival recess, and contralateral cribiform plate were studied.
Results: The facial artery in all specimens had a near vertical course and stayed with the posterior or middle third of the flap in the inferior and superior incisions. The majority of the facial arteries (5/8) were identified in the middle third of the flap incisions. Once transposed into the endonasal cavity, 7 out of 8 flaps covered all of the sellar/planar regions. In 6 out of 8 flaps, complete coverage of the ipsilateral cribriform region was achieved. However, only 4 out of 8 flaps were able to cover the contralateral cribriform region. Lastly, no flaps were able to achieve complete coverage of the middle third of the clival region. Additionally, a clinical case and operative video demonstration can also be presented of the FAB flap harvest and transposition.
Conclusion: The FAB flap holds great promise in anterior skull base reconstruction. In our study, the flap achieved coverage of the ipsilateral cribriform and sellar regions. However, for contralateral cribiform coverage, the reach of the FAB flap is more limited. Additionally, the flap does not have appropriate reach for larger mid-clival defects. The FAB flap should be considered as an alternative when more conventional means of coverage are unfeasible. It is technically challenging and an understanding of the facial artery's course, generally seen in the middle third of the flap, is crucial for its harvest and transposition.

Masqueraders of Appendicitis

Zehra Farzal

Mentor and Collaborators: Anne Fischer, MD, Zainab Farzal BS, Nudrat Khan BS, Sandy Cope-Yokoyama MD
Department of Pediatric Surgery

Purpose: Given the new suggested paradigm of non-operative management of appendicitis, our goal was to identify the incidence of atypical diagnoses detected among appendectomy specimens to better elucidate those potentially missed in non-operative management.

Methods: An IRB-approved (062012-049) retrospective review of pediatric patients (n=6816) who underwent appendectomies at an independent children's hospital over an 11 year period from January 2000 to December 2010 was performed. Inclusion criteria required age <17 and surgery for presumed appendicitis thus excluding incidental appendectomies (n=269) from this sample with a final review of 6547 specimens.

Results: 5998 (91.6%) subjects showed true appendicitis including acute non-perforated, perforated, chronic, suppurative, gangrenous, and catarrhal appendicitis. In 224 subjects (3.4%), diagnoses other than appendicitis were identified: non-inflammatory obstruction (n=71), other infectious etiologies (n=58), non-specific inflammatory changes (n=58), extra-appendiceal pathology (n=31), tumors (n=4), and foreign body (n=2). Additionally, 6 patients with true appendicitis had co-existing carcinoid tumors. 325 specimens (5.0%) were documented as negative appendicitis.

Conclusion: This is the largest analysis of the incidence of pathologies that masquerade as appendicitis in the pediatric population conveying a broad overlap of diagnoses that present similarly. Given the common diagnosis of appendicitis, follow-up for routine appendectomies has been streamlined and expedited in such a way that review of pathology may be overlooked; the number of infectious etiologies and tumors detected reinforces the increasing importance of pathology review in post-operative follow-up to appropriately diagnose uncommon conditions that may necessitate further work-up and treatment. Additionally, the possibility of missing an alternative or co-incidental diagnosis such as carcinoid tumor in the non-operative management of appendicitis merits some reflection in planning operative versus non-operative management.

Analysis of characteristics and outcomes with propranolol use in severely burned adults

Shea A. Finch

Mentor and Collaborators: Steven E. Wolf MD, Melody R. Saeman MD, Agnes Burris RN, & Melanie Evans
Department of General Surgery

Introduction: Severely burned patients experience a hypermetabolic state characterized by a hyperdynamic circulatory response with increased catabolism causing higher energy expenditures. Propranolol has been shown to mitigate these effects in pediatric burns and decrease energy requirements. However, the effects of propranolol in adult burns are unknown, and its use is not universal. Our study focuses on elucidating differences in adult burn patients who are prescribed propranolol versus those who are not.
Methods: We conducted a retrospective case-control study at a regional burn center between 2011 and 2012. Two groups were selected based on propranolol versus non-propranolol use during hospitalization. Selection criteria included: greater than 20% total body surface area (TBSA) burn, older than 18 years, and post-burn survival greater than 2 days. We compared gender, age, race, TBSA burn, burn mechanism, inhalational injury, hospital days, ventilator days, mortality, Charlson comorbidity index, and prior beta-blocker use. Statistical analysis was conducted using SigmaPlot and SPSS with chi-square, t-test, Mann-Whitney rank sum test, and Fisher exact test, where appropriate.
Results: We identified 60 subjects, 30 in each group. The groups showed no significant difference in gender, race, inhalation injury, burn mechanism, mortality, Charlson comorbidity index, or prior prescription of beta-blockers. There was a significant difference in age ($p = 0.05$) with the mean age of 39 (± 3 SEM) years in the propranolol group and 49 (± 4 SEM) years in the non-propranolol group. We found a significant difference in the median TBSA burn ($p < 0.01$) with 31% (27, 60 [IQR]) and 27.5% (22, 34 [IQR]) in propranolol and non-propranolol groups, respectively. Median hospitalization of 24 days (20, 51 [IQR]) was longer in the propranolol group ($p = 0.05$) versus 19 days (10, 34 [IQR]) in the non-propranolol group. Median ventilator duration of 4 days (0, 10 [IQR]) was higher in the propranolol group ($p = 0.04$) versus 1.5 days (0, 3 [IQR]) in the non-propranolol group.
Discussion: We found in our uncontrolled study that severely burned patients prescribed propranolol were younger with larger burns. They had longer hospitalizations and more ventilator days versus those not prescribed propranolol. We did not find a difference in mortality between groups. Identifying these trends gives insight into propranolol use patterns. Future, randomized control trials are needed to determine if propranolol administration results in decreased catabolism and better outcomes in severely burned adults.

Predictors of guideline-concordant colon cancer surveillance recommendations after polypectomy

Zachary Freeland

Mentor and Collaborators: Amit Singal, MD, Ben Kahn, Christian Mayorga MD, Samir Gupta, MD
Department of Internal Medicine

Background: Colorectal cancer (CRC) is the second leading cause of cancer-related death in the United States. Screening colonoscopy can reduce CRC mortality, but its cost-effectiveness is dependent on the use of appropriate surveillance intervals. Prior studies have suggested high rates of both overuse and underuse of surveillance colonoscopy in community practice, but there is a shortage of data regarding surveillance colonoscopy in patients followed at academic centers.
Aims: To quantify and identify predictors for guideline-concordant CRC surveillance recommendations after polypectomy among a large cohort of patients seen in an academic safety-net health system.
Methods: We conducted a retrospective cohort study of patients who underwent colonoscopy with polypectomy at Parkland Memorial Hospital between June 2011 and March 2014. Surveillance intervals shorter than and longer than guideline recommendations were defined as overuse and underuse, respectively. Multivariate logistic regression was used to identify demographic, clinical, and pathologic correlates of guideline-concordant surveillance recommendations, overuse, and underuse.
Results: We identified 537 patients who underwent colonoscopy with polypectomy. Surveillance recommendations were concordant with guidelines in 418 (77.8%) cases. Among the 119 discordant cases, 47 (8.8%) represented underuse and 72 (13.4%) represented overuse. Predictors of appropriate surveillance recommendations on multivariate analysis included incomplete resection, fair prep quality, and presence of ≥3 polyps (Table). Fair prep quality was associated with higher rates of overuse (27.4% vs. 9.7%, p<0.001), while the presence of ≥3 polyps was associated with higher rates of both underuse (11.7% vs. 6.7%, p=0.06) and overuse (16.6% vs. 11.1%, p=0.07).
Conclusions: Surveillance recommendations are divergent from guidelines in nearly 1 in 4 cases. Fair prep quality is a strong modifiable risk factor for colonoscopy overuse, and interventions to optimize prep quality may improve the cost-effectiveness of CRC screening.

Table: Predictors of guideline-concordant surveillance recommendations

Variable	OR	95% CI	Rates of concordance
Incomplete resection (n=33)	4.69	1.10 – 19.87	76.8% if complete resection 93.9% if incomplete resection
Fair prep quality (n=113)	0.49	0.31 – 0.78	80.7% if good/excellent prep 67.3% if fair prep
≥3 polyps (n=223)	0.55	0.37 – 0.83	82.2% if <3 polyps 71.8% if ≥3 polyps

Long Term Central Venous Access in a Pediatric Leukemia Population

Aurelia Fu

Mentor and Collaborators: Adam Alder, MD, Erica Hodgman, MD, Rachel Renkes, BS,& Tamra Slone, MD
Department of Pediatric Surgery

Background: Central venous access devices (CVADs) are used during the treatment of malignancies to facilitate chemotherapy administration and to reduce the pain and trauma of frequent blood sampling. Despite the importance of venous access, there is little recent data on complication rates associated with CVADs among pediatric patients. Our aim was to retrospectively analyze the complication rates among patients with acute leukemia at a single pediatric tertiary referral center.
Methods: After IRB approval, we reviewed the medical records of all patients with a diagnosis of acute lymphoblastic leukemia or acute myeloid leukemia admitted to our institution from May 2009-July 2014. Patient data, including demographics, CVAD type (subcutaneous port or tunneled catheter), peri-operative complications (<24 hours of surgery), long-term complications (>24 hours after surgery), and overall patient outcomes were collected. Chi square, t-tests and backward stepwise multivariate-regressions were used (significance $p<0.05$).
Results: There were 292 CVADs placed in 198 patients. The peri-operative complication rate was 4.8% (14 out of 292). Out of 292 CVADs, 23 did not have any long-term complications. Long-term complications included 93 line-associated infections (blood stream and/or port site infections), 6 episodes of deep vein thrombosis (DVT), and 136 instances of line malfunction without an identifiable cause. Seventy-five CVAD's were prematurely removed: 31 due to infection and 44 to malfunction. Univariate analysis identified age as a risk factor for a hematoma ($p=0.02$), and weight status as a risk factor for blood stream infection ($p=0.02$), DVT ($p=0.009$), line malfunction ($p=0.02$), and premature removal ($p=0.02$). The number of days from diagnosis to CVAD placement ($p=0.008$) and location of the subcutaneous port reservoir ($p=0.01$) were identified as predictors of early CVAD removal by multivariate analysis. There were no significant differences in long term complications between ports or tunneled catheters.
Conclusion: Our rate of peri-operative complications compares to the 1.3-14% range reported in previous studies. Long term complications are high and require additional treatment, catheter replacement, or premature removal. This is costly in health, time, and money for both the patient and our institution, and should be addressed to improve patient care. Our retrospective study is the largest recent evaluation of CVAD complications within a single institution and also represents the largest Hispanic pediatric leukemia population reported upon to date.

Aspiration Pneumonia and Perioperative Antibiotic Use in Transoral Robotic and Laser Microsurgery

Prakash Gajera

Mentor: Baran Sumer, MD
Department of Otolarnyngology

Introduction: Aspiration pneumonia can follow transoral surgery for head and neck cancer due to abnormal swallowing function. While prophylactic post-operative antibiotics may decrease the incidence of this complication, excessive use can be costly, and lead to adverse reactions or antibiotic resistance. The objectives of this study are to 1) determine if the use post-op antibiotics prevent aspiration pneumonia. 2) Identify any complications related to the use of antibiotics.
Methods: A retrospective review of 155 patients who underwent transoral surgery for squamous cell carcinoma (SCCA) between May 2008 and June 2014 was conducted and demographic data was collected. The MD Anderson dysphagia inventory (MDADI) was used to assess swallowing function.
Results: Sixteen of 122 patients that received postoperative antibiotics (13.1%) developed pneumonia, compared to 4/32(12.5%) patients who did not receive antibiotics (p=0.925). Average antibiotic course was 39.2 days (median=23). Average time to infection was 290 days (median=217, range=11-979). Univariate analysis did not show a correlation between patients that developed pneumonia and antibiotic use (p=1.00), location (p=.1642), overall stage (p=.1599), comorbidity status (p=.5327), tobacco use (p=.6328), alcohol use (p=.351), and gastrostomy tube dependence (p=.254). Univariate analysis did show a correlation between pneumonia and tracheostomy placement (p=.0316), T stage (p=.0357), and days post-op of PEG placement (p=.0297). Multivariate analysis showed correlation with tracheostomy placement (p=.0236). No patients contracted C. difficile infection. No trend was observed in post-operative MDADI score.
Discussion: Routine use of post-operative prophylactic antibiotic does not correlate with a decreased rate of pneumonia or improved functional outcomes. Given that tracheostomies are performed mainly for pulmonary toilet, and a larger T stage results in larger resections, the significant correlation was expected. PEG placement in pneumonia patients was significantly later than patients with no pneumonia. This, and the fact that pneumonia generally developed outside of the 30-day perioperative period, supports the idea that aspiration pneumonia development reflects a chronic worsening swallowing dysfunction. Therefore, dysphagia immediately after surgery is probably not a significant risk factor for developing aspiration pneumonia and routine post-operative antibiotic use for pneumonia prevention is not indicated after transoral surgery.

Intubation Hypotension in Trauma Patients After Etomidate Administration

Ryan Glidewell

Mentor and Collaborators: Lynn Roppolo, MD, Brian Hawkins, Benjamin Cooper, MD, Brian Kendall, MD, Scott Knepper, MD, Linda S. Hynan PhD
Department of Emergency Medicine

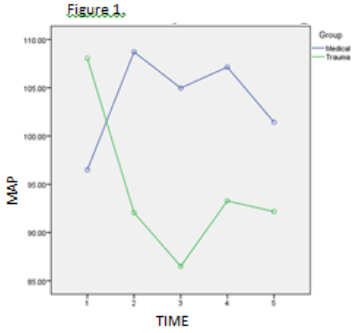
Background: Post-intubation hypotension (PIH) is found in up to 44% of patients emergently intubated in the ED. Etomidate is a popular agent used in rapid sequence induction (RSI) for emergency intubations due to its stable hemodynamic profile. The purpose of this study was to prospectively investigate the incidence of PIH in trauma patients requiring emergent intubation using etomidate as the induction agent.
Methods: All patients intubated in the emergency department (ED) who were induced using etomidate were prospectively recruited for this study. Serial vital signs were recorded just prior to RSI drug administration and every 5 minutes after for 20 minutes.
Results: 20 adult patients were recruited for this study over an 8-week period, 12 (80%) medical and 8 (89%) trauma. Each patient received an average dose of 22 mg. See Table 1 and Figure 1 a comparison of MAP changes observed in medical patients verses trauma patients just prior to the administration of RSI medications and at 5, 10, 15, and 20 minutes intervals.
Conclusion: Etomidate can significantly reduce the MAP in trauma patients. One plausible explanation in the immediate post-intubation period is the reduced sympathetic stimulation that results once unconsciousness is induced. Critically ill trauma patients who require emergent intubation are likely to have concomitant injuries and are at risk for hemorrhagic shock or worsening cerebral injury from precipitous decreases in blood pressure. Resuscitative measures should be cautiously instituted to mitigate any adverse effects of hypoperfusion from PIH in these critically ill patients.

Table 1. Mean Arterial Pressure Changes

Group		Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Medical	Pre-RSI	76.86	6.18	63.87	89.85
	5 min	88.57	5.67	76.65	100.49
	10 min	85.57	4.71	75.67	95.47
	15 min	88.29	4.87	78.06	98.51
	20 min	83.64	6.05	70.93	96.36
Trauma	Pre-RSI	92.17	9.45	72.32	112.01
	5 min	77.00	8.66	58.80	95.20
	10 min	68.67	7.20	53.55	83.79
	15 min	76.00	7.43	60.38	91.62
	20 min	74.67	9.25	55.24	94.09

*Analysis of Variance Results – 1 between (Group) and 1 within (Time) effects (F-tests)
Time * Group Interaction - significant, p=.026

Figure 1



Effect of Extended-Release Niacin on Carotid Intima Media Thickness: Insights from the Atherosclerosis Lesion Progression Intervention Using Niacin Extended Release in Saphenous Vein Grafts (ALPINE-SVG) Pilot Trial

Andres Guerra

Mentor and Collaborators: Emmanouil Brilakis, MD, PhD, Bavana V. Rangan, BDS, MPH, Anna Kotsia, MD, Aristotelis Papayannis, MD, Mohammed Alomar, MD, Ameka Coleman, MS, Howard Chao, BS, Alan Sosa, BA, Henry Han, BS, Michele Roesle, RN, BSN, Georgios Christopoulos, MD, James A. de Lemos, MD, Darren McGuire, MD, Milton Packer, MD, Subhash Banerjee, MD
Department of Internal Medicine/ Cardiology

Background: The Atherosclerosis Lesion Progression Intervention using Niacin Extended Release in Saphenous Vein Grafts (ALPINE-SVG) trial randomized 38 patients with intermediate (30-60% diameter stenosis) saphenous vein graft lesions to extended-release niacin (ER-Niacin) or placebo for 12 months. We evaluated the impact of ER-niacin on carotid intima media thickness (CIMT).
Methods: B-mode ultrasound was used to image the common and internal carotid arteries, at baseline and at 12 months after enrollment (n=11 niacin, n=17 placebo). Mean CIMT was measured using Cardiovascular Suite v2.8 software (Quipu; Pisa, Tuscany); all measurements were performed in triplicate and averaged. The study was stopped early after the Heart Protection Study 2 - Treatment of HDL to Reduce the Incidence of Vascular Events (HPS2-THRIVE) trial results.
Results: Baseline clinical characteristics were similar in both study groups. HDL-cholesterol levels tended to increase more in the ER-niacin group (5.9±8.7 vs. 1.4±7.1 mg/dL, p=0.14). At 12 months, right common carotid artery (0.96±0.44 vs. 0.70±0.24 mm, p = 0.04), and left common carotid artery (0.80±0.30 vs. 0.70±0.20 mm, p = 0.08) CIMT decreased in the ER-niacin group, compared with no change in the placebo group. No correlation was seen in internal carotid arteries (chart).
Conclusions: Administration of ER-niacin for 12 months did not have a significant impact on CIMT compared to placebo; however, the study was underpowered due to early termination of enrollment.

Change in CIMT (mm)	Niacin (n=11)	Placebo (n=17)	P value
RCCA	-0.27±0.37	-0.08±0.43	0.25
RICA	-0.04±0.44	-0.02±0.42	0.91
LCCA	-0.09±0.16	-0.07±0.34	0.8
LICA	0.14±0.29	0.01±0.27	0.24

Evolution of the American College of Cardiology/American Heart Association Clinical Guidelines

Henry Han

Mentor and Collaborators: Emmanouil Brilakis, MD, PhD, Howard Chao, BS, Andres Guerra, BS, Alan Sosa, BS, George Christopoulos, MD, Bavana V. Rangan, BDS, MPH, Spyros Maragkoudakis, MD, Hani Jneid, MD, Subhash Banerjee, MD
Department of Internal Medicine- Cardiology

Background: The American Heart Association (AHA) and the American College of Cardiology (ACC) have been developing clinical guidelines to assist clinicians in clinical practice.
Objective: To evaluate changes in ACC/AHA guideline recommendations between 2008 and 2014.
Methods: We compared the previous and current ACC/AHA guideline documents that were updated between 2008 and June 2014 to determine changes in recommendations. Each recommendation was classified as New, Dropped, Revised, and Unchanged and the changes in evidence were examined.
Results: During the study period, 11 guideline documents (nine disease-based and two interventional/procedure-based) were updated. The total number of recommendations decreased from 2,067 to 1,869 (321 fewer recommendations in disease-based guidelines, and 123 additional recommendations in interventional procedure-based guidelines). The distribution for Class of Recommendations (COR) for the updated versions was 50.2% Class I (previously 50.8%), 39.4% Class II (previously 35.4%), and 10.4% Class III (previously 13.8%) ($p=0.001$). Compared with the previous versions, the proportion of class II recommendations increased, whereas the proportions for Class I and III decreased ($p=0.001$). The distribution for Level of Evidence (LOE) for the updated versions was 15% for LOE A (previously 13.3%), 50.8% for LOE B (previously 41.4%), and 34.2% for LOE C (previously 45.3%) ($p<0.001$). Within all guidelines, 859 recommendations were new, 881 recommendations were unchanged, 1,339 were dropped, and 129 were revised. Of the revised guidelines, 75 recommendations had evidence increased, in the majority from LOE C to LOE B, while 34 recommendations had evidence decreased, and 20 recommendations had class changes. Reasons for evidence increases were the introduction of new randomized controlled trials or drug trials, new studies, and new meta-analyses.
Conclusion: The ACC/AHA guideline recommendations are undergoing significant changes and are becoming more evidence-based and scientifically robust.

Analysis, Classification, and Treatment of the Upper Lip Aesthetic Unit

Ryan Harris

Mentors and Collaborators: Drs. Scott Harris & Peter Raphael
American Institute for Plastic Surgery, Plano Tx

Background: Disharmony of the upper lip aesthetic unit generally stems from tall philtra and/or thin lips. Comprehension and correction of such defects has been stifled by a lack of metrics and organized systems of diagnosis and treatment.
Methods: The philtral-labial score (PLS) was devised to enhance upper lip analysis. A retrospective medical records review identified 200 patients of the senior authors who underwent perioral rejuvenation over a 12-year period. Subjects were assessed in three surveys distributed to two unbiased surgeons that sequentially built on data points provided. Two new treatment modalities were introduced: Perma Facial Implant (PFI), a permanent lip augmentation solution, and Endonasal Lip Lift (ELL), which reduces surplus philtral height using intranasal flaps. The authors performed 832 consecutive PFI insertions and 311 ELLs over a 15-year period and evaluated the results based on photographic documentation, satisfaction surveys, and complications.
Results: When preoperative anteroposterior and lateral photographs, dental show measurements, and PLSs were available, diagnostic concordance approached 100%. Pattern analysis resulted in a lip classification system (LCS), designating patients without maxillary abnormalities as either type 0 (no defects), 1 (thin upper lip), 2 (long philtrum), or 3 (both defects). Characteristic dental show values, PLSs, and suggested treatments were paired with each type. PFIs successfully augmented thin lips, masked excess dentition, and improved vermilion rhytids and pout. However, they neither leveled out asymmetries nor benefitted razor-thin lips without prior lifting or mucosal advancement. ELLs improved scar appearance, minimized tension in visible areas, prevented scar migration (loss of lift), and increased dental and vermilion display. Undercorrection, sill widening, and alar distortion were mostly avoidable/corrigible complications. Nasal sill disruption remained an inevitable drawback, but was minimized through meticulous technique.
Conclusions: The LCS serves as a useful reference for novice surgeons, simplifies discussion, obviates complex algorithms, facilitates documentation and tracking of patients, and provides a method analyzing large sample sizes. When judiciously implemented, it can help surgeons confidently address upper lip defects by streamlining accurate diagnosis and guiding proper management. We consider PFI and ELL to be first-line agents in perioral patients owing to numerous advantages over alternatives.

KMAC value: a measure of resuscitation in severely burned pediatric patients

Elizabeth Harris

Mentor and Collaborators: Steven E. Wolf, MD, Melody Saeman, MD, Andres Guerra, BS, & Agnes Burris, RN
Department of General Surgery

Introduction: The KMAC value is a previously described input-to-output ratio that measures physiologic response to resuscitation in severe burn. It has not been studied in pediatric burns. Our goal was to describe KMAC values in pediatric patients, assess the relationship with outcomes, and determine if these values differ from adults.

Methods: Admissions to a regional burn center from January 2010 through August 2014 were retrospectively reviewed for subjects 18 years or younger with 20% or greater TBSA (total body surface area) burn, admitted within 8 hours of injury, and with survival over 24 hours. Patients without burn were excluded. Demographics, total input including intravenous and oral volume, urine output, and clinical outcomes were recorded. Ratios of input volume (cc/kg/%TBSA/h) to urine output (cc/kg/h) were calculated at 16 and 24 hours. Subjects were classified as over-responders (<0.166), expected(0.166-0.334), or under-responders (>0.334) using the 24 hour KMAC values.

Results: 48 subjects met inclusion criteria; 30 males and 18 females, with a median age of 3 years (1.3, 10.5[IQR]). Median TBSA was 27% (21, 39 [IQR]). The mortality rate was 4%. There were 15 under, 25 expected, and 8 over responders with a median KMAC value of 0.22 (0.15, 0.29 [IQR]). This value differed significantly from the published median adult 24 hour KMAC value of 0.25 (0.15, 0.45 [IQR], p=0.04). Adults showed greater variability and more extreme KMAC values compared to children. Importantly, we found no relationship between the KMAC value and age or TBSA burn. The data did however, support a correlation between the 16 hour and 24 hour KMAC values (r^2=0.55). Contrary to published findings in adult patients, we did not find a difference between responder type and mortality, ICU days, ventilator days, length of stay or complications. We infer that this finding is due to the relative infrequency of poor outcomes in pediatric burn patients compared to adults.

Conclusions: KMAC values in severely burned pediatric subjects are less variable than adults and are independent from age and TBSA burn. Additionally, our findings suggest that pediatric burn patients respond more consistently to resuscitation than adults.

A Prospective Study Comparing Vancomycin and Clindamycin in the Treatment of Soft Tissue Infections in an Emergency Department Observation Unit

Brian Hawkins

Mentor and Collaborator: Lynn Roppolo, MD, Whitney Lewis, MD, Caleb Pierce, MD, Andres Guerra, MS2, Andrew Lin, MS2, & Ngozi Okoro, PhD
Department of Emergency Medicine

Introduction: Many patients who present to the emergency department (ED) with soft tissue infections (cellulitis) are treated for a resistant strain of *Staphylococcus Aureus* known as "community acquired MRSA", which responds only to a handful of antibiotics, most commonly Vancomycin or Clindamycin. Growing resistance to Clindamycin has encouraged wider use of Vancomycin, an arguably more powerful antibiotic, in spite of its less forgiving therapeutic window. Importantly, of the two, only Clindamycin is available in an oral preparation. It is not known whether one of these is a more effective therapy in ED observation units where patients typically receive IV antibiotics over a 24-hour period. Our study seeks to evaluate characteristics of patients receiving Vancomycin over Clindamycin and to compare the effectiveness of each.
Methods: Patients admitted to the Parkland Observation Unit via the ED that presented with a soft tissue infection thought to be due to MRSA were consented and recruited if treated with either Vancomycin or Clindamycin. The largest diameter of the infected area was measured, and pertinent clinical information, to include antibiotic dosage, was recorded. Telephonic followups were conducted 1 to 2 weeks later to evaluate if the infection had resolved.
Results: A total of 35 patients were enrolled over a 16-week period. An additional 15 patients were consented but were lost to follow-up. The average age was 45 years (range 18 to 73), 55% were females. 74.3% (n=26) received Clindamycin; 25.7% (n=9) received Vancomycin. 22% (2/9) of patients receiving Vancomycin had at least one prior skin infection while only 8% (2/26) of patients receiving Clindamycin had a prior skin infection. 66% (6/9) of patients with areas of cellulitis > 10cm received Vancomycin versus 38% (10/26) who received Clindamycin. 55% of patients who received Vancomycin were diabetic versus 27% (7/26) of patients who received Clindamycin. 44% (4/9) of patients who received Vancomycin were back to their baseline versus 65% (17/26) who received Clindamycin. **Conclusion:** This investigation demonstrated that clinicians are reserving Vancomycin for higher-risk patients such as diabetics, those with a history of prior skin infections, or patients presenting with greater areas of cellulitis. However, a larger percentage of patients treated with Clindamycin had returned to baseline when followed up. Because Vancomycin recipients are typically transitioned to oral Clindamycin upon discharge, the data suggest that these patients should either complete a full course of IV Vancomycin therapy outside the observation unit or should be treated with Clindamycin to begin with.

The Disease Burden of HIV in Pregnant Women Within the Catchment of Mamohou Hospital in the Leribe, District of Lesotho

Charles Herrin

Mentors and Collaborators: Dr. Henri Mahadimby, Ryan McClaine
Rachel Neal,
Mamohou Hospital

Background: Current estimates place Lesotho as the third highest rate of HIV infection in the world. The UNAIDS 2013 projections are that 22.9% of the population between the ages of 15-49 are infected with almost 60% of the infected being women. While there are national statistical data available, there is little information specific to the various catchments within the country.
Objective: This study looks at obstetrical records from Mamohou Hospital, whose catchment area includes a large northern section of the Leribe district, to determine the disease burden of HIV on sexually active women. This is possible due to Mamohau hospital's practice that has all women stay at the hospital for the last two weeks of their pregnancy to ensure that all births occur in the presence of trained medical staff.
Methods: Mamohou Hospital is located in the northern region of Lesotho and serves a rural, highly agriculturally based population of ethnic Basotho. The HIV status of each woman who gave birth at the hospital (both vaginal and cesarean) was collected via a retrospective chart review. A total of 1926 eligible OB records between January 2012 and June 2014 were examined. Women are screened for HIV at least once while pregnant (those at risk are screened multiple times), which keeps the "unknowns" in the study very low. Most of the unknown statuses are due to preterm emergency cesarean sections. In addition to the HIV status, the age, educational level, previous births, and methods of contraception used by the women were also collected. **Results:** In total, 20.04% of the women tested positive for HIV while 78.30% tested negative (there was a 1.66% unknown rate). However, these numbers are not consistent across the age demographics. The prevalence for women under 20 years old was only 6.76%, while the prevalence for ages 20-29, 30-39, and over 40 were 20.26%, 34.73%, and 30.65%, respectively. Only 0.88% of the women said that they had ever used a condom.
Conclusion: Although the numbers are suggestive of a massive disease burden, the data allows for slightly more optimism for the catchment area Mamohou serves than the overall national statistics. Additionally, the distribution of the HIV burden towards the older women, coupled with the general low use of condoms, suggests that aggressive educational sexual education campaigns could be effective
in helping to prevent the spread of HIV amongst younger women.

Knowledge, Attitude, and Practices Concerning Leptospirosis in an Urban Slum of Iquitos, Peru

Sarah Ho

Mentors: Jessica Ricaldi, MD, & Jennifer Holmes, MD
Department of Infectious Disease

Background: Leptospirosis is a zoonotic infectious disease that has a worldwide distribution. It is caused by the pathogenic *Leptospira interrogans* species, which colonizes the proximal renal tubules of mammals. The bacteria are shed in the animal's urine, and humans become infected when they come into direct or indirect contact with an infected animal's urine. The study was conducted to determine local knowledge of leptospirosis in Belen, an urban slum of Iquitos, Peru.
Method and Findings: A total of 247 participants living in Belen were interviewed between May and July 2014; 122 were surveyed in their homes and 125 were surveyed at the local health post, Seis de Octubre. Age, sex, level of education, household size, and water sources were recorded. Face to face interviews were conducted using both open and closed questions about leptospirosis transmission, perceived risk, treatment, and preventive practices. Participants reported obtaining health information from local hospitals and health posts, television, and newspapers. Most common sources of health care included local hospitals and health posts, pharmacies, and home remedies. The majority of participants reported using treated water for daily activities; however, a small percentage reported using river water for these activities.
Results: Of the 247 participants surveyed, only 111 (45%) had previously heard of leptospirosis, and 73 (30%) believed the disease occurred locally. 110 (45%) participants identified rats as a carrier animal. The most commonly recognized symptoms associated with leptospirosis included fever (100/247; 41%), headache (98/247; 40%), and death (86/247; 35%). The majority (214/247; 87%) of the sample population was unfamiliar with leptospirosis treatment. Likewise, a large proportion (160/247; 65%) of the respondents were unaware of prevention mechanisms. Of the 111 participants who were familiar with leptospirosis, 87 (78%) believed it to be more severe than dengue.
Conclusions: Unlike other areas where leptospirosis is endemic, the residents of Belen are largely unaware of the presence of the disease, its mechanisms of transmission, and strategies for prevention. Risk factors that have been associated with leptospiral seropositivity in similar environments do not hold true in Belen due to the ubiquity of the bacteria and risky practices, such as not wearing shoes. Hence, the community would likely benefit from a large-scale effort to educate the residents about what leptospirosis is, how it is transmitted and which animals can carry the bacteria, and effective strategies for preventing the disease.

Evaluation of the Sterility of a Vapocoolant Spray for Use in Minor Surgery

Lyahn Hwang

Mentor and Collaborators: James E. Zins, MD, Karolina Mlynek; MD, Michael Kreft
Department of Plastic Surgery, Cleveland Clinic

Vapocoolant sprays (skin refrigerants) are topical agents frequently utilized in a clinical office setting to reduce pain caused by needle injections or minor surgical procedures by rapid cooling of the skin. However, possible flammability and bacterial contamination have limited their use in clinics. The recent introduction of a non-flammable vapocoolant spray, "Pain Ease®" (Gebauer Co., Cleveland, OH), composed of 1,1,1,3.3-Pentafluoropropane and 1,1,1,2-Tetrafluoroethane, has been suggested as a possible alternative product. The purpose of this study is to evaluate the sterility of Pain Ease® and to determine whether this product is suitable for use prior to small skin incisions or injections such as botulinum toxin.

A prospective, blinded, and controlled study was performed on 50 healthy adult volunteers. From each subject, three swab cultures were obtained from the same cheek area: (1) at time 0 prior to any skin preparation (control), (2) after antiseptic preparation with 70% isopropyl alcohol swabs, and (3) after spraying with Pain Ease®. All microbiology specimens were quantitatively and qualitatively analyzed for five days in a blinded fashion regarding the nature and sequence of the culture swabs, and gram stains were obtained when cultures were positive. Three samples of Pain Ease® alone were also cultured to further investigate the microbiologic activity of the product. No injections or surgical procedures were carried out in this study.

Bacterial growth was found in 98% of cultures taken before antiseptic was applied (group I), in 54% of cultures after alcohol was applied, and in 46% of cultures after spraying with vapocoolant. There was statistically significant difference found between group I (no antiseptic) and both group II (after antiseptic but before vapocoolant) and group III (after vapocoolant) ($p < 0.001$), but not between groups 2 and 3 ($p = 0.74$). The pathogens most commonly cultured were gram positive cocci and gram positive bacilli. No positive cultures were observed in samples containing only Pain Ease®.

The widely used and cost-effective topical antiseptic 70% isopropyl alcohol significantly reduces skin colonization when compared to unprepared skin ($p < 0.001$). When Pain Ease® is sprayed on skin prepared with alcohol, there is no statistically significant increase in bacterial colonization than when alcohol is used alone. We present prospective, blinded data using a mock injection clinical model suggesting the use of Pain Ease® as an inexpensive and safe product in clinics from a microbiologic standpoint.

Pain scores with atypical pain regimens in severe burn

Eunjin Jang

Mentor and Collaborators, Steven E. Wolf, MD, Melody R. Saeman, MD, Shawn Banon, Agnes Burris, RSN
Department of General Surgery

Introduction: Severely burned patients receive a variety of medications to alleviate their pain. We wondered if there are differences in reported pain scores and acceptable levels of pain in patients who receive only opioid analgesics versus patients who receive atypical pain medications in addition to opioids.

Methods: The regional burn center's database was queried for subjects with greater than 20% TBSA (total body surface area) burn admitted from January 2011 to March 2014. Subjects who received only opioid medications were categorized into the "opioid" group, and those who received any combination of atypical non-opioid pain medications in addition to opioids were in the "non-opioid" group. Non-opioid medications included typical and atypical antipsychotics, benzodiazepines, SSRIs, and heterocyclic antidepressants. The non-opioid subjects were matched for TBSA burn, age, and gender with opioid subjects. Pain scores and reported acceptable levels of pain were collected from review of the electronic medical record. Scores were averaged from the first five days of hospitalization and compared to scores from the last five days of hospitalization to evaluate for differences. Statistical analysis was performed with SigmaPlot using t-test, Mann-Whitney, chi-square, and Wilcoxon signed rank test where appropriate.

Results: Twenty-eight subjects were identified in each cohort. The median TBSA burn was 25% (21, 31[IQR]) in non-opioid subjects and 28% (24, 32 [IQR]) in opioid subjects. The median length of stay was 31 days and the mean age was 42 years for both groups. There was no statistical difference in TBSA burn, gender, age, or length of stay between groups. We found no differences in pain scores or acceptable pain levels between groups at either time points. Paired t-test demonstrated no statistical change in pain scores over hospitalization in the opioid group. However, those who received non-opioid pain medications had a statistical improvement ($p = 0.018$) in pain scores over their hospitalization from 2.5 (1.6, 3.9 [IQR]) to 1.8 (1.2, 2.5 [IQR]) at the end. There was no statistical difference in the acceptable level of pain over hospitalization in either group.

Conclusions: Our results suggest improved pain scores with atypical pain regimens compared to opioid-only treatments.

Results of Epiphysiodesis for Treatment of Limb Length Discrepancy

Taylor Jackson & Connor Smith

Mentor and Collaborators: John Birch, MD, Marina Makarov, MD, Chanhee Jo, PhD, Department of Orthopaedic Surgery

Background: Epiphysiodesis is a pediatric surgical procedure often used to correct a 2-5 cm limb length discrepancy (LLD) by surgically arresting physeal growth of the longer limb.

Objective: The purpose of the study is to compare three models commonly used to calculate expected LLD in patients who have undergone an epiphysiodesis to determine which most accurately predict the patient outcomes.

Methods: Out of 469 patients who have undergone an epiphysiodesis for LLD at the Texas Scottish Rite Hospital for Children between1991-2011, 84 patients were selected for the study. The inclusion criteria were availability of three pre-operative x-rays and skeletal age data before the surgery, with at least a six months interval between scans. Each patient must have been followed to skeletal maturity with limb length measurements at that time and must not have suffered growth arrest of traumatic etiology or had postoperative complications. Using radiographic limb measurements, we compared the accuracy of the growth remaining methods by assessing predicted limb lengths and predicted LLD with White-Menelaus, Moseley/Rotterdam, and Green-Anderson methods or their variants. Where applicable, the predictions were made with and without accounting for growth inhibition rate (GIR), which is a quantification of the retarded rate of growth in the shorter leg. The differences across methods were assessed with one-way repeated measures ANOVA and reliability measures using intraclass correlation coefficients (ICC). A p-value < 0.05 indicated statistical significance.

Results: Analysis comparing the mean absolute difference between the predicted and actual outcomes for each method demonstrates a similar efficacy.

Conclusion: The White-Menelaus, Moseley/Rotterdam, and Green-Anderson methods of prediction are nearly indistinguishable, with the White-Menelaus being slightly more accurate. Modifying the existing models to include GIR did not improve the accuracy of the predictions. We advocate that the White-Menelaus be the preferred method as it is as accurate as the others and, from the clinical perspective, has the advantage of simplicity: requiring only one measurement and the patient's chronological age, as opposed to skeletal age. It also does not require the physician to create graphs or consult growth charts.

Evaluating Transition from Pediatric to Adult Care in Pediatric Epilepsy Patients

Heidi Kim

Mentor and Collaborators: Susan Arnold, Michelle Lu, Elizabeth Burch, & Nora Gimpel, MD
Department of Pediatric Neurology

Context: Epilepsy is the most common adolescent neurological condition. Pediatric patients with epilepsy are followed at Children's Medical Center (CMC) through the age of 18 years. As they approach adulthood, CMC provides transition education to the patients and families, encouraging them to seek care with adult neurologists. It is plausible that some patients do not follow up with an adult neurologist for various reasons, such as difficulties with health insurance, a lack of understanding, and other complex psychosocial factors.
Objectives: To determine: 1) whether or not former patients have seen adult neurologists, 2) the barriers to finding an adult provider, 3) the facilitators of finding an adult provider, and 4) how CMC can improve its transition services.
Design: Cross-sectional and retrospective chart review.
Setting: The Comprehensive Epilepsy Center at CMC in Dallas.
Participants: Former patients of the Comprehensive Epilepsy Center (≥18 years old) who were advised to transition to adult care during their last visits. The last visit must have taken place between January 2009 and July 2013. Patients or legal guardians of patients must have given verbal consent. (N=75)
Instrument: Demographics and provider notes collected from electronic medical record. Phone surveys (consisting of 8 questions) were conducted to identify specific barriers to and facilitators of transition.
Results: Two hundred and forty-four patients met our inclusion criteria and were called. Seventy-five were surveyed and included in our study. Sixty-three (84.0%) have had their first appointments with an adult neurologist, and 12 (16.0%) have not. Of those who have had their first appointments, 27 (42.9%) found their neurologist through recommendations from CMC. Of those patients without private insurance at their last visits, 37.7% took longer than 6 months to get an appointment compared to the 18.8% of patients with private insurance. Of those who have not had their first appointments, 41.7% cited a lack of health insurance as their reason.
Conclusions: Results show a lack of private insurance and insurance altogether is a barrier to finding an adult provider. Results also show that referrals from the patient's pediatric hospital are facilitators of transition. A structured referral system at the patient's pediatric hospital (with a focus on the uninsured) could be implemented for proper transition of pediatric patients to adult care.

A Prospective, Observational study: Management of Moderate Hyperglycemia in the Emergency Department and Impact on Length of Stay and Return Visits

Jaehyun Kim & Andrew Lin

Mentor and Collaborators: Jillian Horning, MD, Matthew Constantine, MD, & Timothy Chamberlain, MD, Department of Emergency Medicine

Background: Diabetic patients require appropriate diagnostic and therapeutic interventions. No consensus standards have been established for the work-up or treatment of patients presenting with moderate hyperglycemia.
Objective: To identify the strategies utilized by emergency physicians to manage patients with moderate hyperglycemia and evaluate the effects these interventions have on short-term outcome measures.
Methods: Over a 10-week time period (June to August 2014), research assistants recruited diabetic patients presenting to Parkland ED with moderate hyperglycemia (blood glucose between 200 mg/dL and 600 mg/dL) presenting with mild or no symptoms. Patients were excluded from the study if they were less than 18 years of age, newly diagnosed with diabetes, were admitted to the hospital, or were unable to provide a contact number for follow-up purposes. For all enrolled patients, demographic, historical, and clinical data were collected and the ED length of stay was determined. Patient follow-up via phone and review of medical records was conducted one week after the initial ED visit to assess whether the patient sought medical attention for acute hyperglycemia-related complications.
Results: Of the 50 patients recruited to the study, 90% had a basic metabolic panel (BMP) and 72% had a urinalysis (UA). Eighty percent of patients received some form of treatment; of those treated, 100% received IV fluids, 18% received IV insulin, and 15% received subcutaneous insulin. The average POC glucose value at discharge for patients who received treatment and those who did not receive treatment were 272 mg/dL and 280 mg/dL, respectively. ED length of stay was not significantly different between patients that received treatment and those who did not (388 minutes versus 337 minutes, $p = 0.3$). After one week, 26 patients (52%) were able to be reached for follow-up. Of these 26 patients, 22 patients received treatment. Four patients (18%) in the treatment group returned to Parkland or visited an off-site hospital for acute hyperglycemia-related complications within 1 week of discharge. None of the patients who received no treatment had a return visit to the hospital.
Conclusion: While this is a limited study, there are several interesting findings that merit further investigation. The data suggests that there are fairly uniform practice patterns when evaluating patients with moderate hyperglycemia. The majority of patients received a diagnostic work-up including a BMP and/or UA, presumably to rule-out diabetic ketoacidosis (DKA). We also observed a fairly uniform practice pattern in the treatment of this group of patients. Eighty percent of patients received treatment; all of these patients received IV fluids and 33% received some form of insulin. Interestingly, there was no significant difference in the POC glucose at time of discharge (272 mg/dL in the treatment group versus 280 mg/dL in the untreated group, $p = 0.8$). We are unable to draw any formal conclusions in regards to the short-term outcome measures utilized in this study (ED length of stay and return visits). Future studies are warranted to optimize ED resource utilization and reduce unnecessary tests and interventions in patients with moderate hyperglycemia.

Angiographic Progression in adult Moyamoya disease without surgical interventions

Darlene King

Mentors:. Babu G. Welch,MD, & Maki Swada,MD
Department of Neurosurgery

Background. The angiographic progression of moyamoya disease (MMD) occurs from childhood and transiently stabilizes in adolescence. While a number of studies suggest that progression of MMD does occur in an adult population, the inclusion of surgical cases in such reports obscures the understanding of natural progression in the adult MMD.

Objective. We conducted this study to clarify the predictors of MMD progression without surgical intervention.

Methods. A retrospective chart-review analysis of adult moyamoya disease and moyamoya syndrome patients was performed at our institution between January 2005 and June 2013. The angiographic changes between baseline and follow-up images were assessed. Patients with surgical revascularizations before baseline or during the observation were excluded.

Results. A total of 23 cases were assessed, 7 (30.4%) patients demonstrated progression while 16 (69.6%) patients remained radiographically stable. Mean age at progression was 42.9 years and mean period to progression was 23.6 months (4.2-70.8 months). Three cases demonstrated asymptomatic progression. The patients that demonstrated progression had use of statin medications, stroke presentation and classic MMD at baseline. Patients who presented with TIA or unilateral steno-occlusive lesion were more likely to have a stable clinical course.

Conclusion. Angiographic progression in adult moyamoya disease appears to occur with some frequency. Diabetes, statin use, stroke presentation, and bilateral disease appear to be predictors of dynamic and progressive disease.

The BVM Effect

Christopher Leba

Mentor and Collaborators: Ray Fowler MD, Ahamed Idris MD, Paul Pepe MD, Richard King MD, PhD, & Faroukh Mehkri
Department of Emergency Medicine

Background: The most appropriate airway management strategy in the treatment of out-of-hospital cardiac arrest (OHCA) remains to be determined. Many research publications have shown a substantial survival benefit from OHCA with the use of bag-valve-mask (BVM) ventilation rather than advanced airways such as endotracheal intubation (ETI) or supraglottic airways (SGA). These notable findings prompted the authors to investigate this BVM effect further.
Objective: To review recent literature regarding the association between the types of airway management used in OHCA and survival to hospital discharge, noting any factors that seem to produce a benefit through the use of the BVM.
Methods: The authors performed a review of airway management during OHCA in studies published from 1997-2014. The various airways utilized in OHCA treatment that were analyzed included BVM, SGA (LMA, King Tube, combitube), esophageal obturator airway (EOA), and endotracheal intubation (ETI). The focus of the study was to examine the differences in survival from OHCA among patients managed by BVM versus advanced airways. Of note, the primary outcomes in these studies largely focused on survival to discharge, with some studies including neurological outcome as well. We also obtained relevant material through reviewing reference lists within articles and through contacting subject matter experts.
Results: In the majority of papers reviewed, adult patients ventilated with a BVM were more likely to survive to discharge than adults patients ventilated with an advanced airway. There was no effect on pediatric OHCA outcome based on type of airway received. The only difference in survival between adults and children came when controlling for age or when controlling for witnessed arrest. Only two studies demonstrated that ventilation with advanced airways was similar in outcome to BVM ventilation, with one study stating that return of spontaneous circulation (ROSC) for prolonged transport improved with ETI use. One other study stated that survival with BVM ventilation was similar to ETI ventilation in OHCA patients.
Conclusion: The majority of the research reviewed regarding the care of the patient suffering from OHCA indicates that survival is improved in those patients receiving BVM ventilation rather than advanced airways. The finding of this "BVM effect" calls for a future prospective study into ventilatory management of the cardiac arrest patient in the prehospital environment.

Resections Guided by SEEG Recordings: Patters of Implantation and Types of Resections

James Lee

Mentors and Collaborators: Jorge Gonzales-Martinez, MD, Juan Bulacio, Jeff Mullin, Saks Smithasonian, The Cleveland Clinic

Background: Surgical treatment for medically intractable frontal lobe epilepsy is challenging, with long-term seizure-free rate approaching 50%. In many of these patients, invasive monitoring is necessary to better define the epileptogenic zone.

Objective: To report our clinical experience in patients with medically intractable frontal lobe epilepsy who underwent stereo-electroencephalography (SEEG) guided resections, defining patterns of implantation, types of resection and their related seizure outcome.

Methods: From July 2009 to March 2013, consecutive data was collected from all patients with frontal lobe epilepsy who underwent SEEG guided resections. Patients with less than 6 months post- resection follow up were excluded. Data included demographics, type of SEEG implantation, pre-op MRI findings, duration of epilepsy syndrome, side of resection, type of resection, surgical pathology and seizure outcome (according to Engel classification). Seizure outcome at 6, 12, 24 and 36 months were estimated using Kaplan-Meier curve methodology. Univariate statistical analyses were performed in order to compare seizure free outcome with types of resection and other possible variables.

Results: Forty-nine patients were analyzed. The mean age was 28.8 years. 43% of the studied population had non-lesional MRIs. In total, 842 SEEG electrodes were implanted with an average of 14 electrodes per patient. Nineteen patients (38.8%) underwent lobar resections, 21 multilobar resections (42.9%) and the remaining 9 patients underwent sublobar resections. The mean post-operative follow-up was 37 months. In this group, 61% (30 patients) were considered Engel class I at the end of the follow-up. There was no statistical difference between lesion and non-lesional MRI cases. Patients with sub-lobar resections had 1.91 times the risk of recurrence as those with lobar resections.

Conclusions: Frontal lobe resections guided by SEEG recordings improve seizure outcome in patients with difficult to localize epilepsy. Outcome is favorable even in non-lesional patients. Multilobar and sublobar re ections had a tendency towards recurrence seizures after resections.

Increasing documented provider discussion of transition from pediatric to adult epilepsy care: a chart review

Michelle Y. Lu

Mentors and Collaborators: Susan Arnold, MD, Elizabeth Burch, MD, & Heidi Kim, Department of Pediatric Neurology

Introduction*:* As pediatric patients with epilepsy approach adulthood, pediatric neurology providers are expected to discuss the need for transitioning to adult epilepsy care with these patients and their families. To aid providers in these discussions, the Comprehensive Epilepsy Center at Children's Medical Center in Dallas has implemented various resources, including informational transition booklets, EPIC SmartPhrases prompting provider discussion and documentation of transition, and educational "Transition Day" events for patients and families. This study examines the frequency with which providers conducted and documented transition discussions. In addition, the introduction of transition resources was evaluated for increasing the frequency of these documented transition discussions.

Methods*:* This retrospective chart review examined the documented transition process of 402 patients previously followed for epilepsy at the Comprehensive Epilepsy Center who were 17- to 23-years old at their last clinic visit. Associations between availability of transition resources and documented provider discussion of transition were evaluated using chi-squared analysis.

Results*:* From September 2009-June 2014, providers documented discussing transition of care by the last clinic visit with 328 of the total eligible patients (82%) and at the planned penultimate clinic visit with 293 of the total eligible patients (73%). Documented discussion of transition by the last clinic visit increased from 58% of patients in 2010 to 81% in 2011, 79% in 2012, 94% in 2013, and 96% in 2014. Similarly, documented discussion of transition at the planned penultimate clinic visit increased from 42% of patients in 2010 to 71% in 2011, 75% in 2012, 86% in 2013, and 87% in 2014. The combined availability of transition booklets and SmartPhrases beginning in 2011 was found to be positively associated with the frequency of documented discussion of transition by the last clinic visit ($P=0.0015$) and at the planned penultimate clinic visit ($P<0.0001$). Availability of "Transition Day" events starting in 2013 was also found to be positively associated with the frequency of documented discussion of transition by the last clinic visit ($P=0.0002$) and at the planned penultimate clinic visit ($P=0.0033$).

Conclusion*:* Documented discussion of transition by providers at the Comprehensive Epilepsy Center has increased in recent years. This increase is strongly associated with the introduction of new transition resources, including transition booklets, specific SmartPhrases prompting discussion of transition, and "Transition Day" family events.

Predictors and Prevalence of Advance Directives in Hospitalized Heart Failure Patients, Self-Report vs EHR

Neeta Malviya

Mentor: Michael Ong, MD, PhD
Department of Internal Medicine

Introduction: Heart failure patients incur the greatest cost on Medicare as HF is the leading cause of hospitalization in Americans aged 65+. AHA Guidelines for Heart failure state that comprehensive care should address end-of-life care, since it decreases the likelihood of in-hospital death and lowers end-of-life spending. Despite this, HF patients have low rates of advanced directives (AD), reported as 35% at the time of death in a study in MN. Heart failure patients have a 25% mortality rate at 6 months, which underscores the importance of ADs in this population. This study sought to determine the prevalence and predictors of ADs in hospitalized HF patients and documentation rates of ADs in the EHR.
Methods: Baseline survey data from hospitalized patients with heart failure from a larger study, BEAT-HF, was utilized. BEAT-HF sought to reduce HF readmissions via a tele-health intervention and collected patient data from six academic medical centers in California. Individuals admitted as hospital inpatients or on observation status aged 50+ were eligible if they were receiving active treatment for decompensated heart failure. Baseline survey data for advance directives was analyzed using chi-square tests and multivariable logistic regression. All demographic and scale-based variables were included in bivariate analysis, and variables found to be significant in bivariate analysis were selected to be included in the regression model. The EHR of participants in the UCLA subset were searched for documentation of ADs in order to determine the rate of advance directives.
Results: 46.4% of patients reported an advance directive. Predictors of an advance directive in hospitalized heart failure patients included post graduate education 3.06(1.58-5.95), white race, 3.23(1.82-5.56), >$75,000 income 2.73(1.67-4.45), female gender 1.43(1.08-1.90), non-employed status 1.96(1.15-3.45), increased age 4.20 (2.13-8.29), and English-speaking (Ref-Russian) 2.63(1.39-5.00). 20% of the BEAT-HF UCLA patients had an AD documented in the EHR. PPV of self-reporting an advance directive was 31%. For the UCLA subset, predictors of having an AD documented in the EHR were age above 90 10.76(1.09-82.69), income above $75,000 5.63(1.53-20.69), non-employed status 7.69 (1.08-50.0), and English-speaking (Ref-Spanish) 25(1.45-500).
Conclusion: A higher proportion of HF patients across the state of CA (46.4%) report an AD than in Olmstead County, MN (41%). The EHR documentation of ADs at UCLA appears to be poor since they seem to be under-represented, with a low PPV of patient self-report.

The Burden of Orthopaedic Gunshot Injuries on Healthcare Resources in South Africa

Case Martin

Mentors: Sithombo Maqungo, MBChB, FC Ortho,MMed (Project Mentor), & Fiemu Nwariaku, M.D.(UTSW Global Health Mentor), Gerhad Thiart, MBChB

Background: Injuries inflicted by gunshot wounds (GSW) are an immense financial burden on the South African healthcare system. In 2005, Allard et al. estimated South African state hospitals treat approximately 127,000 firearm victims annually and concluded the cost of treating an abdominal GSW is approximately $1,467 per patient. No study has been conducted to estimate the burden from an orthopaedic perspective.
Objective: This study sought to estimate the burden and average cost of treating GSW victims requiring orthopaedic interventions in a South African tertiary level hospital.
Methods: This retrospective study surveyed over 1,500 orthopaedic admissions over a 12-month period in 2012 in Cape Town, South Africa at Groote Schuur Hospital (GSH) – a 893-bed university-affiliated state hospital. Chart review subsequently yielded data on, which allowed for cost analysis of, theatre time, number and type of implants, duration of admission, diagnostic-imaging studies performed, blood products used, laboratory studies ordered, and medications administered.
Results: A total of 111 patients with an average age of 28 years (range 13-74) were identified. Each patient was hit by an average of 1.69 bullets (range 1-7). These patients sustained a total of 147 fractures. The majority of injuries occurred in the lower extremities with 38.8% of all fractures in femurs, 15.6% in tibias, and 11.6% in fibulas. Ninety-five patients received surgical treatment for a total of 135 procedures with a cumulative surgical time of 220 hours 3 minutes. Cumulative anesthesia time was 306 hours 25 minutes. Theatre costs, excluding implants, were in excess of R800,000 (estimated $94,284). Eighty of the patients received a total of 99 implants during surgery, which raised theatre costs an additional R452,935 ($53,381) cumulatively, or R5,661.70 ($667.26) per patient. Total costs were in excess of R1 million for ward admissions, R180,000 for imaging, R190,000 for blood products, R16,000 for laboratory investigations, and R16,000 for discharge medication. Individual patient costs range from $18,603 to $305 for an average of about R24,834.43 ($2,927) per patient.
Interpretation: This study assesses the burden of orthopaedic firearm injuries in South Africa. It estimates that on average treating an orthopaedic GSW patient costs $2,927, utilizes about 3 hours of theatre time per operation, and necessitates a hospital bed for an average period of 10 days. With a greater understanding of not only the high incidence of orthopaedic GSWs treated in a South African tertiary care trauma center but also the costs incurred, the state healthcare system can better prioritize orthopaedic trauma funding and training opportunities while also supporting cost saving measures, including the redirection of financial resources to primary prevention initiatives.

Finding the Limit of Detection of Xpert MTB/RIF in urine samples

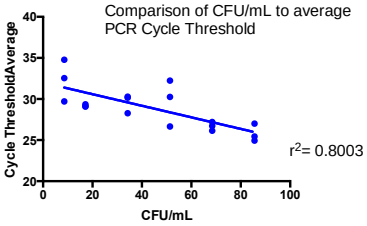
Nirja Mehta

Mentor and Collaborators: Grant Theron, PhD, Keertan Dheda, Anil Pooran, & Liezel Smith
Department of Lung Infection and Immunity, University of Cape Town, South Africa

Background: Xpert MTB/RIF is an automated RT-PCR assay which is able to detect the presence of Mycobacterium tuberculosis and rifampin resistance in sputum specimen within two hours. This test is endorsed by the WHO and the FDA for the frontline diagnosis of TB. A third of TB-HIV coinfected individuals are sputum scarce, thus sputum-based diagnosis is often not possible in these individuals. Urine is readily available and easy to collect, and urine samples have been shown to be an effective method of TB detection in low CD4 count, HIV-infected hospitalised inpatients. The purpose of this study was to determine the limit of detection of the Xpert MTB/RIF assay for urine.

Methods: Known concentrations of Mycobacterium tuberculosis H37 were added to a dilution series of urine, and the Xpert assay was performed in triplicate. The cycle threshold at each concentration was then analyzed for correlations with GraphPad Prism.

Results: The limit of detection for this assay in urine samples was found to be ~ 8 CFU/mL which is substantially lower than the limit of detection in sputum which is known to be 131 CFU/mL. This is perhaps due to the less viscous nature of urine or intrinsic inhibition of the Xpert assay by components of sputum. The correlation between cycle threshold (PCR cycles to positivity) and CFU/mL was found to be negative, which shows some promise in using cycle threshold as a proxy for estimating concentration.



Conclusion: Xpert appears to have a higher analytical sensitivity in urine, compared to what has previously been reported for sputum. Diagnostic accuracy in patients with advanced immunosuppression and disseminated TB warrants further investigation. Because bacteria ought to be filtered out of kidneys, Xpert may also prove to be interesting in providing insight to kidney function in TB patients.

Hepatocellular Carcinoma Surveillance is Associated with Potential Harms

Adam Muffler

Mentor and Collaborators: Amit Singal, MD, Omair Atiq, MD, Adam Yopp, MD
Department of Internal Medicine

Background: Hepatocellular carcinoma (HCC) is the 3rd leading cause of cancer death worldwide and leading cause of death in patients with cirrhosis. HCC surveillance is recommended in patients with cirrhosis to improve early detection rates. A comprehensive assessment of HCC surveillance should weigh both benefits and harms; however, no study to date has assessed potential harms. Although ultrasound and alpha fetoprotein (AFP) have minimal direct harms, there are potential downstream harms from follow-up tests that should be considered.

Objective: To quantify and characterize potential harms of HCC surveillance among a large cohort of patients with cirrhosis

Methods: We conducted a retrospective cohort study among patients with cirrhosis followed at a large safety-net health system. We recorded all surveillance abdominal imaging and/or alpha fetoprotein (AFP) testing between January 2010 and December 2013. We defined a false positive surveillance test as a suspicious liver mass on ultrasound or AFP >20 ng/mL, without HCC development during follow-up. We recorded CT or MRI scans, biopsies, or any procedures performed as a direct result of surveillance testing. Predictors of harm were identified using logistic regression, with significance being defined as $p<0.05$.

Results: We identified 571 patients with cirrhosis, with median follow-up of 2.8 years. HCC surveillance was performed at least once in 551 (96%) patients. Surveillance testing led to diagnostic CT or MRI testing in 123 (21.5%) patients – 74 with one CT/MRI and 49 with multiple studies. Rates of unnecessary diagnostic testing increased from 15% if followed for ≤1 year to 25% if followed for 1-2 years to 37% if followed for ≥2 years. An additional two patients had a biopsy and one patient angiogram for false positive surveillance tests. Follow-up tests were performed due to false positive ultrasound in 47 cases, false positive AFP in 35 cases, and indeterminate ultrasound results in 41 cases. In multivariate analysis, surveillance harm was associated with viral liver disease (OR 1.60, 95%CI 1.04-2.46), receipt of hepatology subspecialty care (OR 2.32, 95%CI 1.52-3.59), and coverage by Parkland Health Plus (OR 2.21, 95%CI 1.45-3.40).

Conclusion: This study is the first to demonstrate HCC surveillance can be associated with potential harms. One in five patients have at least one unnecessary diagnostic test, and nearly 10% have multiple tests. Better HCC surveillance tools, with a higher positive predictive value, are urgently needed.

Before and After Study of Care Protocol for Patients Admitted to the Observation Unit

Alexander Nasr

Mentor and Collaborators: Lynn Roppolo, MD, Kavita Joshi MD, Mani Alavi MD, Angela Gardner MD, Linda S. Hynan PhD
Department of Emergency Medicine

Background: Transition of care programs within emergency departments (ED) are not uniformly established. Furthermore, errors in communication during patient care handoffs account for an estimated 80% of medical errors. Emergency departments are particularly complex necessitating efficient information transfer during patient handoffs. Patients requiring short-term admission from the ED are often placed in the observation unit, which is primarily staffed by advanced level practitioners (ALP) working under the direction of emergency medicine attendings. These physician extenders have raised concerns over the inconsistencies and general lack of patient information conveyed to them during handoffs.
Methods: All Parkland ED patients placed in the observation unit over an 8-week period were identified using the electronic medical record. Residents were instructed to implement a new transition of care protocol, referred to as a CAP note (C – clinical evaluation; A – assessment of concerns; P – plan of care). Research assistants verified that this note was properly documented in the patient's medical record. The ALP provided verbal consent to participate in the study. All patients were consented as their medical record numbers were used to identify which ALP was in charge of their care. The ALPs were then surveyed to evaluate the quality and content of the new protocol. The CAP protocol was graded on a 1-4 scale with 4 being the best quality and 1 being the worst quality.
Results: 14 ALPs completed surveys on the 116 patients. The CAP protocol was graded as follows:

	Grade 4	Grade 3	Grade 2	Grade 1
Clinical evaluation	46.6% (54/116)	37.9% (44/116)	11.2% (13/116)	4.3% (5/116)
Assessment	47.4% (55/116)	30.2(35/116)	19.8 (23/116)	1.7 (2/116)
Plan	46.6 (54/116)	30.2% (35/116)	18.1 (5/116)	0.9% (1/116)

The vast majority of the ALPs, 97.4% (113/116) and 93.1% (108/116), thought that the new protocol simplified, and improved, the transition of care process, respectively. 91.4% (106/116) of patients had no deviation in their plan of care from that documented in the ED physician's transition of care note.
Conclusion: This investigation demonstrates that the new transition of care protocol improves both the efficacy and quality of the transition of care process between emergency medicine residents and midlevel providers in the observation units.

The Impact of Diurnal Changes and Inter-Visit Variability on the Concentration of Insulin-like Growth Factor-1 in Human Tears

Roshni Patel

Mentor: Danielle Robertson, OD, PhD
Department of Ophthalmology

Introduction: There is a growing body of research focused on the use of tear film-derived proteins as biomarkers of disease. Previous studies have reported quantitative changes in tear-derived growth factors and related proteins associated with various systemic and ocular diseases. Major challenges when working with human tears however, includes sample volume limitation and the high potential for reflex tearing. One method of tear collection that is increasingly being reported involves the use of microcapillary tubes to draw tears from the inferior tear reservoir. The purpose of this study was to investigate the impact of diurnal changes and inter-visit variability on the concentration of a known growth factor present in human tears, the insulin-like growth factor-1 (IGF-1).
Methods: Nine healthy volunteers without any reported symptoms of dry eye were recruited for this study. At visit 1 (baseline), all participants underwent a standard dry eye examination to assess tear volume, tear film break up time (TFBUT), and tear production. Subjects were asked to return to clinic for an additional 5 visits (morning and afternoon on a total of 3 days). Tears were collected at the start of each visit from the inferior temporal tear meniscus of both eyes using 1 – 10 µl glass microcapillary tubes and frozen at -80C until use. Total protein was measured for each patient using a bicinchoninic assay. IGF-1 levels wear assessed using ELISAs.
Results: 8.8 ± 2.1 µg/µl of total protein was obtained from each subject. Total protein was unchanged at each visit. There was no difference in IGF-1 between morning and afternoon. Tear levels of IGF-1 did vary with visit, with the final visit showing a 2 fold-increase over baseline ($p<0.05$). Tear levels of IGF-1 were correlated with TFBUT ($R=0.856$, $p=0.007$).
Discussion: While diurnal variation did not affect basal levels of IGF-1 in tears, there was a visit-dependent increase. This increase was likely due to a reduction in reflex tearing during tear collection as patients became more comfortable with the technique. Similarly, the decrease in IGF-1 that corresponded with increased tear evaporation was likely due to changes in reflex tearing. Together, these findings suggest that low abundant proteins, such as IGF-1, are highly susceptible to changes in reflex tearing. These findings also suggest that a participant training phase may be required.

Nutritional study of Puerto Lopez, Ecuador

Shalvi Patel

Mentor: Maria Zuluaga, MD
Department of Pediatrics

Background & Objective: A problem seen in many underdeveloped towns is a lack of nutritional knowledge. This contributes to the improper growth & development of children, as well as prevalence of preventable chronic diseases. The purpose of this study was to analyze the level of nutritional education in Puerto Lopez, Ecuador & see how it correlated with local child growth and general prevalence of disease.
Methods: In the first study for child growth, data was collected by visiting various day cares where name, exact age, gender, height & weight were measured, as well as by going through files of those under the age of 18 in the clinic's records in order to obtain data points. Collectively, the data was plotted on CDC growth charts. The second study involved of a week of going door to door in an assigned sector of town (77 families, 130 inhabitants) with a nutritional knowledge survey, & collecting data from children to apply to the first study. The results of the survey were quantified & organized into a presentation and handout in Spanish. Announcements for the presentations were broadcasted over the local radio, resulting in good attendance.
Results: Based on the survey results, it was found that only 55% of the sector boiled their water correctly. When asked what foods contained protein, 69% gave a correct response, 16% did not know & 15% gave a wrong answer. For carbohydrates, less than 20% gave a correct response, 52% did not know & the rest gave wrong answers. For sugar, 80% were able to answer correctly & 20% did not know. For iron, 39% did not know what foods contained iron. For vitamin A, 9% gave a correct response, 50% did not know & the rest named wrong foods. For calcium, 24% responded correctly, 42% did not know, & the rest gave wrong answers. When looking at meal portions, it was found that most families served more than 50% carbohydrates & very little vegetables and protein. As for the growth chart for children, a stunted growth trend was seen compared to those children in urban areas. Out of 250 girls under the age of 18, 58% were under the 10th percentile for height & 26% under the 10th percentile for weight. For 143 males, 64% were under the 10th percentile for height & 33% under the 10th percentile for weight. Based on the survey of known chronic illnesses, 10.6% had diabetes, 15% had HTN, & 16.6% had cholesterol, although local doctors claimed that these rates were much higher due to poor diet.
Conclusion: Based on the outcome of the growth chart analysis & nutritional survey, a correlation between poor nutrition choices and stunted growth & disease prevalence could be seen. Therefore, proper nutritional education plays an important role in lifelong health.

Family history (ies) of glaucoma

Andrew Plummer

Mentors and Collaborators: Karanjit Kooner, MD, David Eng, David Seamont; Beverley Huet, MS; Xilong Li, MBA, Department of Ophthalmology

Purpose: To determine the prevalence of family histories of glaucoma and other diseases in patients with primary open angle glaucoma (POAG) and to evaluate overall influence of positive family history of glaucoma in this cohort.

Methods: In an IRB-approved cross-sectional study, patients with POAG were interviewed at a university –based clinic, a county hospital and a VA hospital. The following data were collected: family history (FHx) of glaucoma, cup/disc (C/D) ratio, intraocular pressure (IOP), visual field defects, medications, refraction, central corneal thickness (CCT), and average thickness of the retinal nerve fiber layer (NFLA). FHx of other comorbidities were grouped into several categories: cardiovascular, hematology, oncology, renal, gastrointestinal, autoimmune, metabolic, neurological, skin and psychiatric.

Results: Among 304 patients, 164 (53.9%) had FHx of glaucoma. Both groups had a similar C/D ratio, CCT and NFLA. Significantly, patients with FHx of glaucoma were diagnosed at a younger age (54.09 vs. 59.37yrs. p=.001), and had higher rates of laser surgery (62.92% vs. 37.08%, p=.05) as well as FHx of type 2 diabetes (60% vs. 40% p=.03). Patients with FHx of hypertension (HTN) had higher IOP than those without (16.00 vs. 15.00mmHg, p=.01). Among our most frequent FHx of comorbidity (HTN, type-2 DM and breast cancer), females predominated at rates of 60% or more. Our sample population was 51.3% male.

Discussion: Higher rates of the above factors and younger age at diagnosis among patients with FHx of glaucoma suggest a more severe course of POAG. Correlation between FHx of glaucoma and FHx of diabetes, as well as elevated IOP in patients with FHx of HTN, may indicate an intricate association between these diseases and the progression and severity of POAG.

Conclusions: Patients with FHx of glaucoma were diagnosed at an earlier age and required more vigorous treatment. Females in this cohort had a much higher frequency of other family histories, including HTN, DM and Breast Cancer.

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Efficacy of Device Algorithms in Attenuating the Competitive Effects Of Atrial Fibrillation on Cardiac Resynchronization Therapy; Study Design and Rationale

Ramon Luis Ramirez III

Mentor and Collaborators: Owen Obel, MD, Disha Kohli, MD, Daniel Sohinki, MD, Shining Sun, MD
Department of Internal Medicine- Cardiology

Cardiac resynchronization therapy (CRT) through biventricular (BiV) pacing is an effective therapy for heart failure (HF) associated with bundle branch block (BBB). CRT operates by preempting the dysynchronous cardiac activation that results from BBB with a BiV paced beat. CRT is compromised in AF by rapid native conduction of AF, which preempts BiV pacing, and results in ongoing cardiac dysynchrony. Device manufacturers have begun implementing programmable algorithms into their devices for the purpose of attenuating these effects. The purpose of this study is to test the efficacy of these algorithms in restoring effective CRT in the presence of conducted AF. Patients implanted with a BiV pacemaker (PPM) or implantable cardioverter defibrillator (ICD) with BiV pacing capacity, who are in AF, will be included. Patients who have heart block will be excluded. A 12-lead ECG will be recorded at rest with the pacemaker programmed to back up mode in order to observe the patient's ventricular rate during conducted AF and acquire a non-paced template. The pacemaker will then be programmed to 20 bpm above the patient's intrinsic ventricular rate to serve as the BiV paced template. The pacemaker will then be programmed to the patient's intrinsic ventricular rate. 12-lead ECGs will be recorded at rest: 1) with all algorithms off; 2) with ventricular sense response (VSR) algorithm on; 3) with VSR-plus-additional algorithms on (if available). In order to study patients during moderate activity, this procedure will be repeated after the patient performs three, two-minute walk tests. In order to determine the percentage of adequately BiV paced beats during conducted AF, two investigators, blinded to whether (and which) of the algorithms were turned 'on' or 'off', will evaluate the ECG strips on a beat-by-beat basis using the templates as a reference. The endpoints for this study are: 1) the percentage of patients who achieve >95% BiV pacing by ECG criteria as the result of the action of the device algorithms; 2) in each patient we will evaluate the relative increase in the percentage of conducted beats that meet the ECG criteria for adequate CRT as a result of programming the device algorithms on. AF has the potential to interfere with the delivery of CRT. Modern BiV pacing devices come equipped with algorithms aimed at ameliorating some of this effect, however the efficacy of these algorithms has not been formally evaluated. The hypothesis is that these algorithms are not effective at restoring CRT in the presence of conducted AF and more definitive therapy aimed at restoring sinus rhythm or effectively blocking the conduction of AF are required.

Urology: Prolapse Recurrence after Transvaginal Mesh Removal

Tanner Rawlings

Mentor: Philippe Zimmern, MD, Department of Urology

Introduction: Due to patients' concerns regarding pelvic organ prolapse (POP) recurrence after transvaginal mesh removal (TMR), we reviewed our rate of POP recurrence after TMR.

Methods: Following IRB approval, a prospective database of women undergoing TMR for complications after transvaginal mesh placement with at least 1 year minimum follow-up was queried for POP recurrence. Exclusion criteria included TMR via an abdominal approach (3). Recurrent POP was defined as either > Stage 1 on examination or need for re-operation at the site of TMR. Outcome measures were based on POP-Q at last visit.

Results: From 2007-2014, 52 of 82 women met inclusion criteria (Table 1). Twenty one women had less than one year follow up and 9 underwent mesh removal via abdominal approach. Mesh types included Avaulta (7), Prolift (23), Perigee (8), Elevate (3), Pinnacle (2) Prosima (1) and unknown (8). Interval between insertion and removal was 45 months (10-165). Indications for mesh removal included dyspareunia /vaginal pain (43), mesh extrusion (31), pelvic pain (20), buttocks pain (1), rectal pain (2), abscess (1), groin pain (1), defecatory problems (2), and urethrovaginal fistula (1) with 73% of women presenting with multiple indications. Baseline demographics are shown in Table 1.POP recurrence rate at the same compartment as TMR was 13.5% (n=7), at a mean follow-up of 30 months (12-84). Five patients underwent surgery for recurrent POP at mean 9 months (5-13). Two patients chose observation. Repair procedures included native tissue repair with anterior vaginal wall suspension with cystocele repair (4) and mesh sacrocolpopexy (1). 25% of patients had prolapse at the time of TMR, with one patient ultimately undergoing repair for persistent anterior prolapse at 8 months post TMR. 9.6% had POP develop in a different compartment than the location of their TMR, with 3 undergoing surgical repair at a mean of 27 months (10-52).

Conclusion: At a mean of 2.5 years follow-up, POP recurrence at the site of TMR was 13.5%, with 9.6% electing surgical repair.

Mean age	58 (38-77)	POPQ Before Excision	
Mean parity	2 (0-6)	Aa	-2.5 (-3-0)
Mean BMI	28 (17-39)	Ap	-2.8 (-3-0)
Post-menopausal patients (n) (50/53)	39	POP Before Excision	
Hormone replacement therapy (n) (52/53)	21	Stage II	12
Patients reporting sexual activity (n) (50/53)	24	Stage III	0
		Stage IV	0

What is the contemporary cost of Stress Urinary Incontinence Procedures

Tanner Rawlings

Mentor: Philippe Zimmern, MD, Department of Urology

Introduction: To review the literature on cost economic analysis (CEA) related to surgical procedures for stress urinary incontinence (SUI).
Methods: A MEDLINE search related to the economic analysis of SUI surgical procedures for the years 2000 – 2014 included the MeSH terms "tension-free vaginal tape", TVT, "trans-obturator tape", "TOT", "Burch colposuspension", "stress urinary incontinence", "economic analysis", and "cost-effectiveness analysis". Important criteria for evaluating articles were selected from panels that set out criteria to evaluate CEA as summarized in Table 1.
Results: Thirteen articles compared cost of TVT, TOT, or Burch colposuspension (BC). Six compared TVT to BC, 1 TVT to other surgical procedures for SUI (1), open BC to laparoscopic BC (1), TVT to TOT (3), 1 analyzed various slings and meshes for various types of incontinence and 1 compared the single-incision mini sling to TVT. Three articles originated from the United States, 4 from Europe, 4 from UK and 2 from Canada. Eight described CEA, 2 cost-utility analysis (CUA), and 3 cost comparison. Follow- up time for patients ranged from 6 to 24 months in 8 articles, with 4 having a minimum of 24 months of follow-up. All studies adhered to criteria for including incremental costs. Eleven included some type of long-term cost in their analysis, with 8 including the cost of reoperation. Four included a Markov Model with a decision tree.
Conclusion: The contemporary literature on CEA for SUI is a burgeoning field, with established reporting criteria not always well-adhered to, thus hampering study comparison. As women live longer, more use of long-term data and its associated costs will be important as complications and reoperations can affect the real overall cost of an anti-incontinence surgical procedure.

Criteria	
Target population and subgroups	*Measurement of effectiveness*
Setting and location	*Estimating resources and costs*
Study perspective	*Currency, price date, conversion*
Comparators	*Study parameters*
Time horizon	*Incremental costs and outcomes*
Discount rate	*Characterizing uncertainty*
Choice of health outcomes	*Long term costs*

Cost analysis of the Anterior Vaginal Wall Suspension Procedure to the repair of stress urinary Incontinence with early grade anterior Compartment prolapse

Tanner Rawlings

Mentor: Philippe Zimmern, MD, Department of Urology

Introduction: To evaluate the contemporary cost of the Anterior Vaginal Wall Suspension (AVWS) procedure to correct SUI with early grade compartment prolapsed.

Methods: The cost of AVWS for women undergoing AVWS alone (with no associated procedure) was analyzed from a prospective long-term database. Costing data was obtained from a tertiary care institution for operating room expenses, medical and surgical supplies, pharmacy, anesthesia supplies, and room and bed. Professional fees for the AVWS procedure were obtained from the Medicare Fee for Service Schedule. Costs for 2012 were adjusted by 3% to match 2013 costs. Due to non-normality in the data, the non-parametric Wilcoxon Rank Sum test was used to test for differences in cost by fiscal year or payer type. The Student *t*-test was used to ensure this population was a representative sample by testing for differences between the patients in this sample compared to the remainder of the patients that have undergone AVWS without concomitant surgery at our institution

Results: For 2012 – 2013, 34 of 48 women met inclusion criteria. One charity case was excluded, and others had concomitant procedures like hysterectomy. With the 3% inflation adjustment for 2012, the mean total cost was $3681 ± $764, with a median cost of $3664. Anesthesia, operating room, and room and bed costs differed significantly from 2012 to 2013. Only pharmacy cost differed between payer mix and Medicare. The sample analyzed had a shorter mean surgery time (69.6 min) compared to the overall AVWS population (86 min).). This cost data compares favorably to the average cost reported in contemporary U.S. literature for Tension free vaginal tape (TVT)($8082 – 9579), transobturator tape (TOT) ($9017), and BC ($9320 - $105450)

Conclusion: The AVWS mean total cost was $3681, with an increase in cost from 2012 to 2013 related to anesthesia, operating room, and room and bed costs, a figure much lower than most reported costs for comparable anti-incontinence procedures.

Long-Term Use of Nitrofurantoin Prophylaxis for Urinary Tract Infections In The Older Patient: a Critical Analysis Of The Beers Recommendations

Lauren L Rego

Mentor: Philippe E Zimmern, MD, Department Of Urology

Introduction and Objectives: To review the current literature on reported pulmonary adverse reactions (ARs) of long-term Nitrofurantoin (NF) suppression in older patients treated for urinary tract infections (UTIs), as well as the use of safer alternatives.

Methods: In the wake of the recent Beers criteria (2012), an extensive literature search was performed on PubMed for the search terms “Nitrofurantoin,” and “Nitrofurantoin and lung, pulmonary, or ARs”. Relevant cited papers were also analyzed. Articles not in English, or related to children, or pregnant women were excluded.

Results: In 69 articles and other texts meeting the inclusion criteria from 1969 to 2014, rates of long-term NF-related pulmonary ARs compared to total NF prescriptions differed worldwide, but remained extremely small at 0.0001% (USA) and 0.001% for pulmonary and hepatic ARs (France). The breakdown of pulmonary ARs compared to all NF ARs also differed across the literature from 2% (UK), 3% (Holland), 5% (Sweden), to 7% (Australia). Case study reports for NF-related chronic pulmonary ARs in women (N=21) confirmed their occurrence both above and below the age 65, underscoring their unpredictable nature. Bacterial resistance to NF alternatives has increased over the past decade: from 3% to 17.1% for fluroquinolones, and from 17.9% to 24.2% for TMP-SMX.

Conclusion: Pulmonary risks of long-term NF prophylaxis in older patients treated for UTIs are extremely minimal, and should not deter from the use of NF in this population. Antibiotic alternatives to NF exist, but may lead to more antibiotic resistance.

"Regular Monitoring" in Older Patients On Long-Term Nitrofurantoin Prophylaxis: What Does It Mean Practically?

Lauren L Rego

Mentor: Philippe E Zimmern, MD Department of Urology

Introduction and Objectives: To review the current literature for recommendations or guidelines for "regular monitoring" of older patients on long-term Nitrofurantoin (NF) prophylaxis to prevent/detect adverse reactions (ARs).

Methods: The recent Beers criteria (2012) recommended avoiding NF for long-term suppression due to the "potential for pulmonary toxicity and availability of safer alternatives". A literature search was performed on PubMed for national organizations, textbooks, and any report or publication advocating methods of follow-up to detect and or prevent long-term NF-related ARs. Articles not in English, or related to children or pregnant women were excluded.

Results: Thirteen sources recommended various methods to improve the safety of patients on long-term NF suppression. Monitoring recommendations were vague, calling for increased scrutiny and education either in general (N= 5), or on the part of the physician (N=10) and/or patient (N=3). Two studies (2008, 2012) recommended biannual chest x-rays, liver function tests, and kidney function monitoring, but with no supportive prospective data to justify these guidelines. No studies documented the role of these preventative guidelines in the early detection of long-term NF-related AR, and none addressed the cost/effectiveness of these additional monitoring tests.

Conclusion: While many sources give a variety of recommendations on monitoring an older patient on long-term NF prophylaxis, none appeared to be scientifically tested in the long-run to either detect ARs or prevent them altogether.

Upper Tract Imaging Abnormalities Related to Recurrent Urinary Tract Infections Rarely Found in Women

Lauren L Rego

Mentor: Philippe E Zimmern, MD, Department of Urology

Introduction and Objectives: To investigate the rate of upper tract imaging abnormalities as possible source for UTI recurrence in women with documented RUTIs.

Methods: Following IRB approval, a prospective database of non-neurogenic women with documented RUTIs (≥ 3 UTI/year) was reviewed for relevant demographic and clinical data (Table 1), as well as radiology-interpreted upper tract imaging study (renal ultrasound (US), CT scan, IVP) findings. Patients were excluded for irretrievable image (3), no imaging study performed (13), an obvious source for RUTI (intermittent catheterization, indwelling catheter, > stage 2 anterior prolapse)(8), or history of pyelonephritis (1). Any upper tract imaging anomaly was recorded.

Results: From 2006 to 2014, 170 of 280 women with RUTIs were studied, including US alone (N=76), CT alone (N=47), US and CT (N=38), and IVP with US or CT (N=9). Out of total imaging findings (N=84 in 76 women), 81/84 (96.4%) were noncontributory: duplicated systems (10), non-obstructing renal stone (16), renal cyst (46), renal tumor (1), questionable small renal lesion (8). In 3/76 women (3.6%), mild hydronephrosis appeared related to RUTI; but no clinical parameters (BMI, gravida, parity, immunosuppression, history of urethral dilation or kidney stones, degree of cystocele, infecting strain, post-void residual) were correlated with these upper tract findings. Six of 15 (40%) patients with kidney stone history had stones on imaging (ranging from .13 mm to .31 cm) versus 10/155 (6.5%) of patients that did not have such history had stones on imaging ($p < 0.0001$).

Conclusions: In this cohort of predominantly Caucasian post-menopausal women, upper tract imaging yielded a low percentage of significant findings associated with RUTIs, thus questioning the routine practice of upper tract studies in this population.

Safety of Chemoembolization for unresectable hepatocellular carcinoma in patients with a pre-exisiting transjugular intrahepatic portosystemic shunt

Katherine Rief

Mentors: Sanjeeva Kalva, MD (UTSW Interventional Radiology),
& Suvranu Ganguli, MD (Massachusetts General Hospital)

Study Aim: To assess the safety of transarterial chemoembolization (TACE) for unresectable hepatocellular carcinoma (HCC) in patients with a pre-existing transjugular intrahepatic portosystemic shunt (TIPS).

Methods: A multi-institutional, IRB approved, retrospective review was conducted of patients with a pre-existing patent TIPS who underwent TACE to treat unresectable HCC between 2009 and 2014. Patients (7 male, 4 female) ranging from 39 to 74 years of age (mean 61, SD 11) were included. Parameters of interest included type of TACE (drug-eluting beads or traditional), number of TACE procedures, 30-day mortality from last TACE procedure, and any complications or toxicity following TACE.

Results: Ten of the eleven patients underwent super-selective drug-eluting bead TACE, using doxorubicin at a dosage ranging from 50mg to 150mg (Median 100mg). Number of TACE procedures per patient ranged from 1 to 4 (Median 1). Three of the patients (3/11, 27%) experienced toxicity (CTAE v4) grade 2 or higher immediately following the TACE procedure. Two of these patients experienced Grade 2 Albumin Toxicity. Another had Grade 3 Toxicity of AST, ALT and bilirubin. 73% of patients were discharged within 24 hours. The remaining 3 patients were hospitalized for pain, edema, or acute pancreatitis for 3, 5 and 20 days respectively. All eleven patients were alive and discharged from the hospital 30 days after the most recent TACE procedure.

Discussion: TACE can be well tolerated by patients with a patent TIPS given adequate liver function. As additional cases are performed we hope to clarify the efficacy and most appropriate TIPS patient population for TACE.

Peritoneal Drainage After Surgical Intervention for Congential Heart Disease

Christine Ritchie

Mentor: Peter Pak, MD, Department of Pediatrics

Purpose: Patients who undergo surgical intervention for congenital heart disease frequently develop abdominal ascites and elevated intraabdominal pressures. In this study, we review a single institution's experience with peritoneal drainage (PD) catheters in patients who have undergone surgical intervention for congenital heart disease.

Methods: We retrospectively reviewed medical records of all patients in whom PD catheters were placed after cardiac surgery for congenital heart disease over 5 years.

Results: Sixty-six patients received PD catheters after cardiac surgery. Twenty-seven (40.9%) were male. The mean age was 2.5 years (Range: 5 days – 23.3 years). Mean duration of therapy was 42.5 days (Range: 1-401 days). Thirty-seven (56.1%) patients received PD catheters within 30 days (Mean 11.2 days). Thirty-three (50%) patients survived. There were no differences in sex, age, duration of therapy, drain output, vasopressor requirement, or creatinine between survivors and nonsurvivors.

Conclusion: While peritoneal drainage catheters may facilitate end organ perfusion and venous return, it is unclear whether they confer a survival advantage. In the setting of PD catheter placement, factors other than patient sex, age, and drain effectiveness, likely play a larger role in patient outcomes.

Pediatric obstructive sleep apnea (OSA): Differences between normal-weight, overweight, obese and morbidly obese children

Brian Scott

Mentors: Romaine Johnson MD, Ron Mitchell MD
Department of Pediatrics

The severity of obstructive sleep apnea (OSA) in children determines perioperative management and is an indication for postoperative polysomnography (PSG). There is a paucity of data on differences and predictors of OSA severity in children in different weight categories. The primary objective was to compare demographic, clinical and polysomnography parameters in normal-weight, overweight, obese and morbidly obese children and to identify factors that are associated with OSA severity. Healthy children aged 2-18 who underwent polysomnography at an academic children's hospital were included in the study. Demographics, clinical findings, and polysomnogram parameters were recorded. Children were categorized as normal-weight, overweight, obese, or morbidly obese based on CDC criteria. Differences were assessed with linear and logistical regression models. Significance was set at $p<0.05$. 290 children were included. Morbidly obese were older than normal-weight children (mean 8.0±0.5 versus 5.8±0.3; $p<0.001$) but less likely to have a normal PSG (16% versus 48%; $p=0.02$). There were no differences in gender, ethnicity, birth status (term or pre-term), tonsil size or AHI between the different weight categories. Sleep efficiency and %REM were decreased in morbidly obese children ($p<0.05$). The AHI was positively correlated with increasing BMI z-score as a function of increasing age ($p<0.001$). There are important differences in children with OSA in different weight categories. OSA severity is correlated with a combination of increasing age and weight but not with either variable independently. This study suggests that obese and morbidly obese older children are most likely to have severe OSA and should undergo routine PSG.

Do males have more severe glaucoma?

David Seamont

Mentor and Collaborators: Karanjit Kooner, MD, David Eng, Andrew Plummer, Xilong Li, PhD, Beverley Adams-Huet, MS
Department of Ophthalmology

Purpose: To understand the role of gender in the development and progression of primary open angle glaucoma (POAG) by contrasting the severity of glaucoma, health differences and risk factors in male and female patients with POAG.
Methods: In an IRB approved cross-sectional study, 304 patients with POAG were interviewed across 3 hospitals (a county hospital, university based clinic, and VA hospital). Detailed family and medical histories were recorded from patients through a review of systems interview and verification from patient charts. Markers of the severity of glaucoma, such as family history of glaucoma, myopia, visual field (VF) defects, nerve fiber layer thickness, central corneal thickness (NFLA), C/D ratio, IOP, number of medications, and glaucoma surgeries were recorded. These markers, as well as patient comorbidities, were stratified by gender and compared using Fisher Exact test for categorical variables, analysis of variance for Gaussian distributions, and Kruskal-Wallis test for non-Gaussian continuous variables.
Results: There were 148 females and 156 males. Men had more VF damage of 1.99 vs 1.68 ($p=0.0168$) based on a 0-3 severity scale, higher C/D ratio of 0.77 vs 0 .73 ($p=0.0373$) and needed more glaucoma medications (2.72 vs 2.11, $p=<0.0001$) than women respectively. No significant difference was found for CCT or IOP. 55.41% of women and only 39.1% of men had a first degree relative with POAG ($p=.0057$). Women were more likely to have immunological disease (51.35% vs 28.21%; $p= <0.001$) and disease of the GI system (36.49% compared to 23.08%; $p= 0.012$).
Discussion: The severity of VF defects in male patients points to a more severe disease course while the increased medications point to an increased difficulty in management of the disease. Family history of POAG was more associated with female patients than males. Women also seemed to carry higher burden of immunological and GI diseases, a finding that requires further exploration. With larger sample sizes and a control group, specific diseases can potentially be isolated as gender-specific co-morbidities in POAG.
Conclusions: Our study suggests that men develop a more severe form of glaucoma. In addition, it stresses that we need to consider both ocular and systemic associations in developing the picture of an “at-risk” patient, with implications both in gender-specific treatment plans and patient screening.

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Evaluating patient perception of differences in effectiveness of oral versus parenteral non-steroidal anti-inflammatory drugs

Jeremy Semeiks

Mentors and Collaborators: Lynn Roppolo, MD, Simone Neuwelt, MD, Larissa Velez, MD
Department of Emergency Medicine

Background: Pain is a very common reason for emergency department (ED) visits. Providing safe, effective analgesia is not only central to providing good health care, but also to overall patient satisfaction. Prior work has shown that although parenteral administration of NSAIDs is more expensive and has greater risk of adverse effects than oral administration, there are no significant differences between the two routes in amount or efficiency of pain relief. However, some clinicians believe that patients presenting with pain to the ED prefer parenteral over oral NSAIDs, due to an assumed patient perception that shots are more effective than pills. Additionally, prior studies in this area have not examined patient ethnicity as a factor in administration preference.
Objective: To determine the extent to which patient preference for oral versus parenteral methods of NSAID administration can be influenced by education.
Methods: All patients who presented to a county hospital ED with a chief complaint of pain and were subsequently prescribed any type of NSAID were included. After obtaining consent, a survey was given in English or Spanish to obtain demographic data and question the patient on three items: (1) Which NSAID form (pill or shot) is better at taking away pain (2) Which NSAID form is faster at taking away pain (3) Which NSAID form is preferred to take away pain. This preference survey was repeated after educating the patient that the shot and the pill are equally effective but the shot costs more and causes pain. Statistical analysis was performed using standard methods.
Results: N=270 patients were surveyed, with mean age 42; 49% female; and 37% African American, 37% Hispanic, and 23% Caucasian. Before education, overall subjects were equally likely to prefer the pill versus the shot but believed the shot to be faster (82%) than the pill (17%). Patient education on NSAIDs significantly influenced patient beliefs on all three items: 73% found the pill to be as effective as the shot, 55% found the pill to be as fast as the shot, and 75% preferred the pill ($p<0.001$ in all three cases). There were no statistically significant differences in any of these beliefs across patient ethnicity, education, or narcotic preference.
Conclusion: Despite clinician assumptions, most patients have favorable attitudes toward NSAID pill versus shot effectiveness and overall preference, and can be easily influenced by briefly educating these patients in the ED. This suggests brief patient education is effective to reduce cost of treating minor pain in the ED. Future work should compare effectiveness of various education methods.

Interrater Reliability of Point of Care Ultrasound for Inferior Vena Cava Distensibility in Mechanically Ventilated Patients

David Serrano

Mentors and Collaborators: Jonathan Purcell, MD, Jeremy Brady, Ben Cooper, Eric Lopez
Department of Emergency Medicine

Background: The inferior vena cava (IVC) is ideally suited for monitoring plasma volume by virtue of its large capacitance and distensibility. Small changes in central venous pressure lead to large changes in vessel diameter, therefore allowing the use of imaging modalities to track changes in its contraction and expansion as a measure of intravascular volume. For this reason, the use of bedside ultrasound (US) to measure volume responsiveness in patients requiring fluid resuscitation has become increasingly popular despite inconsistent evidence supporting its validity in all patients. Previous studies that have attempted to measure the interrater reliability of IVC US to measure volume responsiveness have focused on spontaneously breathing patients. However, most validated uses of the IVC to predict volume responsiveness are in mechanically ventilated patients.
Objective: We sought to determine the interrater reliability of IVC distensibility measurements by emergency medicine physicians using point of care US on mechanically ventilated patients.
Methods: We conducted a prospective study of adult emergency department patients who were mechanical ventilated. Each patient that was enrolled had two IVC US scans performed by two different 2nd or 3rd year emergency medicine residents. Each scan was performed in both B-mode and M-mode and caliper measurements were taken at maximum and minimum vessel diameter.
Results: In total 32 US scans were performed on 16 patients by 18 different emergency physicians. Using B-mode, the ICC for maximum inferior vena cava diameter was .855 ($p<.05$) and for minimum diameter was .831 ($p<.05$). Using M-mode, the ICC for maximum inferior vena cava diameter was .855 ($p<.05$) and for minimum diameter was 0.887 ($p<.05$). The ICC for the calculated IVC distensibility when using B-mode was .624 ($p<.05$) and insignificant when using M-mode.
Conclusion: Despite having a high interrater reliability for absolute maximum and minimum IVC diameter, the interrater reliability for IVC distensibility in mechanically ventilated patients was moderate (B-mode) to low (M-mode). Given that the cutoff for IVC distensibility to detect volume responsiveness is small (12-18%), our data cautions against the use of IVC US to guide fluid administration in mechanically ventilated patients.

A multi-parametric investigation of vascular alterations in elderly with hypertension

Adam Sheffield

Mentor and Collaborators: Kevin King, MD, Hanzhang Lu, PhD, & Min Sheng, MD
Advanced Imaging Research Center

Background: Along with aging comes many cardiovascular and cerebral changes that impact a person's health. These changes manifest as variances in blood pressure, brain volume, cerebral blood flow (CBF), oxygen metabolism, and neurological functioning.
Objective: The purpose of this study is to provide evidence to support new or previously known biomarkers for declining cerebrovascular health, such as cerebral arterial stiffness, reduced vessel capacity, and thickening of the extracellular matrix.
Methods: 45 participants ranging from the ages of 61 to 79 with a mean of 67 were studied using a 3 Tesla MRI. Several MRI techniques were employed to acquire and analyze data. Phase-contrast (PC) MRI was used for acquiring images of moving fluid, so that arteries containing blood flow to the brain could be isolated in order to calculate total CBF. Blood-oxygen-level dependent contrast images and end-tidal CO_2 and O_2 measurements were also obtained using MRI after the participants were given a different sequence of gases to breathe containing varying amounts of oxygen, carbon dioxide, and nitrogen. This allowed the cerebrovascular reactivity (CVR) and venous cerebral volume (vCBV) of the vessels to be determined. Venous oxygenation (Yv) was assessed using T2-relaxation-under-spin-tagging (TRUST) MRI technique. Linear regressions were performed to account for age, sex, and blood pressure. Data were also analyzed by putting participants with a systolic blood pressure greater than 140 into a hypertensive category for comparison. Other data acquired during or immediately prior to the MRI scans include systolic and diastolic blood pressure, brain volume, and the oxygen saturation level of venous and arterial blood.
Results: A p-value of <0.05 was used to determine significance. The CVR for the hypertensive group was lower than that of the non-hypertensive group ($p<0.01$) and CVR decreased as systolic blood pressure increased ($p=0.02$). CVR also decreased with increasing age ($p=0.02$) and was higher in males than in females ($p<0.01$). CBF increased with systolic blood pressure ($p=0.03$) and was higher in females ($p=0.03$). Yv also increased with systolic blood pressure ($p=0.02$) and correlated strongly with CBF values ($p<0.001$).
Conclusion: These results support certain relationships between blood pressure and the vascular markers within the brain, which may appear before cognitive decline or clinical symptoms emerge. This study is an early step on the path to discovering easily identifiable precursors to neurological changes that take place as normal aging processes occur.

Paclitaxel-Eluting vs. Bare Metal Stent Implantation in Saphenous Vein Graft Lesions: Very Long-Term Follow-Up of the SOS (Stenting Of Saphenous vein grafts) Trial

Alan Sosa

Mentor and Collaborators: Emmanouil Brilakis, MD, PhD, Howard Chao, Andres Guerra, Henry Han, George Christopoulos, MD, James A. de Lemos, MD, Owen Obel, MD, Tayo Addo, MD, Michele Roesle, RN, BSN, Donald Haagen, RCIS, Bavana V. Rangan, BDS, MPH, Subhash Banerjee, MD
Department of Internal Medicine- Cardiology

Background: The very long-term (>3 year) outcomes after implantation of drug-eluting as compared with bare metal stents (BMS) in saphenous vein grafts (SVGs) have received limited study.

Methods: In the Stenting Of Saphenous vein grafts (SOS) trial 80 patients were randomized to BMS or paclitaxel-eluting stents (PES). During a median follow-up of 35 months use of PES was associated with better clinical outcomes. We report very long-term outcomes on 62 patients enrolled at the highest enrolling institution.

Results: Of the 62 studied patients 31 received a BMS and 31 a PES. Both study groups had similar baseline characteristics. During a median follow-up of 6.9 years the study patients experienced 116 major adverse cardiovascular events (MACE). Compared with patients who received BMS those who received PES had lower incidence of MACE (hazard ratio [HR]=0.56, P=0.04), target lesion revascularization (HR=0.20, P=0.001), target vessel revascularization (HR 0.41, P=0.02), target vessel failure (HR=0.35, P=0.001), and definite or probable stent thrombosis (HR=0.14, P=0.03). There was no significant difference in all-cause mortality (HR=1.77, P=0.15) and myocardial infarction (HR=0.52, P=0.10) between the two groups.

Conclusion: The early benefit observed with use of PES vs BMS in SVGs persisted during very long-term follow-up.

Confetti Depigmentation as a sign of rapidly progressing vitiligo

Juan Jesús Sosa

Mentor and Collaborators: Amit G. Pandya, MD, Sharif D. Currimbhoy, MD, Uzoamaka Ukoha, Samantha Sirignano, Ryan O'Leary, Travis Vandergriff, MD
Department of Dermatology

Objective: Vitiligo is a common disease causing disfiguring depigmentation. Assessment of disease activity is important to determine prognosis and select appropriate treatment. Confetti depigmentation may be a clinical sign of rapidly progressing vitiligo.

Design: Retrospective review of charts and images of patients with vitiligo.
Setting: University-affiliated tertiary health care center in Dallas, Texas
Patients: Records of 178 patients with vitiligo were reviewed of which 7 fit the inclusion criteria of having confetti-like lesions of depigmentation, baseline and follow up images and lack of any treatment. Images of 13 lesions from these 7 patients were evaluated for percent depigmentation by three independent reviewers.

Main Outcome Measures: Percent depigmentation of vitiligo lesions in image.

Results: The median time between baseline and follow-up images was 16 weeks. The mean percentage of depigmentation at baseline was 19%, which increased to 51% in follow-up images. Two with additional follow-up images at median 31 weeks had mean depigmentation of 71%. A skin biopsy of a confetti lesion in one patient revealed an inflammatory infiltrate in the papillary dermis including CD 8+ T cells at the dermal-epidermal junction.

Conclusions: A confetti-like pattern of depigmentation may be a negative prognostic indicator for patients with rapidly progressing vitiligo. Patients identified with this pattern of depigmentation may require more aggressive treatment in order to stabilize their disease. Further, prospective studies evaluating this physical finding should be performed.

The Clinical Presentation, Treatment, and Outcomes of Pediatric Thyroid Surgery in Children

Nicholas Spendlove

Mentor and Collaborators: Diana Diesen, MD, Lorrie S. Burkhalter, & Michael Skinner MD
Department of Pediatric Surgery

Purpose: Children have thyroidectomy for hyperthyroidism, nodules, and cancer. Pediatric thyroid cancer is aggressive but with treatment, has a favorable prognosis. This study characterizes the clinical presentation, treatment, and outcomes in patients requiring thyroidectomies.

Methods: After IRB approval, we performed a retrospective review of all 45 patients who had thyroid operations at Dallas Children's Medical Center between 2009 and 2014.

Results: At diagnosis, our patient had a median age of 13 with 82% females, 69% Caucasian, 6.7% with history of irradiation, 6.7% personal history of cancer and 16% family history of thyroid cancer (13% MEN-2A). Patients underwent total thyroidectomy (42%), near total/subtotal thyroidectomy (24%), and lobectomy (31%) with 51% having lymph node dissections and 33% having a parathyroid autotransplant. Fifty-three percent of patients had malignancy with 24% and 2% having malignant lymph node and distant metastases, respectively. Sixty-seven percent of patients with cancer received postoperative I131. Risk factors for complications were palpable mass, palpable nodes, malignancy, and type of surgery ($p<0.05$). Our complications included temporary nerve injury (9%), temporary hypocalcemia (7%), and wound infection (2%) with the rate of complications by procedure being total thyroidectomy (21%), near/subtotal thyroidectomy (36%), and lobectomy (0%). Of the 7 patients who had complications, 6 had Central Neck Dissections and 4 had Lateral Neck Dissections. FNA was performed on 73% of patients with a sensitivity and specificity of 93% and 100%, and a PPV and NPV of 100% and 75%, respectively. Indeterminate FNA or suspicious FNA had malignancy on final pathology was 21% and 100%, respectively. Follicular FNA was found in 17 patients. Ten patients had lobectomies after which 2 required completion thyroidectomies for malignancy. Seven patients had total thyroidectomies, two of whom had complications. Patients with follicular FNA had a 35% risk of carcinoma on final pathology.

Conclusions: Malignancy is a common indication for thyroid cancer in children. Certain characteristics are associated with increased complications. In the case of follicular lesions, lobectomy may be performed understanding the risk of needing completion thyroidectomy

A Four-Year Experience at a Level I Pediatric Trauma Center: 2009-2012

Audrey Stevens

Mentor: Robert P. Foglia, MD & Rachel Renkes
Department of Pediatric Surgery

Background: In the United States, trauma is the leading cause of death and disability in children. Annually 140,000 children are seen in the Emergency Department(ED) at our single Level-I verified pediatric trauma center. 12,000 – 13,000 are due to trauma, with approximately 1,400 admissions. We reviewed the trauma experience at our hospital to assess its impact based upon the management, outcome, and hospital charges for these patients.
Methods: With IRB approval, the hospital Trauma Registry was accessed to identify the severity of injury, management and outcomes for patients admitted from Jan. 2009 – Dec. 2012. Data points included age, gender, Trauma Activation (TA), Injury Severity Score (ISS), admit service, ICU admission, length of stay (LOS), operative need, mortality, and hospital charges. ED deaths were excluded.
Results: There were 5,514 trauma admissions, 8.18% of all of the 67,429 hospital admissions; 60% were boys and 40% girls. Age was 6.82±4.41 years, and ISS was 8.21±7.54. 54% had a minor ISS (0-7), 32% moderate (8-15), 9.5% severe (16-24), and 5.2% very severe (>24). TAs were called in 1346(24.4%) patients, 1014(75.3%) ALERTs and 332(24.7%) STATs. 2607 (47.3%) patients required an operation. The majority of patients were assigned to Pediatric Surgery (44%) and Orthopedic Surgery (41%). Trauma ICU admissions were 14.2% of all trauma admissions, comparable to all hospital ICU admissions at 17.4%. The trauma ICU LOS was 3.59±5.64 days; this doubled to 7.02±15.96 days for all hospital ICU admissions. The trauma LOS was 2.48±4.57 days; again, this doubled to 5.17±10.31 days for all hospital patients. There were 64 trauma deaths (1.16%). The trauma cohort accounted for $188,472,675 of hospital charges, which was 4.3% of all hospital charges ($4,375,099,917) for four years. The average charge per trauma patient was $36,746 vs. $65,324 for all admits.
Conclusion: If trauma were a single disease, it would be the third most frequent admission diagnosis. The trauma population is heterogeneous; 24% of the trauma patients required TA, 14% ICU admission, 47% needed surgery, and 46% had a moderate or higher ISS. The mortality rate of 1.16% is less than the national average of 2.26%. Hospital charges and the LOS (total and ICU) for trauma patients were half that of all patients. The lower cost may be due to an efficient use of resources, management, and care of trauma patients. Our patient management and hospital charges for these trauma patients, coupled with good outcomes, may be a model for other hospital admissions and other trauma programs.

The Use of Vapocoolant in the Adult Population to Improve Patient Perception of Pain with Peripheral Intravascular Access

Jacob Tausiani & Alexander Yau

Mentor and Collaborators: John P. Pease, MD, Christina Noah, MSN, RN, CEN, & Courtney Edwards, MSN/MPH, RN, CCRN-CEN
Department of Emergency Medicine

Importance: Patient anxiety and perception of pain during peripheral intravenous (PIV) cannulation can unfavorably impact both patients and treatment provided. Topical analgesics are rarely used due to a long time to effectiveness and treatment delay, but vapocoolant has a more immediate effect.

Objective: To investigate whether the use of a topical vapocoolant anesthetic spray at the site of intravenous access reduces pain and anxiety associated with PIV insertion in an adult emergency room population.

Design, Setting and Participants: A randomized, doubleblind, placebo-controlled, single-center trial, conducted from July 2014 to August 2014 in an emergency department with 72 patients with orders for PIV placement receiving either topical vapocoolant spray (n=38) or a placebo spray (n=34).

Interventions: Vapocoolant spray or placebo was applied to the IV site and allowed to evaporate prior to cleansing and needle insertion.

Main Outcomes and Measures: The primary outcome was patient perception of pain and anxiety with PIV needle insertion using a 0-10 Likert scale. Secondary outcomes included patient/staff preference for the use of the topical anesthetic for future procedures and staff perception of the procedure and patient anxiety.

Results: The patient groups did not vary significantly in previous history of IV placement ($p>0.999$) nor anxiety pre-procedure ($p=0.785$). Median scores for patient perception of pain did not vary significantly between vapocoolant (2.0) and placebo populations (2.5), nor did the scores vary significantly for patient-forecasted anxiety regarding the procedure should the same procedure be used again (0.5 for vapocoolant, 0.0 for placebo; $p>0.05$). Additionally, when asked if they desired the spray for future procedures, nurses and patients responded identically: 89% expressed the desire for vapocoolant, while 74% desired future use of placebo; however, the difference was not significant ($p>0.05$). Neither placebo nor vapocoolant affected the nurses' ability to obtain IV access ($p<0.05$). No skin blanching or lesions due to the spray were noted.

Conclusion: Among adult patients in the Parkland Emergency Department receiving PIV access, no significant differences in pain relief or alleviation of anxiety were found between treatment using a vapocoolant spray or placebo.

Assessing the Reliability of Greilich Evaluation Tool (GET) for Measuring OR to ICU Transfers of Care Following Cardiac Surgery

Neela Thangada

Mentors: Philip Greilich MD & Mandy McBroom
Department of Anesthesiology

A transfer of care (TOC) involves shifting patient care responsibilities between healthcare teams. This study focuses on post- sternotomy OR to ICU TOCs, which prove challenging because the OR team must monitor patient's vitals, perform life-sustaining measures such as manual ventilation, and educate the ICU team about the patient's health status in a chaotic ICU setting. Cognitive aids—such as checklist tools that facilitate effective information transfer—have been shown to reduce TOC-related medical errors.

This study tests the reliability of the Greilich Evaluation Tool (GET), a checklist designed for trained observers to evaluate OR to ICU TOCs.

The GET was developed by clinicians through an iterative process of five cycles, which identified essential elements of sender-receiver communication in the TOC. The GET measures the following eight essential elements of a TOC: clear initiation of handoff process, distinct sequence to handoff process, bedside presence of providers during handoff, anesthesiologist communicates necessary information, surgeon communicates necessary information, receiving nurse repeats back care goals, clear termination of handoff process, and the presence of a noise and distraction free "sterile cockpit." Trained observers assigned a "yes," "no," or "partial" scoring for each of the eight essential elements. A cardiac anesthesiologist trained two observers on how to use the GET for evaluating TOCs. The reliability of the GET was measured using unweighted Cohen's kappa, a statistical measure of inter-rater agreement, with κ of 0.8-1 suggesting strong agreement between raters. The two trained observers used the GET to evaluate five (n=5) TOCs; these paired observations served as a baseline adjusting for inter-rater variability. The remaining paired observations measured the reliability of GET.

A total of nineteen paired observations (n=19), assessing 180 inter-rater agreements, were conducted. The trained observers agreed 89% of the time on the outcomes of the essential elements. An inter-rater reliability, k= 0.8, was achieved for the paired observations. The GET showed that 58% of the essential elements were covered during the TOCs. Certain essential elements, such as nursing repeat back and the distinct sequence of TOC, were almost never addressed.

This study illustrates that the GET has an acceptable reliability for rating TOCs when utilized by trained observers. There is still significant room for improving the quality of TOCs since providers covered less than 60% of essential elements during a handover.

Diffusion Kurtosis Imaging as a Diagnostic Tool for Parkinson's Disease

Joseph Vento

Mentors: Dr. Maria Otaduy & Dr. Ellison Cardoso
Magnetic Resonance Department, University of São Paulo

Reliable diagnosis of Parkinson's disease requires long-term assessment of a patient's motor performance tests and response to medication. Though the development of magnetic resonance imaging (MRI) presents an additional tool in making a diagnosis, limited imaging biomarkers have been reported that support a clinical diagnosis of Parkinson's disease or its differentiation from similarly presenting diseases.

Diffusion Kurtosis Imaging (DKI) is an MRI method that quantifies deviation of water diffusion from normal Gaussian distribution. DKI is a more sensitive technique than conventional diffusion tensor imaging (DTI) for assessing tissue microstructure. The parameters provided by DKI analysis, particularly the mean kurtosis, reflect structural changes within brain regions and demonstrate potential as a diagnostic tool for Parkinson's disease where the basal ganglia are known to markedly change.

Here we examine the DKI maps of 86 patients from Hospital das Clinicas da FMUSP in Sao Paulo, Brazil. 49 patients presented with a previous diagnosis of Parkinson's disease based on the UK Parkinson's Brain Bank criteria (mean age, 65.3 + 8.7 [standard deviation]), 19 patients with a previous diagnosis of essential tremor based on the Movement Disorder Society standards (mean age, 64.7 + 6.7) and 27 patients were age-matched healthy controls (mean age, 64.5 + 10.9). All patients underwent the same 3T MRI procedure, consisting of a DTI scan with 32 different gradient directions and b values of 0, 1000, and 2000 s/mm^2, necessary to construct a DKI map.

Using a region of interest (ROI) analysis on the substantia nigra (rostral, middle, and caudal) and putamen for each patient and comparing mean kurtosis values, we find no significant differentiation of Parkinson's disease patients in the substantia nigra, but significantly higher mean kurtosis values in the putamen of Parkinson's patients (0.82 + 0.05 [standard deviation]) than healthy controls (0.60 + 0.04, $p = 0.0158$). Neither analysis demonstrated significant difference from essential tremor patients.

Higher mean kurtosis estimates in the basal ganglia of Parkinson's disease patients may reflect changes in the microstructural environment of these structures related to disease progression. Further studies should investigate the histological correlates of these values and the reliability of DKI estimates as a diagnostic tool in various stages of the disease.

A Novel Thighplasty Technique for Patients after Massive Weight Loss

Shelly M. Xie

Mentor and Collaborators: Jeffrey M. Kenkel, MD, Kevin Small, MD; Ran Stark MD; Ryan S. Constantine, Jordan P. Farkas, MD;
Department of Plastic Surgery

Background: Medial thighplasty is a challenging operation often associated with post-operative complications. It has undergone significant changes over the course of the last few decades from Pitanguy's original lift to Lockwood's technique and more recent changes regarding the care of the weight loss patients. While the Lockwood technique, which embraces a horizontal resection and a vertical lift, may be effective for non-massive weight loss (MWL) patients, it does not provide the same result for MWL patients with more extensive skin laxity down to and often below the knee, leading to traumatic dissection and prolonged edema. Recently, our group suggested that tension of medial thighplasty in massive weight loss (MWL) patients should be oriented in the horizontal rather than vertical direction, negating the need for Colles fascia anchoring. In this study we compare the morbidities, complications and outcomes between Colles fascia suture fixation (CFSF) and our modified method, horizontal vector fixation (HVF) in medial thighplasties in MWL patients.
Methods: A 10-year retrospective study was performed on an IRB-approved database of patients who had medial thighplasty between October 2004 and March 2014. MWL patients were extrapolated. Patient demographics and surgical outcomes were reviewed between those patients who had anchoring of Colles fascia (CFSF group) and those who received medial thighplasties with our novel approach, horizontal vector fixation (HVF group).
Results: In this series, 86 patients had medial thighplasty, of which 65 patients were post MWL. In the MWL subset, 26 (40.0%) patients were in the CFSF group and 39 (60.0%) patients in the HVF group. The two groups were statistically equivocal with respect to age, gender, body mass index, diabetes, smoking, hypertension, coronary artery disease, pulmonary disease, renal disease and cancer history. Intra-operatively, HVF group had increased use of barbed suture (92.3% vs. 30.6%, $P < 0.0001$) and liposuction (71.8% vs. 26.9%, $P < 0.0001$). Post-operatively, HVF group had significantly decreased incidence of seroma (2.5% vs. 30.76%, $P = 0.002$), and the rate of infection also decreased in HVF group compared to CFSF group (5.1% vs. 23.0%, $P = 0.051$). No statistical differences were observed between the two groups for dehiscence, necrosis, hematoma, or lymphocele.
Conclusion: Our group has demonstrated that a horizontal vector fixation for medial thighplasties in MWL patients is a safe and efficient technique, with lower incidence of seroma formation and infection than Colles fascia anchoring, suggesting that Colles fascia fixation is not needed and may even increase complications in MWL patients. Furthermore, the comparison infers that barbed sutures and/or liposuction may optimize results.

Pupillometer Inter-Device Reliability

Weidan Zhao

Mentor: Venkatesh Aiyagari, MD, Department of Neurological Surgery

Introduction: Assessment of the pupillary reflex is one of the fundamental aspects of the neurological examination. Traditionally, it comprises of a subjective assessment of the size and shape of the pupil prior to the manual application of a light source and the speed of pupil reactivity when exposed to light. We have recently shown that there is a striking degree of disagreement between trained observers in interpreting pupillary size and reactivity, partly because examiners are allowed to use a variety of non-standardized handheld light sources. Automated hand-held pupillometers are commercially available that are able to provide an objective measurement of the initial and final size of the pupil and to grade the speed of pupil contraction in response to a light stimulus. The purpose of this prospective study was to assess the inter-device reliability of the pupillary examination performed with NPi^{TM}-100 pupillometers (NeuroOptics, Inc.).

Methods: To determine the inter-device reliability, 33 practitioners (28 RNs, 2 MDs, 1 NP, 1 medical student and 1 PhD research coordinator) obtained 210 paired pupillometer measurements from 20 patients at risk for cerebral edema. Paired pupillometer assessments were completed within a five-minute period and consisted of two separate assessments by two different clinicians using two different pupillometers.

Results: There was no statistically significant difference between the mean maximum pupil size at rest for both OS ($p=0.27$) and OD assessments ($p=0.74$) when measured by the different pupillometers (PM1 and PM2) prior to the light stimulation. Similarly, there was no statistically significant difference between the mean minimum pupil size for both OS ($p=0.64$) and OD (0.44) when measured after the light stimulation. The mean pupil reactivity for both OS ($p=0.36$) and OD ($p=0.82$) are also not statistically significantly different. In addition, Cohen's Kappa assessments of pupil size and reactivity revealed an almost perfect agreement between PM1 and PM2 for both the maximum pupil size of both OS ($k=0.97$) and OD observations ($k=0.91$) and the minimum pupil size of OS ($k=0.96$) and OD observations ($k=0.98$). Including the non-reactive pupil results, there was also a high correlation for the OS ($k=0.99$) and OD readings ($k=0.90$).

Discussion: The NPi^{TM}-100 pupillometers have a high inter-device reliability, even when two different pupillometer devices are used on the same subject by different practioners. The data provide sufficient support to conclude that the use of NPi^{TM}-100 pupillometers is likely to improve the precision of the pupillary examination.

NOTES