THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
AT DALLAS

56th ANNUAL
MEDICAL STUDENT RESEARCH FORUM

TUESDAY, JANUARY 23rd, 2018
Oral Presentations 3-5:00 pm
Poster Presentation 5-6:00 pm

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

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56th ANNUAL MEDICAL STUDENT RESEARCH FORUM

LIST OF ORAL PRESENTATIONS

Calvin Geng
"Mechanistic study of insulin and exercise combination therapy to recover muscle function in burn and hindlimb-unloaded rats"
Mentor: Steven Wolf MD, Department of Surgery

Matthew Gillings
“Carnosine and Anserine Deficiency in a Mouse Model for Mitochondrial Myopathy”
Mentor: Prashant Mishra. MD, PhD, Children’s Research Institute

Sami Horani
“Altered Levels of the Transcription Factor PTF1A Result in Abnormal Sensitivity to Itch”
Mentor: Jane Johnson PhD, Department of Neuroscience

Shan Su
“Feedback Regulation of HMG-CoA Reductase in Livers of Mice”
Mentor: Russell Debose-Boyd, PhD, Department of Molecular Genetics

PRESENTATION OF GUEST SPEAKER

Beth Levine, M.D.
Investigator, The Howard Hughes Medical Institute
Professor, Internal Medicine and Microbiology
Charles Cameron Sprague Distinguished Chair in Biomedical Science

RECEPTION AND POSTER SESSION IMMEDIATELY FOLLOWING

56th Medical Student Research Forum

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Basic Research and Disease Models

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Effects of Altering Ets1 Expression on B Cell Antibody Production and the Development of Autoimmunity

Samantha Black

Mentor: Anne Satterthwaite PhD, Department of Immunology
Collaborator: Kristina Ottens MS

B cells are adaptive immune cells elicit the humoral immune response. When activated by foreign antigens, they differentiate into plasma cells (PCs) that secrete antigen-specific antibodies. This process is under tight control through various B cell inhibitory mechanisms such as the Lyn-dependent inhibitory cascade that promotes expression of inhibitory transcription factor Ets1. Increased Ets1 expression prevents plasma cell differentiation while decreased expression allows plasma cell differentiation in vitro. In this study, we hypothesize that B cell expression of Ets1 stops antibody production in response to foreign antigens. We utilized a triple-transgenic mouse with a tet-inducible promoter to turn on Ets1 expression in B cells when mice were fed doxycycline (Dox). Transgenic and control mice were treated or not with Dox and immunized with a T-dependent antigen and immune responses measured at various time points post immunization. Antibody production was measured through ELISA and ELISPOT. Spleens were analyzed via flow cytometry, observing distribution of B cell subpopulations and enumerating plasma cell and germinal center B cell numbers. B cell expression of Ets1 was measured in purified B cells via Western blot and Real Time PCR. Our results showed no significant difference in immune response in immunized wildtype mice versus immunized transgenic mice in the presence of Dox. We attribute this lack of immune response difference to low levels of Ets1 expression in the transgenic mice, despite Dox feedings. When Ets1 expression was measured via Western Blot, Ets1 expression in transgenic mice was not significantly higher than wild type mice. Measurement of mRNA transcript levels via Real Time PCR further followed this trend, as transcription levels were not significantly increased in the transgenic mice. These results explained the minimal immune inhibition observed when transgenic, doxycycline-fed mice were immunized. We concluded that Ets1 expression levels in our transgenic mouse model were not sufficient to inhibit the humoral immune response when mice were fed Dox and immunized. Since our transgenic mouse only contained one copy each of the Ets1 transgene and Dox-inducible transactivator (rTTA) controlling the Ets1 transgene, we hope for better results with a mouse that contains two copies of each of these transgenes. This should, in theory, increase Ets1 expression in response to Dox. We will also develop a system in which Ets1 is overexpressed constitutively but can be turned off by Dox. Once Ets1 is expressed at sufficient levels, the effect on the immune response in these mice can be better measured in vivo.

Structure, Function, and Biochemistry of ChTOG, ZYG9, and XMAP215 TOG Domains

Analise Doney

Mentor: Luke Rice PhD, Department of Biophysics
Collaborators: Elizabeth Geyer BS, Shreoshi Majdar BS, & Xuecheng Ye PhD

Background: Tumor Overexpressed Gene (TOG) domains are ab-tubulin binding components of regulatory microtubule 'polymerases' that promote fast elongation. TOG domains use conformation-selective interactions with ab-tubulin to achieve their function. Whereas TOG1 and TOG2 domains prefer to bind unpolymerized ab-tubulin, the conformational preference of other TOGs has not yet been defined, limiting our understanding of the mechanism. A recent study suggests TOG5-type domains may prefer to bind polymerized ab-tubulin (microtubules). For this project, I aimed to express, purify, and study the tubulin binding patterns of TOG5-type domains from ChTOG, XMAP215, and ZYG9, the human, Xenopus, and C. elegans polymerases.

Methods and Results: I expressed the three TOG5-type domains in E. Coli cells. All three domains showed strong overexpression when analyzed with SDS-PAGE Gels, but the domains from ChTOG and XMAP215 were insoluble and consequently not pursued. I purified the ZYG9 domain using a combination of Ni-affinity and ion exchange chromatography.

Having purified the TOG5-type domain from ZYG9, I next turned to binding assays in order to assess conformational selectivity. To assay binding to unpolymerized ab-tubulin, I used analytical ultracentrifugation. This assay showed the sedimentation coefficient of the TOG5-type domain to be 2.3 S. Unfortunately, while the TOG domain was well-behaved, the tubulin showed severe aggregation, precluding further analysis.

To assay binding to polymerized tubulin, I used "co-sedimentation" experiments with GMPCPP-stabilized microtubules. Surprisingly, the TOG-5 type domain did not bind to the microtubules. This may have been due to specificity of the ZYG9 TOG3 for C. elegans microtubules, a change in the TOG conformation in the experimental conditions, or that this TOG5-type domain does not prefer to bind microtubules.

Conclusion: Future direction includes more binding assays to test the affinity of ZYG9 TOG3 and its mutants to unpolymerized and polymerized ab-tubulin. Questions still remain about the function of TOG5 domain and its structural qualities that would appear to assist in binding polymerized tubulin.

The Role of long non-coding RNA NORAD in Mitochondrial Function and Aging

Mahmoud Elguindy

Mentor: Joshua Mendell MD, PhD, Department of Molecular Biology
Collaborators: Florian Kopp PhD, Mehmet Yalvac PhD, Beibei Chen PhD, Sungyul Lee PhD, Frank Gillett BA, Sushama Sivakumar PhD, Hongtao Yu PhD, Yang Xie PhD, Prashant Mishra MD, PhD, & Zarife Sahenk, MD, PhD

Long non-coding RNAs (lncRNAs) are increasingly being recognized for their critical functions in numerous important biological and pathological processes. Here, we describe a novel role for lncRNA NORAD in regulating mitochondrial function. NORAD (non-coding RNA activated by DNA damage) was first characterized by the Mendell Lab as a highly conserved and abundant lncRNA that regulates genomic stability in human cells by interacting with and negatively regulating PUMILIO proteins, which bind to target messenger RNAs and trigger their deadenylation and degradation.

Recently, we generated a global knockout of the mouse homologue of NORAD (Norad) using CRISPR/Cas9-mediated genome editing. Interestingly, Norad−/ − mice were viable and fertile with no apparent phenotype at birth. As the mice grew older, however, a premature aging phenotype became apparent, with early onset of kyphosis, alopecia, greying of hair, weight loss, and loss of adipose tissue. Histological and biochemical analyses of skeletal muscle and brain tissues revealed the accumulation of abnormal-appearing mitochondria in Norad-/- mice. We also analyzed mitochondrial electron transport chain function in isolated mouse embryonic fibroblasts (MEFs). Norad−/ − MEFs showed dissipated mitochondrial membrane potential, reduced mitochondrial respiration, and increased reactive oxygen species (ROS) production. Moreover, using gain-of-function and loss-of-function approaches, we confirmed the role of PUMILIO hyperactivity in mediating the Norad knockout effect on mitochondrial homeostasis. Specifically, PUMILIO overexpression in wild-type MEFs leads to similar mitochondrial defects as those seen in Norad−/ − MEFs, while PUMILIO knockdown in Norad−/ − MEFs alleviates increased ROS levels. These findings were also supported by RNA-sequencing, which revealed downregulation of several key PUMILIO targets implicated in mitochondrial function and homeostasis in Norad-/- animals.

Mitochondrial dysfunction has been shown to be associated with major aging phenotypes as well as cardiomyopathy, skeletal muscle atrophy, and several neurological disorders. This study reveals a previously unanticipated role for lncRNA NORAD in regulating mitochondrial function and aging through its interaction with PUMILIO. With less than 2% of our genome being protein-encoding, deciphering the function of non-coding RNAs will be crucial for understanding normal physiological processes and may help uncover novel approaches to remedy and/or prevent aging-associated pathologies and other diseases.

Expansion of Dermal White Adipose Tissue in Colonized Versus Germ-Free Mouse Skin

Whitney Gao

Mentor: Tamia Harris-Tryon MD, PhD, Department of Dermatology
Collaborators: Jeffrey McDonald PhD & Lora V. Hooper PhD

In the skin, lipids have been shown to have an antimicrobial effect (Drake, 2007; Feingold, 2009; Fischer, 2014). Of particular interest to us is how the dermal white adipose tissue (dWAT) layer of the skin can be affected by bacterial colonization. Zhang et al. (2015) showed that mice infected with *Staphylococcus aureus* demonstrated a rapid proliferation of their dWAT. We now observe that mice that are housed in conventional mouse facility (fully colonized by the microbiota) have grossly more opaque skin in comparison to the skin of germ-free mice. This project aimed to quantify this observed difference in dWAT between germ-free and conventional mice, and to explore the possible mechanism of this fat expansion. Using ImageJ software, we analyzed high-power fields of skin to count the number of adipocytes and to measure adipocyte size. We observed both hyperplasia and hypertrophy in the conventional mouse skin compared to germ-free mouse skin. In the germ-free mice, the mean number of adipocytes was 41.6; in conventional mice, the mean number was 61.5. In the germ-free mice, the mean size of the adipocytes was 336 μm^2; in conventional mice, the mean was 928 μm^2. We also analyzed and compared the lipid composition of the skin of germ-free and conventional mice. Triglycerides dominate both landscapes. Additionally, there was no significant difference in saturation or number of carbons. We conclude that there is no significant change in the skin's lipid composition between the two populations. This preliminary conclusion will need further confirmation, specifically looking at isolated dWAT without other components of mouse skin. At this point, however, it seems that the dWAT expansion in colonized mouse skin represents an expansion of general adipose, and not of any specific lipid class. Our next step will be using genetic mouse models to explore specific mechanisms that drive adipose expansion in response to bacterial colonization.

Mechanism Study of Insulin and Exercise Combination Therapy Recovering Muscle Function in Burn and Hindlimb Unloaded Rats

Calvin Geng

Mentor: Steven Wolf MD, Department of Surgery
Collaborator: Juquan Song MD

Introduction: Severe burns induce the hypermetabolic state, which results in a loss of muscle mass and function. Like burns, disuse of muscle also results in muscle loss. Resistance exercise and insulin both attenuate burn and disuse induced muscle atrophy, though neither is fully compensatory. To date, no data describe efficacy of insulin and exercise as a combination therapy to recover muscle mass and function. This project investigates molecular mechanisms supporting musculoskeletal improvements in a burn and disuse rat model with these treatments.
Methods: Twenty-four Sprague-Dawley rats received full thickness 40% total body surface area burns and hindlimb unloading, and were randomly grouped into vehicle without exercise (V/N), 5U/kg of insulin without exercise (I/N), vehicle with exercise (V/E), and insulin with exercise (I/E) groups. Fourteen days after injury, hindlimb muscle function was measured and muscle tissues were harvested for genomic profile and western blot analysis.
Results: The isometric force including tetanic (Po) and twitch (Pt) were significantly elevated in the plantaris of I/E rats ($p < 0.05$). The soleus also had significant elevation of Po, Pt, fatigue maximum, and fatigue minimum in I/E rats ($p < 0.05$). Transcriptome analysis showed that 70, 62, and 116 genes were upregulated more than 2 fold in insulin, exercise, and combination treatment, respectively. Western blots showed that p-PDK 1, which activates AKT, was significantly increased in all treatment groups compared to control ($p<0.01$). p-AKT S473 was significantly increased in the combination group ($p<0.05$). eEF2 controls the elongation step in translation and was increased in the exercise and combination ($p<0.05$). Muscle RING-finger protein-1 (MuRF-1), an E3 ubiquitin ligase, was reduced in the combination group ($p<0.05$).
Discussion: Insulin and resistance exercise have a positive combined effect on muscle function recovery. Signal pathway examination showed that the combination treatment decreased protein degradation and increased protein synthesis genetic markers. The observed changes at the transcriptional and protein levels are supported by muscle function improvements.
Implications: Muscle loss is a sequela of burn and disuse that increases cost and risk of complications. By identifying the molecular basis of these changes, treatments that target critical proteins can be developed to mitigate muscle loss and improve patient outcomes.

Carnosine and Anserine Deficiency in a Mouse Model of Mitochondrial Myopathy

Matthew Gillings

Mentor: Prashant Mishra MD, PhD, Department of Children's Research Institute

Background: Mutations and deletions in the mitochondrial genome are known to cause myopathies in humans at a rate of approximately 1:5000 newborns, and currently no effective treatment options are available. In mitochondrial myopathies, the threshold for metabolic acidosis is lowered and can occur at resting muscle activity. Recent findings indicate that mutant muscle exhibits altered expression of solute carrier (SLC) family members and altered metabolomics. We report here metabolic disturbances present in a mitochondrial myopathy mouse model and hypothesize that a carnosine/anserine deficiency promotes the development of resting metabolic acidosis.

Methods: A mitofusin 1,2 knock-out mouse model was used, in which mtDNA deletions accumulate, resulting in severe mitochondrial myopathy. Muscle samples were taken from mutant and wild-type tibialis anterior muscle and processed for metabolomic measurements using LC and GC-MS, as well as for gene expression using RT-QPCR. Results were compared using a two sample t-test assuming equal variances; 95% confidence was chosen as the cutoff for demonstrating significance.

Results: LC and GC-MS analysis of muscle samples indicated clear metabolite differences, and unsupervised clustering was able to clearly distinguish the control and experimental groups. Of note, the following metabolites were decreased in mutant mice: carnosine (-95%), anserine (-89%), histidine (-80%), beta-alanine (-71%). Carnosine and anserine, synthesized from histidine and beta-alanine, are utilized in muscle for intracellular pH buffering. These changes prompted an examination of the expression of the several genes involved in carnosine biosynthesis and transport. Using RT-QPCR, we found significant elevations in SLC7A5 (+1800%), SLC38A2 (+230%), SLC7A1 (+1200%), SLC15A4 (+170%), and CNDP2 (+400%). These results suggest that mutant myofibers are operating with a histidine and beta-alanine deficiency and are attempting to compensate by increased expression of histidine transporters. We hypothesize these changes contribute to lowering the threshold for the development of lactic acidosis due to the role of carnosine and anserine in intracellular pH buffering.

Quantification of Itch Behavior in Ptf1a Enhancer Mutants

Sami Horani

Mentor: Jane Johnson PhD, Department of Neuroscience
Collaborators: Bishakha Mona & Juan Villarreal

A specific balance between excitatory and inhibitory neurons is critical for proper central nervous system development; even a slight alteration in this balance has been implicated as a cause for multiple neurological disorders. PTF1A is a bHLH transcription factor that specifies inhibitory neurons over excitatory neurons in regions that function in somatosensation and motor coordination. Mutant mice null in *Ptf1a* result in neonatal lethality, with a loss of inhibitory neurons and an excess of excitatory neurons in the dorsal spinal cord, brainstem, cerebellum, and retina. Dorsal spinal cord inhibitory neurons modulate sensory signals from the periphery, such as itch, pain, touch, and proprioception. Regulatory enhancers of *Ptf1a* have been identified; they include an autoregulatory enhancer ~13kb 5' of the gene, and a dorsal neural tube (DNT) enhancer ~13kb 3' of the gene. Using CRISPR-CAS9 strategies, these enhancers were mutated generating two new mutant mouse strains, BM35E and BM36A. In contrast to *Ptf1a* null mice, these mutants survive past neonatal stages, but by 4-6 weeks of age they express a severe scratching phenotype, causing such severe skin lesions that euthanasia is required days after symptom initiation. We hypothesize that there is a specific loss of inhibitory input into itch circuits and/or an increase in excitatory modulation, due to decreased expression of *Ptf1a*. To test whether the scratching phenotype resulted from hypersensitivity to itch, BM35E and BM36A homozygous mutant mice along with their wild type littermates, were injected with 0.6 microliters of chloroquine, inducing a non-histamine itch response. Hindpaw scratch bouts were recorded over a 30-minute period immediately after injection. The BM36A mutant mice were hypersensitive to the chloroquine treatment relative to wildtype controls. The BM35E trended towards hypersensitivity but the difference was not significant with a simple student T-test. These findings support the hypothesis that inhibitory/excitatory input into the itch circuit is altered. Additional behavior tests such as von Frey's for mechanical pain and Hargreave's for thermal pain revealed no difference between mutants and wildtype. Future experiments will test different types of itch such as histamine-induced itch. Furthermore, alternative explanations such as obsessive-compulsive behavior, excessive itch as a consequence of organ failure, or disruption of other *Ptf1a*-dependent neural circuits must be considered and tested.

Molecular Characterization of Novel FOXN1 Mutations Casual to Thymic Aplasias in Human Patients

Larry Huynh

Mentor: Nicolai van Oers PhD, Department of Immunology
Collaborators: Maite de la Morena MD & Dr. Qiumei Du PhD

The Forkhead Box N1 (FOXN1) transcription factor plays a crucial role in thymic epithelial cell development. Humans and mice harboring FOXN1 mutations have a profound T-cell deficiency caused by their thymic aplasia. They also present with alopecia and nail dystrophy. Recently, two patients were identified with T-cell immunodeficiency. Both patients have normal hair and nailbed development. Genetic workup revealed that each patient carried distinct compound heterozygous mutations in FOXN1 not previously reported. Molecular characterization of these FOXN1 mutations will provide new insight into how this transcription factor functions in thymus development.

To characterize these mutations, CRISPR/Cas9 technologies were used to create similar compound heterozygous mutations in mouse models. The mice are currently being intercrossed to determine the impact of these novel FOXN1 mutations on thymus development. To determine how these mutations impact FOXN1 function, we undertook transcriptional reporter assays. Preliminary results suggest only one of these mutations led to loss of transcriptional activity. Western blot analysis indicated that this mutation led to a truncation of the protein. Further experiments including co-immunoprecipitation assays, transcriptome analyses, and functional studies will reveal how these compound heterozygous mutations impact the functions of FOXN1.

Findings from this study may lay the foundation for novel therapeutic strategies at restoring thymopoiesis in a number of distinct clinical settings. These can include patients undergoing radiation treatment, chemotherapy, and in any other conditions that can lead to a thymic aplasia.

Eradicating Metal-Associated Bacteria with Alternating Magnetic Fields

Kasey Kreutz

Mentor: David Greenberg MD, Department Internal Medicine-Infectious Disease
Collaborators: Rajiv Chopra MD & Reshu Saini MD

Purpose: As with other medical implants, prosthetic joints provide a hospitable surface for bacterial adherence and biofilm formation. We are developing a non-invasive thermal technique to destroy biofilm on the metal surfaces of prosthetic joints using alternating magnetic fields (AMF). One hypothesized benefit of AMF therapy is that it could be used in conjunction with traditional antibiotics to produce a synergistic bactericidal effect. The purpose of this study is to characterize the thermal sensitivity of bacteria in the presence of antibiotics to aid in the development of appropriate parameters for AMF dosing.

Methods: Planktonic solutions of Pseudomonas aeruginosa were thermally shocked in heating blocks with and without minimum inhibitory concentrations of ciprofloxacin. Bacterial solutions were plated on blood agar at intervals throughout the experiment to create a time-kill curve of the combined effects of heat shock therapy and ciprofloxacin.

Results: A single 10-minute dose of 55°C thermal shock reduced bacterial concentrations by 1.47-log CFU/mL, but subsequent ncubation allowed bacteria to quickly reach and surpass original starting concentrations. Ciprofloxacin alone achieved a 3.78-log reduction within six hours and prevented significant regrowth during 24 hours of incubation. In combination, thermal shock and antibiotic achieved a 6.20-log reduction within 24 hours.

After 24 hours allowing for regrowth, combination therapy produced superior bactericidal effect when compared to antibiotic or heat shock alone. When multiple doses of heat were applied in conjunction with antibiotic exposure, a step-down effect over time was observed as the log reduction achieved by each successive heat shock was either preserved or accentuated by the simultaneous inhibitory activity of the antibiotic.

Conclusion: The results of this study demonstrate that the bactericidal effects of thermal shock are enhanced by the addition of antibiotics, and appear to show a promising synergistic benefit over either treatment being used alone. Future steps will focus on applying combination therapy to biofilm in an AMF coil in order to determine how dose requirements may differ.

Discovery of Novel Anesthetic Compounds Using Zebrafish Larvae

Maria Lima

Mentors: Stuart Forman MD, PhD & Cindy Yang MD,
Department of Anesthesia and Critcal Care

Introduction: Novel general anesthetic compounds for use in medicine can provide increased treatment options for patients undergoing invasive medical procedures such as surgery. Zebrafish larvae have recently emerged as a platform for high throughput screening of neuroactive compounds. In our lab, we are using zebrafish larvae to conduct a high throughput screen of over 2,000 uncharacterized drug compounds for possible anesthetic properties. Furthermore, we are testing new combinations of etomidate and MPAB, two known anesthetics acting on the GABA-A receptor, to determine agonistic or antagonistic interactions; we aim to reduce toxic side effects of various drug combinations and to exploit the beneficial properties of these drugs to improve treatment efficaciousness.

Methods: After a 0.2 second bright white light stimulus in dark-adapted 7 day old post-fertilization Tu zebrafish larvae, the Photomotor response (PMR) was analyzed using a specialized motion tracking video system (ViewPoint Zebralab). This bright stimulus startles the zebrafish into a brief burst of movement. Anesthetic effects of new compounds were qualified by calculating the PMR inhibition, representing the decrease in movement after the stimulus and sedative effects were quantified by recording pre-stimulus basal activity inhibition, representing the normal zebrafish movement during periods of no stimulus.

Results: Several prospective novel anesthetic compounds have been identified and our lab is currently performing more screens to assess the reversibility and potency of each drug. Specifically, we discovered Compound 84 which shows a significantly higher potency (IC50 = 8.99 μM , 95% IC: 6.38 to 12.7 μM) and normal reversibility (representing the zebrafish ability to recover from drug PMR inhibition overnight).

Conclusion: Zebrafish photomotor response is a promising method for high throughput identification of novel anesthetics. Additionally, co-administration of MPAB with etomidate can potentially reduce dosage requirements in anesthetics, therefore, providing beneficial drug combination options to reduce side effects in higher risk patients.

Role of Vitamin D Metabolism in the Timing of Birth

Kelsi Morgan

Mentor: Carole Mendelson PhD & Alina Montalbano PhD,
Department of Biochemistry & Obstetrics & Gynecology
Collaborator: Ailing Yang BS

Preterm birth (PTB) is the leading cause of infant mortality during the first four weeks of life world-wide. This is due, in part, to our incomplete understanding of the mechanisms that mediate uterine quiescence during most of pregnancy and promote the transition to labor at term. Term and preterm labor are associated with increased levels of proin¬flammatory cytokines within maternal reproductive tissues where they activate inflammatory transcription factors (e.g. NF-□B) that enhance expression of genes encoding contraction-associated proteins (CAP) (i.e. connexin-43 (CX-43)), oxytocin receptor (OXTR)). By contrast, uterine quies¬cence is main¬tained throughout most of preg-nancy by increased progesterone (P4) levels and enhanced progester-one recep¬tor (PR) activity, which silence expression of proinflamma¬tory mediators and CAP genes. Treatment of pregnant women at risk for preterm labor with progestins has negligible effects - underscoring the need for novel therapeutic targets. To identify such targets, our lab surveyed the myo¬metrial transcriptome of timed-pregnant mice at 15.5-18.5 days post-coitum (dpc) and during labor at term (19.0 dpc) using RNA-sequenc¬ing. Interestingly, Cyp27b1 was one of the most highly downregulated transcripts at 18.5 dpc and in-labor, compared to 15.5 dpc. Cyp27b1 encodes 1□-hydroxylase, the key enzyme respon¬sible for synthesis of the active form of vitamin D, 1,25-dihydroxyvitamin D3 (calcitriol) which binds to the vitamin D receptor (VDR). Calcitriol/VDR have anti-inflammatory actions and are reported to mediate maternal tolerance to the hemi-allogeneic fetus. Interest¬ingly, we previously observed that P4 treatment of timed-pregnant mice caused a significant increase in myo¬metrial CYP27B1 mRNA levels, compared to controls. In the present study, we sought to assess effects of calcitriol treatment on CAP gene expression in timed-pregnant mice. To this end, pregnant mice were injected s.c. daily from 13.5–17.5 dpc with vehicle (n=3) or with 3□g/kg of calcitriol (n=4). Mice were sacrificed and myometrial tissues were collected at 18.5 dpc. RT-qPCR revealed significantly reduced levels of CX43 ($p<0.0001$) and OXTR ($p<0.05$) in myometrium of calcitriol treated mice, compared to controls. Collectively, these data suggest that the decrease in Cyp27b1 expres¬sion, coupled with the decline in PR function near term may contribute to increased CAP gene expres¬sion leading to myometrial contractility and labor. Cyp27b1 may serve as a key P4/PR target gene that acts cooperatively to maintain myo¬metrial quiescence via its anti-inflamma¬tory actions. Thus, calcitriol may be a safe and effective treatment for the prevention of PTB.

Exploring a Novel, Non-Invasive Treatment for Prosthetic Joint Infection

Ajay Narayanan

Mentor: David Greenberg MD, Department Internal Medicine-Infectious Disease
Collaborators: Qi Wang, Christine Pybus, Sumbul Shaikh, Imalka Munaweera, Carolyn Sturge, & Rajiv Chopra

Periprosthetic joint infection (PJI) is a very prevalent consequence of implant surgery. The surface of the prosthesis provides a favorable environment for the growth of bacterial biofilms, which are notorious for being resistant to conventional antibiotics. The current treatment for PJI involves re-opening the surgical site and replacing the prosthesis, a very costly procedure that diminishes patient quality of life. Recently, a non-invasive procedure has been developed that utilizes high frequency alternating magnetic fields (AMF) to destroy biofilms via induction heating. Our research was focused on both optimizing and further characterizing the cytotoxicity of this treatment method on Staphylococcus aureus and Pseudomonas aeruginosa, two biofilm-forming pathogens commonly implicated in PJI.

The organisms used for these experiments were Staphylococcus aureus and Pseudomonas aeruginosa. Biofilms were grown on stainless steel rings or washers, to model the surface of implanted prosthetics. P. aeruginosa was grown statically in MH2 media at 37°C for 48 hours. S. aureus was grown statically in Tryptic Soy Broth media supplemented with 0.5% glucose and 3.0% NaCl at 37°C for 48 hours. Soaking the stainless steel ring/washer in a 20% Human Plasma solution overnight at 4°C greatly enhanced S. aureus biofilm formation. AMF continuous dosing was performed at 20 watts, up to 15 minutes. AMF intermittent dosing was performed using 1 second duration, 670 watt pulses every 10 minutes, up to 6 hours.

The results indicated that S. aureus biofilms were eradicated more effectively than P. aeruginosa biofilms when treated with intermittent AMF exposure. Specifically, there was a 2.6-log reduction in S. aureus biofilm CFU after 30 minutes of AMF exposure, with CFUs reaching the limit of detection after 3 hours. Corresponding studies in P. aeruginosa showed a 1.3-log reduction in biofilm CFU after 30 minutes of AMF exposure, with CFUs not reaching the limit of detection after 6 hours. In an ongoing study, ciprofloxacin was administered alongside AMF exposure to investigate any potential synergistic effects on P. aeruginosa biofilm eradication.

While the data produced this summer was exclusively in vitro, the results give insight on how AMF might be applied in the clinical treatment of PJI. The observed cytotoxicity combined with the non-invasive nature of AMF suggest significant promise for a much more desired method of PJI treatment for common pathogens.

Distinct Tau Strains: Exploring Variability in Cell Uptake and Seeding Using Heparinoids

William Prueitt

Mentor: Marc Diamond MD, Department of Center for Alzheimer's and Neurodegenerative Disease
Collaborator: Barbara Stopschinski MD

Background: Tauopathies (including Alzheimer's Disease) are incurable, progressive neurodegenerative diseases caused by tau protein aggregation. Evidence suggests that tau aggregates spread pathology as do prions, infectious proteins that transmit a pathologic conformation to native proteins via disease-specific conformers (strains). Evidence shows tau aggregates enter cells through heparan sulfate proteoglycan (HSPG) mediated macropinocytosis. In this project, I explored whether distinct tau strains bind cell surface HSPGs uniquely or generically to trigger uptake and used heparinoids to measure the relative importance of heparin size and sulfation patterns.
Methods: I used a "biosensor" cell line responsive to tau aggregates that scores induction of intracellular aggregation based on FRET flow cytometry. Using cell lysate from various strains of tau, I measured (1) the ability of different heparin-like molecules to block tau aggregate uptake and seeding, and (2) seeding in HSPG gene knockout cells.
Results: All tau strains tested were highly sensitive to heparin inhibition of seeding and most maintained a highly similar dose response. Some strains, however, showed subtle differences. At maximal heparin concentrations, noticeably higher seeding vs baseline was observed in DS 5 & 6 (17%, 9%) as compared to the other strains (<5%). Heparinoid titrations revealed highly similar inhibition patterns between DS 9 and 10. Seeding reduction: DS 9: dp4= 21%; dp8= 27%; dp12= 70%; dp16= 63%; De-2-O= 65%; De-6-O= 52%; De-N= 35%. For DS 10: dp4= 19%; dp8= 33%; dp12= 64%; dp16= 46%; De-2-O= 53%; De-6-O= 25%; De-N= 13%. Seeding in HSPG genetic knockout cells was reduced substantially in two knockouts, but increased in another.
Conclusions: Cellular uptake of many tau strains is similarly inhibited by heparin, hinting that the same heparinoid (or small molecule analog) could be used to treat diverse tauopathies. But the unique behavior of some strains suggests a one-size-fits-all treatment approach may not always be sufficient. Certain size and sulfation patterns on heparin have specific importance for tau binding. Larger heparinoids better inhibit tau seeding (dp16 & dp12 > dp8 & dp4) and the importance of N-sulfation > 6-O-sulfation > 2-O-sulfation. This pattern remains consistent in recombinant tau, DS 9, DS 10, and in the genetic knockout data gathered here (using strains) and by others in the lab (using recombinant tau). This data shows many similarities and some differences between strains of tau. Parsing these differences could have important implications for understanding the diversity of tauopathies and finding unique approaches to diagnosis and treatment.

The Role of KIRREL in Mammalian Myogenesis and Rhabdomyosarcoma

Shannon Reinert

Mentor: Rene Galindo MD, PhD, Department of Pathology
Collaborator: Usha Avirneni PhD

Rhabdomyosarcoma is an aggressive soft-tissue malignancy comprised microscopically of neoplastic skeletal muscle-lineage precursors that fail to exit the cell-cycle and fuse into syncytial muscle - the underlying pathogenetic mechanisms for which remain unclear. We previously identified that misregulated myoblast fusion signaling via the TANC1 adaptor molecule promotes neoplastic transformation in RMS cells driven by the PAX-FOXO1 oncogenic transcription factor. Unknown from these studies are the upstream elements that participate with TANC1 in wild-type myoblasts to orchestrate myoblast fusion, and how these elements likewise participate in RMS.

We are now interrogating the Immunoglobulin Superfamily Receptor Kirrel receptors in these processes. Three Kirrel orthologs are present in mammals, two of which, Kirrel-1 and -3, are expressed normally in myogenesis. Using loss-of-function (shRNA) and gain-of-function (misexpression) strategies, our preliminary data are showing a requirement for Kirrel-3 during myoblast fusion, as tube formation is significantly altered in these studies. We are now extending these for Kirrel-3 activity in RMS using cultured neoplastic rhabdomyoblast. Our data and most recent findings will be presented and discussed.

Administration of Fatty Acid Emulsions to Reduce Secondary Brain Injury in Mice

Clifford Rodgers

Mentor: Joshua Gatson PhD, Department of Surgery
Collaborators: Ashish Chowdary, Ming-Mei Liu, Deborah Carlson, Steven E. Wolf, & Joseph P Minei

Background: Mild traumatic brain injuries are the most common type of injury to the head. Seventy-five to eighty percent of all traumatic brain injuries (TBI) are considered a mild TBI, or concussions, and involve only a short interruption of mental state and consciousness. Although the FDA reports no nutrition supplements for TBI therapy and/or symptom prevention, preclinical data has suggested that omega-3 poly unsaturated fatty acid (PUFAs) treatment decreases apoptosis, inflammation, and neurodegeneration following brain trauma. In this study, we hypothesized that Smoflipid® reduces inflammation in the brain of adult mice that have suffered a mild-to-moderate brain injury. Smoflipid® is an injectable liquid emulsion solution that contains omega-3, omega-6, omega-9, and medium chain triglycerides.

Methods: In this study, mice were subjected to a moderate brain injury using the controlled skull impact device (Leica microsystems) and we administered Smoflipid® intraperitoneally at day 1 and 3 after injury. At Day 14 after injury and treatment the mouse brains were harvested, processed, and stained using immunohistochemistry for the inflammatory markers, glial fibrillary acidic protein (GFAP) and Iba1.

Results: In this study after TBI, within the corpus callosum (C.C.) and cerebral cortex there was a significant increase in the levels of activated microglia (Day 14 $p=0.05$) compared to the control animals. Treatment with Smoflipid® shortly after injury, resulted in a significant decrease in the number of active microglia within these brain regions.

Conclusions: Chronic activation of microglia and heightened inflammation in the cerebral cortex/C.C. after TBI, results in cognitive decline and long-term memory deficits. As a therapeutic strategy, by targeting these pro-inflammatory cells with Smoflipid®, we hypothesize that a reduction in the activity of microglia will improve results in better neurological outcomes. More definitive studies will be conducted to test the efficacy of Smoflipid® at reducing secondary brain injury after TBI.

Feedback Regulation of HMG-CoA Reductase in Livers of Mice

Shan Su

Mentor: Russell Debose-Boyd PhD, Department of Molecular Genetics
Collaborators: Kristina Garland BS, Youngah Jo PhD, Seonghwan Hwang PhD, Gennipher Young MS, Iris Fuentes MD, Marc Schumacher PhD, Rania Elsabrouty MD, PhD, & Brittany Johnson, MS

Introduction: HMG-CoA reductase is a membrane protein of the endoplasmic reticulum (ER) that catalyzes the reduction of HMG-CoA to mevalonate, a rate-limiting step in the synthesis of cholesterol and nonsterol isoprenoids. Sterol and nonsterol isoprenoids exert stringent feedback control on HMGCR through multiple mechanisms. This ensures constant synthesis of essential nonsterol isoprenoids, while avoiding toxic overaccumulation of cholesterol. One of these mechanisms involves sterol-induced ubiquitination of HMGCR, which marks the enzyme for degradation from ER membranes that is augmented by nonsterol isoprenoids. In this study, we examine the contribution of this sterol-accelerated ubiquitination/degradation to overall regulation of HMGCR in the livers of mice.
Methods: Forty mice, including 20 wild-type (WT) and 20 knock-in (Ki) mice that express ubiquitination-resistant HMGCR, were fed diets containing only chow, or chow supplemented with 0.1%, 0.3%, or 1% cholesterol. After five days of feeding, livers were harvested for measurements of cholesterol and triglycerides, immunoblot analysis of six proteins, and qRT-PCR of 26 genes related to cholesterol, nonsterol isoprenoid, and fatty acid synthesis.
Results: Normalization of mRNA levels to protein levels indicates that HMGCR Ki mouse livers contain a higher level of HMGCR protein despite mRNA downregulation. Protein and gene expression of SREBP-2 and its target genes, which contribute to cholesterol synthesis, decreased as expected with increased dietary cholesterol. Conversely, protein and gene expression of SREBP-1 and its target genes increased, likely due to SREBP-1c predominance toward fatty acid synthesis, which prevents cholesterol accumulation.
Conclusion: The increase in HMGCR protein relative to mRNA suggests that significant post-transcriptional regulation exists in the form of impaired degradation. Furthermore, these normalized values indicate that accumulation of protein is primarily due to impaired degradation at lower cholesterol levels (chow, 0.1%); however, at high cholesterol levels (0.3%, 1%), a greater degree of transcriptional control from sterol-mediated inhibition of SREBP-2 regulates HMGCR due to negative feedback. This study demonstrates the role of degradative control on inhibition of HMGCR and may assist in reducing HMGCR accumulation during statin therapy.

Antisense Blockade of Efflux Systems in Gram-Negative Pathogens

Naveen Subramanian

Mentor: David Greenberg MD, Department Internal Medicine-Infectious Disease & Microbiology
Collaborators: Christina Felder-Scott BS & Carolyn Sturge PhD

Antibiotic resistant bacteria, aka “super bugs”, are a critical threat to public health worldwide, as the medical community is running out of effective antibiotics against a growing number of bacteria. One of the ways that bacteria develop resistance to antibiotics is by utilizing efflux systems that are used to pump the antibiotic out. A strategy that is currently being investigated is to restore the susceptibility of these bacteria to antibiotics by using peptide-conjugated phosphorodiamidate morpholino oligomers (PPMOs) to suppress genes within these bacteria that encode components of efflux pumps. This project studied the effectiveness of PPMOs that target the AcrAB-TolC efflux pump, which is a major component of the intrinsic antibiotic resistance mechanisms of E. coli and K. pneumoniae. Experiments tested for the effect of the PPMO targeting the acrA gene, specific sequences within the acrA gene, and the tolC gene. The effect of the PPMO was measured by a change in the minimum inhibitory concentration (MIC) of common antibiotics such as Piperacillin/Tazobactam (Pip/Tazo), Azithromycin, and Levofloxacin on strains of these two bacteria. The results show that PPMOs targeted to the acrA gene have a 4-8 fold effectiveness at lowering antibiotic MICs for the bacterial strains. PPMOs that targeted the tolC gene, on the other hand, have no synergistic effect in lowering antibiotic MICs for the bacterial strains. In addition, changing the sequence of the PPMOs targeting the acrA gene was shown to have an effect, albeit small, on susceptibility to antibiotics, which suggests that targeting specific regions of a gene of interest can induce more or less susceptibility in the bacteria to antibiotics.

Correlates of Neural Response to Energy-Dense Food

Gray Umbach

Mentor: Bradley Lega MD, Department of Neurosurgery
Collaborators: Irina Podkorytova MD & Jui-Jui Lin BE

Obesity is a condition of grand cost and detriment at times and in part resulting from excessive consumption of energy-dense foods. Functional MRI (fMRI) literature demonstrates that high-calorie food activates the brain's reward pathway and brain regions linked to drug use and addiction. However, to understand the circuit such foods activate to a sufficient level that would enable the use of exogenous neural stimulation to combat unhealthy food's enticing influence on our brains requires technology with more temporal specificity and functional insight than fMRI. To work towards this, we designed a cognitive task that presented images of foods of various energy-densities in a controlled manner. We then ran this task with patients suffering from refractory epilepsy, who, to localize their epileptogenic foci to guide future brain tissue resections, were implanted with intracranial electroencephalography (EEG) electrodes. Using the EEG data from these electrodes, we sought to define not only the regions activated by energy-dense foods, but also key functional characteristics of the neurons involved such as their oscillatory frequencies, the intensity of neuronal population activation, and functional connectivity between various brain regions. Data is still being gathered, but we expect a stronger induction of gamma band oscillations (36-120Hz) in the orbitofrontal cortex (OFC), a region involved in reward, for energy-dense food presentations. We also expect energy-dense food to induce functional connectivity between the OFC and other members of our reward pathway, such as the hippocampus. Such information would lay the foundation for determining if there are any patterns of neural activation unique to high-calorie food stimuli. If that is the case, then exogenous neural stimulation could offer an unconventional modality of obesity treatment by antagonizing such neural activation, thus reducing the drive to eat specifically energy-dense foods.

Synergy of AcpP PPMO and Piperacillin/Tazobactam in the Breakdown of Pseudomonas Aeruginosa PA01 Biofilms

Ashley Wallace

Mentor: David Greenberg MD, Department of Microbiology
Collaborators: Christine Pybus MS & Carolyn Sturge PhD

Introduction: Pseudomonas aeruginosa is an opportunistic Gram-negative bacterium and one of the most common causes of hospital-acquired infection, especially in immunocompromised patients. It is particularly pathogenic because of its ability to form biofilm, an extra-cellular matrix that makes it more resistant to host defenses and antibiotic therapies. Combination therapies have proven to be more effective at clearing biofilms because they target different processes or cell populations, but concerns about toxicity and antibiotic resistance have led to the exploration of alternative therapies that target biofilm formation at a genetic level. One such alternative is the use of peptide-conjugated phosphorodiamidate morpholino oligomers (PPMOs), which are sequence-specific antisense oligomers that target the mRNA of bacterial genes and prevent translation of particular proteins.

Hypothesis: PPMOs targeting the essential gene AcpP will act synergistically with the antibiotic Piperacillin/Tazobactam (Pip/Tazo) in the breakdown of Pseudomonas aeruginosa PA01 biofilms in vitro.
Methods: To test synergy between the PPMO and antibiotic, PA01 biofilms were grown in filtered Mueller Hinton broth II (MHII) on minimum biofilm eradication concentration (MBEC) plates. MBEC plates are 96-well plates that have pegs attached to the lid to provide additional surface area for biofilm growth. After 24 hours of growth, the biofilm-covered pegs were switched to another 96-well plate containing fresh media with different combinations of antibiotic and PPMO in each well. Three such doses were administered every 8 hours, and at 48 hours of total growth, the biofilm remaining on the pegs was analyzed by one of four methods: 1) crystal violet assay, 2) resazurin assay, 3) CFU count, and 4) confocal microscopy.

Results: Crystal violet and resazurin assays demonstrated that Pip/Tazo and AcpP PPMO were potentially synergistic in biofilm breakdown for Pip/Tazo 0.5-0.0625 ug/mL and AcpP 5-0.625 uM. For several combinations, CFU measurements yielded 2-log or 3-log reduction in CFU compared to the control and synergistic effects on biofilm breakdown, particularly in cases where the antibiotic alone had no effect. While confocal microscopy demonstrated a decrease in viable bacteria with antibiotic treatment and PPMO treatment, the most significant eradication of biofilm occurred with combined treatment.

Conclusion: The synergy demonstrated in vitro between AcpP PPMO and Pip/Tazo in the breakdown of P. aeruginosa PA01 biofilms is promising for in vivo studies as well, since PPMOs have the potential to increase biofilm sensitivity to lower doses of traditional antibiotics.

The Role of Vitamin D Metabolism in the Timing of Birth

Ailing Yang

Mentors: Carole Mendelson PhD & Alina Montalbano PhD,
Department of Biochemistry & Obstetrics & Gynecology

Preterm birth (PTB, <37 weeks of gestation) is the leading cause of neonatal mortality and morbidity. Both term and preterm labor are associ-ated with increased levels of proinflammatory cytokines within fetal and maternal reproductive tissues. Uterine quiescence is maintained throughout most of pregnancy by increased circulating progesterone (P4) and enhanced progesterone receptor (PR) activity, which silence expression of proinflam¬matory mediators and contraction-associated genes. To identify novel genes that maintain uterine quiescence during pregnancy and promote the initiation of term and preterm labor, our lab conducted RNA sequencing of myometrium from timed-pregnant mice at 15.5-18.5 days post-coitum (dpc) and during labor (19.0 dpc). Novel genes of interest were identified through transcriptome profiling and validated by quantitative real-time PCR. Cyp27b1 was one of the most highly downregulated transcripts in pregnant mouse myometrium at 18.5 dpc and in-labor, compared to 15.5 dpc. Cyp27b1 encodes 1□-hydroxylase, the key enzyme in synthesis of the bioactive form of vitamin D, calcitriol, which binds to the vitamin D receptor (VDR), a member of the steroid/nuclear receptor family, which was also downregulated at term. Calcitriol/VDR mediate anti-inflammatory actions in various tissues; calcitriol synthesized by human placenta, decidual macrophages and uterine natural killer cells was reported to regulate maternal immunologic tolerance to the hemi-allogeneic fetus during pregnancy. The effect of P4 and of the PR antagonist, RU486, on Cyp27b1/VDR mRNA expression was analyzed. We observed that P4 treatment of timed-pregnant mice caused a significant increase in myometrial CYP27B1 mRNA levels compared to time-matched controls in labor at term. In RU486-treated mice, CYP27B1 mRNA decreased signifi-cantly 8 hours post-injection and remained significantly reduced during preterm labor, compared to vehicle-injected mice. Based on these collective findings, we postulate that CYP27B1 and VDR are key P4/PR target genes in the pregnant myometrium that act cooperatively with P4/PR to maintain myometrial quiescence via their anti-inflammatory actions. Thus, the decline in PR function near term, accompanied by a parallel decline in CYP27B1/VDR, permit increased inflammatory gene expression leading to myometrial contractility and labor. We hypothesize that calcitriol may provide a safe and effective treatment for prevention of PTB.

Analyses of the Link Between Amyloid and Tau Pathology in an AD Mouse Model (3xTg-AD): Disease Progression Due to Increased Levels of Abeta Peptide and Tau.

Lucio Zapata, Jr.

Mentor: Doris Lambracht-Washington PhD,
Department of Neurology & Neurotherapeutics
Collaborator: Hannah Ismail

Introduction: Pathological features of Alzheimer's disease (AD) include the accumulation of extracellular amyloid plaques composed of aggregated amyloid-β (Aβ) peptide and intracellular neurofibrillary tangles consisting of phosphorylated tau protein. Mutations in the genes that encode amyloid precursor protein (APP), and presenilin 1 and 2 (PS1/PS2) have been shown to cause familial AD in humans. Studies provided evidence that Aβ accumulation may initiate phosphorylation of tau protein, via the Ras/MEK/Extracellular Signal-regulated Kinase (ERK) signaling cascade, activation of the mitogen-activated protein kinase (p38 MAPK), Cyclin dependent kinase 5 (CDK5) and/or glycogen synthase kinase-3β (GSK3β). We studied distribution of Aβ and tau oligomers, Erk activity in different brain lysate fractions from different age groups of a triple transgenic mouse model (3xTg-AD) and wild-type mice, and Erk activity in DNA Abeta42 immunized mice.

Methods: Brain lysates of 4-, 6-, 12-, and 20-month-old 3xTg-AD and wild-type mice were prepared via a 4-step extraction protocol in TBS (soluble), TBS-T, SDS, and formic acid. DNA Abeta42 vaccination administered via gene gun. Abeta and Tau concentrations and Tau phosphorylation levels were monitored by Dot blot, Semidenaturing detergent agarose gel electrophoresis (SDD-AGE), and ELISA using anti-Abeta and anti-Tau antibodies. Erk1/2 levels were monitored by Western blot using monoclonal antibodies.

Results: There was a significant increase of total tau concentrations with increasing age and we found also an increasing insolubility (more tau in the non-soluble brain lysate fractions). 4- and 20-month-old 3xTg-AD soluble brain lysates indicated the presence of aggregated tau peptide, which was not present in wild-type control mice. Kinases involved with tau phosphorylation were measured and showed an increase of activated/phosphorylated Erk1/2 with increasing age, with a drop in concentration at 12 months in half of the mice analyzed (n=5). Immunized 3xTg-AD mice showed a decrease in activated Erk1/2 when compared to non-immunized, age matched mice.

Discussion: The 3xTg-AD mouse model provides a good model to study pathologies and possible treatments for human Alzheimer's disease. Abeta 42 peptide and tau increase due to age in this mouse model. A link between the amyloid pathology is likely found in the wide spectrum of cellular kinases which are upregulated due to Abeta in Alzheimer's disease. Therefore, immunization against Abeta and generation of anti-Abeta antibody will indirectly reduce tau pathology.

Cellular Sources of CXCL9 and CXCL10 in Cutaneous Lupus Erythematous

Jane Zhu

Mentor: Benjamin Chong MD, Department of Dermatology

Lupus erythematosus (LE) is an autoimmune disease that can affect many organs including the skin, kidney, heart, lungs, joints, and/or central nervous system. Up to 20% of LE patients with skin limited disease (cutaneous lupus erythematosus (CLE)) eventually develop systemic lupus erythematosus (SLE). A biomarker that helps identify this at-risk population of CLE patients would aid in their management and provide a better understanding of the pathophysiology behind disease progression. Preliminary data have demonstrated a stepwise up-regulation of CXCL9 and CXCL10 in CLE and SLE patients suggesting that these two chemokines may be promising biomarkers for lupus disease progression. While CXCL9 and CXCL10 are both up-regulated in dermal inflammatory infiltrates of CLE skin lesions, a knowledge gap remains in fully understanding the cellular sources of these chemokines in CLE. In allograft rejections and bacterial infections, CXCL9 and CXCL10 are known to be produced by macrophages, dendritic cells, and B cells.1 However, the secretion of CXCL9 and CXCL10 by these inflammatory cells have yet to be confirmed in CLE lesions. The aim of this project is to characterize and compare expression of CXCL9 and CXCL10 in multiple skin cell subsets including CD20+ B cells, CD3+ T cells, CD68+/CD163+ macrophages, CD123+ plasmacytoid dendritic cells (pDCs), and basal keratinocytes in CLE lesional skin. We hypothesize that basal keratinocytes, CD68+ macrophages, and CD123+ pDCs express higher levels of CXCL9 and CXCL10 in CLE than other cells. Skin biopsies were taken from CLE and normal control patients recruited from the outpatient dermatology clinics at Parkland Health and Hospital System and UTSW Medical Center. CXCL9, CD3, CD68, and CD163 antibodies were tested in positive control tissue (inflamed tonsil) and positive staining for each marker was confirmed. Single stains with CD3 and CXCL9 antibodies have been successfully performed in normal skin. Double immunofluorescence studies are currently being optimized. Because the CD163 antibody did not have strong staining in normal skin, an alternative marker, CD68, has been chosen for future studies. Future directions for this project include optimizing single immunofluorescence staining protocols for CXCL10, CD20, CD68, and CD123 antibodies. Then double immunofluorescence studies focusing on CXCL9 or CXCL10 and a cell surface marker (CD3, CD20, CD68, and CD123) will be performed in both normal and CLE lesional skin samples.

References: 1Park MK, Amichay D, Love P, et al. J. Immunol. 2002;169:1433-43.

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Clinical Research

KEY

Ω Oral Presenter - UT Southwestern Medical Student Research Forum
Δ Dean's Research Scholar, τ T35 NHLBI Training Grant Funded
∗ Poster Presenter

Antibody-Mediated Rejection in Cardiac Transplant Patients at UT Southwestnern

Carol Abousaab

Mentor: Sonia Garg MD, Department of Internal Medicine-Cardiology
Collaborators: Steve Ring MD & Gunjan Singh BS

Background: Antibody mediated rejection (AMR) is a form of rejection in cardiac transplant patients associated with worse over-all outcomes. Identifying clinically relevant AMR is difficult, as patients are often asymptomatic and have normal cardiac allograft function. Changes in diagnostic standards from the International Society for Heart and Lung Transplantation in 2013 focused the diagnosis on pathologic findings that included markers of complement activation. We sought to assess the correlation between the amount of complement found in our biopsies with the presence of allograft dysfunction as assessed by echocardiogram.
Methods: A retrospective chart review of 205 patients that underwent heart transplants at William P. Clements Jr. University Hospital between 2010 and 2016 was performed. Percentage of complement factors, C4d and C3d, were collected from clinical pathology reports. We excluded biopsies that had evidence of advanced cellular rejection. Assessment of cardiac allograft function was determined from the reported left ventricular (LV) ejection fraction (EF) on clinical echocardiogram reports. Biopsy data was paired with an echocardiogram performed within 3 months of the biopsy. Left ventricular dysfunction was characterized by qualitative description or an EF below 55%.
Results: A total of 3,592 echocardiograms were performed in 205 patients after cardiac transplant. Of these, 695 echocardiograms showed left ventricular dysfunction in 145 patients. Left ventricular dysfunction was noted in 22% of echocardiograms associated with C4d positive biopsies and 29% of echocardiograms associated with C3d positive biopsies. Of the 42 biopsies showing both C4d and C3d positivity, 5% of biopsies with less than 50% C4d were associated with left ventricular dysfunction, while 64% of biopsies with 50% or higher C4d were associated with left ventricular dysfunction. Of the 10 C3d/C4d positive biopsies that corresponded to echocardiograms showing left ventricular dysfunction, 9 biopsies showed a combined C3d/C4d percentage of 80% or higher.
Conclusions: Patients with normal left ventricular function have varying amounts of combined C4d and C3d; however, patients with left ventricular dysfunction tended to display higher amounts of combined C4d and C3d. Further information is required to better delineate which patients are at increased risk of allograft dysfunction.

Cholesterol Efflux Capacity: Biological and Clinical Determinants in a Large Multi-ethnics Population Study (Dallas Heart Study)

Oludamilola Akinmolayemi

Mentor: Anand Rohatgi MD, MSCS, Department of Internal Medicine-Cardiology

Background: Cholesterol efflux capacity characterizes the ability of HDL to accept cholesterol from extrahepatic cells in the periphery to the liver, which is a crucial step in reverse cholesterol transport. Cholesterol efflux capacity has been shown in clinical studies to be inversely correlated with prevalent coronary disease and incidence of cardiovascular events, but it is still unclear what biological and clinical determinants drive cholesterol efflux capacity.

Objectives: To determine the biological and clinical variables that associate with cholesterol efflux capacity measured with two different methods in a large multi-ethnic population study (Dallas Heart Study 2) and how these associations differ by sex, race, history of diabetes, and history of cardiovascular disease.

Methods: Cholesterol efflux capacity was measured in the cohort (DHS-2) using both fluorescence (BODIPY) and radiolabeled methods. Statistical analysis was performed using Jonckheere-Terpstra trend test, Mann-Whitney test, and multivariate linear regression. Two-sided p values <0.05 were considered to indicate statistical significance.

Results: A total of 2373 participants were included. The median age was 51 years, 57% were women, 51% were black, 5% had history of CVD, and 17% had history of diabetes. Cholesterol efflux capacity measured by radiolabeled method was significantly higher in women than in men (P<0.001). Blacks had the lowest cholesterol efflux capacity measured by both BODIDY (p=0.010) and radiolabeled (p<0.001) methods. Participants without history of CVD had higher cholesterol efflux capacity measured by radiolabeled method compared to those with history of CVD (p=0.048). In multivariate regression, risk factors and circulating markers explained more of the variance in efflux using radiolabel than the variance in efflux using BODIPY (R2 0.195 vs. 0.099) with some overlapping and some distinct markers. Stratification by history of CVD, history of diabetes, race, and sex categories did not alter the findings.

Conclusion: Our analysis revealed that biological and clinical variables that associate with cholesterol efflux capacity vary with measurement methods, but further studies with different study population validating these differences are needed. An understanding of these differences will be useful in identifying targets to improve cholesterol efflux capacity.

The Effect of Melasma on Self-Esteem: A Pilot Study

Oyindamola Akinseye
Janice Jiang

Mentor: Amit Pandya MD, Department of Dermatology
Collaborator: Andrea Tovar-Garza MD

Background: Melasma is a common disorder of hyperpigmentation characterized by tan or brown macules and patches mainly affecting sun exposed areas. It can affect men and women of all ethnicities and skin types, but is especially prevalent in women with darker skin types who are exposed to ultraviolet (UV) light. It has been shown to have a significant impact on the quality of life of those affected. While several studies measuring the effect of melasma on women's quality of life have been conducted, there is little research regarding the effect of melasma on self-esteem.

Methods: In this study, we used an inductive qualitative approach to understand the effect of melasma on self-esteem using semi-structured interviews as the means of collecting data. This method has been used to gather information about the psychosocial impact of other skin diseases. We interviewed patients with moderate to severe melasma regarding the effect of their disorder on their self-esteem.

Results: We interviewed 6 patients. All reported a significant negative effect of melasma on their quality of life and self-esteem despite different racial/ethnic background. Four key themes emerged in our analysis: decreased self-esteem/increased self-consciousness, decreased freedom, frustration with costly and ineffective treatments, and improvement in QOL after treatment with oral tranexamic acid and triple combination cream.

Conclusions: Our interviews revealed that quality of life and self-esteem appeared to be significantly impacted by melasma. Patients refused to leave the house, felt inferior to others, and incessantly thought about their melasma. Physicians treating patients with melasma should aim to not only improve the pigmentary changes but also improve quality of life and self-esteem.

Association of African Ancestry with Left Ventricular Hypertrophy Assessed by Electrocardiographic Voltage and Cardiac Magnetic Resonance: the Dallas Heart Study

Aya Alame

Mentor: Mark Drazner MD, MSc, Department of Internal Medicine-Cardiology
Collaborators: Sonia Garg MD, Julia Kozlitina PhD, & Colby Ayers MS

Introduction: Left ventricular hypertrophy (LVH) is more common in blacks than whites, despite adjusting for differences in blood pressure. Whether environmental or genetic factors lead to this increased prevalence of LVH in blacks is unknown. If genetic factors are involved, we hypothesized that the proportion of African ancestry among self-reported blacks would be associated with an increased risk of LVH in this ethnic group.
Methods: Participants from the Dallas Heart Study underwent genotyping, an electrocardiogram (ECG), and Cardiac Magnetic Resonance (CMR) imaging. Ancestral admixture proportions were estimated using genetic markers (Illumina Exome Chip) and ADMIXTURE software assuming 3 ancestral populations. In this analysis, we included participants that self-identified as black or white (n=2077). First, we tested the association of genetically inferred African ancestry (AFR) and self-reported black race, separately, using multivariable linear regression models, with three LVH phenotypes: 12-lead ECG voltage, LV concentricity0.67 (LV mass/volume0.67, a marker of concentric LVH), and LV Wall Thickness (LVWT). Next, we entered both AFR and black race into the same models to determine if the association of black race with LVH would be accounted for by AFR. Finally, we tested the association of AFR with LVH phenotypes among self-reported blacks.
Results: The study cohort consisted of 1,251 black and 826 white participants. Black race and AFR were individually associated with ECG voltage, LV concentricity0.67, and LVWT (Table 1). When AFR and black race were entered together into multivariable models, AFR, but not black race, was significantly associated with the LVH phenotypes (Table 1). Among self-reported blacks, AFR remained significantly associated with these LVH phenotypes (Table 1).
Conclusions: The association of black race with LVH phenotypes can be captured more robustly with a genetic estimate of African ancestry. Further, within blacks, the proportion of AFR was associated with LVH phenotypes. These data support a genetic basis, related to African ancestry, for the increased prevalence of LVH in blacks.

Table 1. Association of African ancestry and self-reported black race with LVH phenotypes in Multivariable Linear Regression Models

Cohort	Variable	ECG Voltage		LV Concentricity$^{0.67}$		LV Wall Thickness	
		β	p-value	β	p-value	β	p-value
Blacks and Whites	AFR	21.7	<.0001	0.36	<.0001	0.50	<.0001
	Black race	18.6	<.0001	0.30	<.0001	0.42	<.0001
Blacks and Whites	AFR*	21.1	0.02	0.64	0.04	0.77	0.03
	Black race*	0.49	0.95	-0.24	0.38	-0.25	0.42
Blacks Only	AFR	20.3	0.04	0.70	0.045	0.88	0.02

*AFR and black race entered together in this model. All models in table adjusted for age, sex, systolic blood pressure, antihypertensive medications, lean mass, and fat mass. Raw β estimates are provided.

Resident Complications of Intravitreal Injections at a Large County Hospital

Neeraja Balachandar

Mentor: Zachary Robertson MD, Department of Ophthalmology
Collaborator: Keerthana Bolisetty MD

Introduction: Intravitreal injections (IVIs) have now surpassed cataract surgery as the most frequently performed procedure in ophthalmology. Their incidence has increased from less than 3,000 in 1999 to more than 2.3 million in 2012. The most common pharmacologic agents administered intravitreally inhibit angiogenesis by blocking vascular endothelial growth factor. Diabetic macular edema, exudative age-related macular degeneration, and venous-occlusion associated macular edema are the most common indications. As such, IVI usage will only increase in the future as the population ages, new medications become available, and indications broaden. With IVIs being performed at increasing rates at the Parkland county hospital's resident ophthalmology clinic, identification of an accurate risk profile must be delineated, including possible complications during cataract surgery.

Methods: A retrospective chart review of patients who received one or more IVIs by an ophthalmology resident at Parkland between 01/2010 and 07/2016 was conducted. Charts were reviewed for a variety of IVI-related complications as well as the incidence of posterior capsule rupture (PCR) during cataract surgery, after one or more IVIs.

Results: 1893 eyes (from 1300 subjects) that had undergone at least one IVI were included. Of a total of 8642 IVIs that were reviewed, 76 complications (0.88%) were noted. Their nature ranged from relatively non-vision threatening (corneal abrasion, ptosis, and posterior vitreous detachment) to severely vision threatening (endophthalmitis, intraocular pressure (IOP) elevation, retinal detachment (RD), and other patient movement-related complications). The majority of complications did not occur at a significantly higher or lower rate than those reported in the literature. However, a significantly lower rate of RD ($p=0.039$) and a significantly higher rate of acute and chronic IOP elevation ($p=0.001$) was found. Further, of 354 cataract surgeries included and reviewed on eyes with prior IVIs, PCR occurred 12 eyes. Of these 13 eyes, 7 eyes were excluded for a prior history of pars plana vitrectomy, a known independent risk factor for PCR. This resulted in a PCR rate of 1.41% compared to average rates in literature of 1.9-2.1% ($p=0.677$).

Discussion: Resident administered IVIs at Parkland pose an overall low risk of complication, minimally different from IVIs administered at other institutions. The PCR rate in eyes with a history of IVIs at Parkland, excluding previously vitrectomized eyes, is not significantly different than the standard rate in literature. This data will prove useful in analyzing the unique risks of IVIs and subsequent cataract surgeries in individual patients. The etiology of the increased rates of IOP elevations at Parkland requires further investigation.

Does Age Affect Surgical Outcomes Following Ileo-Pouch Anal Anastomosis in Children?

Nora Bismar

Mentor: David Schindel MD, Department of Pediatric Surgery
Collaborators: David T. Schindel MD & Ashish Patel MD

Introduction: To determine if younger children having a laparoscopic restorative proctocolectomy, mucosectomy and ilea-pouch anal anastomosis (LRS-IPAA) have comparable outcomes to older counterparts in the treatment of ulcerative colitis (UC) and familial adenomatosis polyposis (FAP).

Methods: After IRB approval, a review of 65 children with FAP and UC who underwent LRS-IPAA at a children's hospital from 2002 to 2017 was performed. The study population was separated into two groups based on age: Young group (YG) (5- 12yrs); Older group (OG) (13-18yrs).
Patient demographics, post-procedure course and outcomes data was collected. A statistical analysis of the data was performed using Graphpad® San Diego, CA.

Results: There were 65 children identified. YG, n=22 (13 with UC; 9 with FAP). There were 15 females and 7 males in YG. OG, n=43 (UC; n=28), (FAP; n=15). There were 20 females and 23 males in OG. Following LRS-IPAA, continence, appetite recovery, use of antidiarrhea medications, and complications were not significantly different between groups. The incidence of pouchitis was 21.5% (14): YG (n=5); OG (n=9) (p=NS). The incidence of anastomotic stricture was 13.8% (9): YG (n=2) and OG (n=7) (p=NS). Two children (one in each group) required re-operative adhesiolysis after presenting with a bowel obstruction (p=NS). Three children elected to have a loop ileostomy constructed secondarily to chronic rectal pain and failure to achieve full continence following LRS-IPAA: all three were in the OG (p=NS).

Conclusion: There are no significant differences in the outcomes of younger children when compared to older pediatric patients following LRS-IPAA in the treatment of FAP or UC. While numbers are small, these data suggest that a younger age should not be a deterrent when contemplating LRS- IPAA in the treatment of UC and FAP in the pediatric population.

Adiposity and Aging: Assessing the Relationship Between Telomere Length and Patterns of Adipose Tissue Distribution

Benjamin Bleiberg

Mentor: Ian Neeland MD, Department of Internal Medicine
Collaborators: Colby R. Ayers MS

Background: A telomere is a region of repetitive nucleotide sequences at each end of a chromosome, which protects the end of the chromosome from deterioration. Telomere shortening, a surrogate marker of cellular aging, may accelerate from the inflammatory stressors of obesity. The association between adipose tissue depots and telomere length is unknown.
Methods: Data were analyzed from 2,551 participants in the Dallas Heart Study, a prospective multiethnic cohort. The sample composition was 41% male, 59% female, 48% African American, 35% Caucasian, 15% Hispanic and participants had a mean age of 51 years with 23.4% >60 years of age. Leukocyte telomere length (LTL) was determined using qPCR on DNA isolated from circulating leukocytes. Visceral (VAT) and subcutaneous (SAT) abdominal fat masses were measured by MRI, lower body fat (LBF) by dual x-ray absorptiometry, and liver fat by MR spectroscopy. Linear regression was used to evaluate the association between LTL and body fat depots.
Results: In univariate analysis, shorter LTL was associated with higher VAT (p=.0002) and less LBF (p=.02). Shorter telomeres were also associated with older age, male sex, hypertension, diabetes, smoking, decreased kidney function and decreased physical activity (p<0.05 for all). Adjustment for age and sex attenuated the relationships between LTL and VAT, SAT, LBF, and liver fat. No significant interactions were seen by stratification within age groups or by severity of obesity.

Variable	Beta unadjusted	p unadjusted	Beta adjusted	p adjusted
VAT	-0.072	0.0002*	0.009	0.6
SAT	0.021	0.29	0.016	0.38
Lower Fat	0.048	0.02*	0.024	0.19
Liver Fat	0.03	0.41	0.032	0.4

Adjustments for age and sex and * p<0.05
Standardized β coefficients = estimated unit change in 1-SD of the log-transformed variable for a 1-SD increase in the telomere parameter
Conclusions: While LTL is associated with pathogenic patterns of adipose tissue, this association is confounded by the close relationship between LTL and temporal aging. These findings suggest that cellular aging is not independently linked to variation in adipose tissue distribution patterns.

Non-Home Discharge and Prolonged Length of Stay after Cytoreductive Surgery and HIPEC

Daniel Burguete

Mentor: Patricio Polanco MD, Department of Surgical Oncology
Collaborators: Ali A. Mokdad MD, PhD, Martin M. Augustine MD, PhD, Rebecca Minter MD, John C Mansour MD, & Michael A. Choti MD, MBA

Introduction: The ability to preoperatively anticipate prolonged length of stay (PLOS) or transition to an extended care facility (non-home discharge, i.e., NHD) may facilitate discussion of patient expectations and improve utilization of hospital resources. No data has been reported on the rate and risk factors associated with NHD and PLOS in patients following cytoreductive surgery/hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) for peritoneal carcinomatosis. The aim of this study is to identify risk factors for NHD and PLOS following CRS/HIPEC in a national cohort of patients.

Methods: Patients that underwent CRS/HIPEC from 2011-2012 were identified from the National Surgical Quality Improvement Project (NSQIP) dataset. NHD/PLOS and home discharge (within 30 days) groups were compared using Pearson's chi-squared test and two-sample t-test with unequal variances. A univariate analysis was used to compare patient demographics, diagnosis, comorbidities, CCI, operative details and types of resection and post-operative complications among both groups. A multivariate analysis was used to identify independent predictors of NHD and PLOS.

Results: A total of 556 CRS/HIPEC patients were identified, 44 (7.9%) of which were not discharged to home within 30 days. From these 44 patients, 12 were discharged to a skilled care facility and 11 were discharged to a rehabilitation facility, accounting for a NHD rate of 4.1%. Twenty-one patients remained hospitalized at □30 days accounting for a PLOS rate of 3.7%. On univariate analysis, advancing age, COPD, HTN, and low preoperative albumin were identified as preoperative risk factors for NHD/PLOS ($p<0.05$). On multivariate analysis, age ≥ 65, pre-op albumin < 3.0 g/dL, and having a multi-visceral resection were identified as independent predictors of NHD/PLOS. If all three predictors are met preoperatively, the probability of NHD/PLOS is 30.2%.

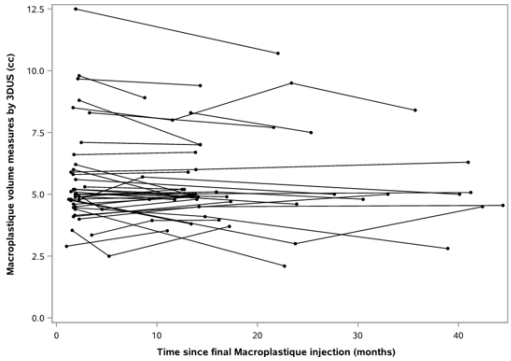
Conclusion: In this national cohort of patients, advanced age, hypoalbuminemia, and multi-visceral resection constituted the main risk factors for NHD/PLOS following CRS/HIPEC. Timely identification of these risk factors may facilitate preoperative discussions with patients, and improve discharge planning and resource utilization.

Durability of Macroplastique in Women With Stress Urinary Incontinence Secondary to Intrinsic Sphincter Deficiency

Tim Carroll

Mentor: Philippe Zimmern MD, Department of Urology
Collaborators: Alana Christie BS, MS, Melissa Foreman RDMS, RVT, FSDMS, & Gaurav Khatri MD

Introduction/Objectives: Macroplastique (MPQ) is a urethral bulking agent used in the treatment of stress urinary incontinence (SUI) in women with intrinsic sphincter deficiency (ISD). MPQ has been emerging as a viable bulking agent in the United States since 2011 when Collagen (Contigen) became no longer available. Prior studies with Collagen suggest that a stable volume and circumferential configuration of bulking agent around the urethra result in improved clinical outcomes. However, little is known about the durability of the volume/configuration of MPQ over time. Three-dimensional ultrasound (3DUS) is an ideal modality to image the irregularly shaped and echogenic MPQ. Our goal is to evaluate the durability of MPQ in women with SUI secondary to ISD using serial 3DUS measurements. We hypothesize that MPQ will maintain its volume/configuration around the urethra over time.
Methods: Following IRB approval, charts of non-neurogenic women with SUI and ISD (low VLPP; lateral imaging of urethral support with no hypermobility) who underwent MPQ were reviewed from a prospectively maintained database. All had at least two 3DUS measurements after their last MPQ injection. Excluded were women with prior bulking agent injection, urethral hypermobility, or follow-up <6 months. 3DUS was performed using the Philips IU22 ultrasound system with endovaginal 3D 9-3V end-fire probe (Philips Healthcare, Bothell, WA) at 6-8 weeks post-injection and yearly thereafter. The same senior sonographer blinded to clinical outcomes evaluated volume and configuration circumferential/symmetric or asymmetric) at each 3DUS.
Results Obtained: Between 2011 and 2016, 38 of 146 women met study criteria. Those excluded were due to prior other bulking agent injection (21%) or insufficient 3DUS follow-up (79%). The average age and BMI were 64 and 28, respectively. 63% of patients had prior anti-incontinence surgery. The mean time from first to last 3DUS was 19 months (range: 6-42 months). The mean time between first and second ultrasound was 13 months. An average of 5.6cc were injected total in each patient (range 2.5-10cc). 76% of patients had 1 injection, while the remainder had 2 or more (24%). The change in volume from first 3DUS measurement to last 3DUS measurement decreased from a mean of 5.8cc to 5.5cc (mean change = -0.3 (95% CI: -0.5, -0.04); p = 0.0262). 29 patients had symmetric MPQ at first 3DUS, out of whom only 4 (14%) had a follow-up 3DUS showing asymmetric MPQ distribution.
Conclusions: At mid-term follow-up, MPQ maintains both its volume and configuration in the urethral wall.



Mid-Term Macroplastique Outcome in Women with Stress Urinary Incontinence Secondary to Intrinsic Sphincter Deficiency

Tim Carroll

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Introduction/Objective: Macroplastique (MPQ) is a urethral bulking agent used in the treatment of stress urinary incontinence (SUI) secondary to intrinsic sphincter deficiency (ISD). MPQ has been emerging as a viable bulking agent since 2011 when Collagen (Contigen) became no longer available. Little is known regarding the mid-term efficacy of MPQ as it relates to prior anti-incontinence treatment exposure. Therefore, our goal is to evaluate the efficacy of MPQ in women with SUI secondary to ISD with varying backgrounds of anti-incontinence treatment.

Methods: Following IRB approval, charts of non-neurogenic women with SUI secondary to ISD who underwent MPQ injection were reviewed from a prospectively maintained database. ISD was defined as low VLPP and absence of hypermobility on voiding cystourethrogram. Patients were divided into 3 groups: Naïve (Group I), Prior Anti-Incontinence Surgery (Group II), and combined Prior Bulking Agent and Anti-Incontinence Surgery (Group III). Excluded were women with follow-up <6 months. Baseline data collected included questionnaire scores (UDI-6 question 3 and VAS Quality of Life) and urodynamic study values. Patients were followed with repeat questionnaires, patient symptomatic self-report, and three-dimensional ultrasound (3DUS) evaluating volume/configuration of MPQ. Success was defined as a UDI-6 question 3 score of 0-1, patient self-report of improvement of at least 75%, usage of ≤ 2 pads/day, or a VAS QoL score of ≤3, as well as not requiring additional anti-incontinence therapy.

Results Obtained: Between 2011 and 2016, 106 of 149 women met study criteria. The average age and BMI of the whole population was 66 and 28, respectively. 67% of patients had 1 injection, while the remainder had 2 or more. The mean baseline UDI6 Question 3 score was 2.6 and the mean baseline QoL score was 8. The success rate was 46% for Group I, 49% for Group II, and 62% for Group III at 30 months mean follow-up (p=.61). Over the same period, the mean overall UDI6 question 3 score and QoL score improved to 1.7 and 4.3, respectively. Of the success group (N=54), Group II contributed the largest proportion (56%) followed by Group I (24%). Of the failure group, 6 patients progressed to sling and 2 patients required an artificial urinary sphincter. 3DUS measurements confirmed only a 0.2cc decrease in MPQ volume each year after the final injection.

Conclusion: At mid-term follow-up, MPQ was effective as both a primary and secondary treatment alternative for SUI secondary to ISD.

Obstructive Sleep Apnea in Children with Down Syndrome: Demographic and Clinical Factors

Bahir Chamseddin

Mentor: Ron Mitchell MD, Department of Otolaryngology
Collaborator: Romaine F. Johnson MD, MPH, FACS

Introduction: OSA is a disease characterized by obstruction of the airway during sleep leading to periodic reductions in airflow, hypoxemia, and hypercapnia and is the most common reason for this demographic to visit an otolaryngologist. Current research of factors predicting OSA in this population are non-linear, scarce, and inconclusive. Objective: The primary objective of this study was to use relatively large patient population to describe the demographic, clinical and polysomnographic characteristics of children with Down Syndrome (DS) suspected of having obstructive sleep apnea (OSA). The secondary objective was to identify demographic and clinical factors that predict severe OSA in children with DS.
Methods: A retrospective case-control study of children with DS who received PSG over 5 years was performed. Criteria for inclusion were age 2-18, negative history of adenotonsillectomy, data available on ethnicity, BMI z-score, medical comorbidities, clinical data including tonsil size and polysomnographic data. Severe OSA is defined by Apnea Hypoxia Index (AHI)>10 using polysomnography, the gold standard test for diagnosing OSA.
Results: Of a total of 106 children, 90% were diagnosed with OSA (AHI>1) and 44% were diagnosed with severe OSA (AHI≥10). Obese compared to non-obese children had a significantly higher prevalence of severe OSA (56% versus 35%).The mean SaO2 nadir was significantly lower in obese compared to non-obese children (80 versus 85%). In children older than 12 years, the obese compared to non-obese children had a significantly higher mean AHI of 23 compared to 5.6. Tonsillar hypertrophy (grade III/IV) was not a predictive for OSA. Presence of other medical comorbidities including allergies, asthma, congenital heart disease, and hypothyroidism were not significant in predicting OSA. A multivariable logistic regression model predicting the likelihood of severe OSA in children with DS showed increasing weight (OR: 1.1, 95% CI 1.0-1.1, p=.015) was important in prediction of Severe OSA. Age (OR: .87, 95% CI: .6-1.3, p=.560) did not predict the risk of having severe OSA.
Conclusions: In conclusion, a cohort of 106 children with Down Syndrome prior to corrective OSA surgery showed that weight was the primary risk factor of increasing AHI on PSG. Our study did not find an independent association between age and OSA severity in children with DS with older children, without obesity, showing no increased likelihood of severe OSA. This suggests that a major effort should be directed at avoiding obesity as children with DS as they reach adolescence.

Obstructive Sleep Apnea Demographics in Children Under Three Years Old

Danielle Collado

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Collaborator: Romaine Johnson MD

Introduction: Pediatric obstructive sleep apnea (OSA) most commonly affects children 3 years or older. Very few studies describe the epidemiology and predictors of pediatric OSA in children under 3 years of age.
OBJECTIVES: To describe the demographic, clinical, and polysomnographic characteristics of children under 3 years of age referred for polysomnography (PSG). To identify demographic and clinical features that predict severe OSA in this cohort of children.

Methods: This study reviewed all children under 3 years of age who underwent PSG between 08/01/2012-06/01/2017 at UT Southwestern/ Children's Medical Center in Dallas and had complete data. Demographic, clinical, and PSG data were obtained from the electronic medical records. The following comparisons were made: obese versus non-obese; age 0-1 and 1-3; children with or without significant comorbidities. Pearson chi-squared was used for categorical data and ANOVA for continuous data. Logistic regression was used to look for predictors of severe OSA. A $P<0.05$ was considered significant.

Results: Three hundred thirty-two patients were included in this study, 17% of which were between 0-1 years, and 82% were between 1-3 years. Two hundred sixteen patients were male (65%).The cohort was comprised of 86 (26%) Caucasian, 86 (26%) African American, 138 (42%) Hispanic, and 22 (6.6%) patients that identified as Other. Co-morbidities included 59 (18%) preterm patients, 64 (19%) with allergic rhinitis, 88 (27%) with gastroesophageal reflux, 55 (17%) with asthma, 14 (4.2%) with down syndrome, 25 (7.5%) with cardiac issues, 31 (9.3%) with craniofacial issues, and 6 (1.8%) with sickle cell disease. A total of 163 (49%) patients had tonsillar hypertrophy (tonsil size of 3+ to 4+). Comparison of the two age groups 0-1 and 1-3 years, obese versus non-obese and with or without comorbidities showed no significant differences in clinical or PSG data. Severe OSA was predicted by tonsillar hypertrophy (OR=1.97: p=0.005).

Conclusion: Children under 3 with OSA are more likely to be male and have a variety of comorbidities. Tonsillar hypertrophy is the primary predictor for severe OSA in young children. Additional research is needed to determine the outcomes of surgical therapy for OSA in children under 3.

Role of NT-proBNP in Late-Onset Anthracycline-Induced Cardiotoxicity Screening in Adult Survivors of Pediatric Cancer

Kylie Cullinan

Mentor: Angela Orlino MD, Department of Internal Medicine
Collaborator: Daniel Bowers MD

Purpose: Anthracyclines are chemotherapeutic agents with well-characterized cardiotoxic effects that can occur years after treatment. Current screening techniques in the cancer survivorship population are centered upon noninvasive cardiac imaging; however, this is effective in identifying cardiomyopathy only after significant remodeling has occurred. This study is a continuation of efforts to identify early biomarkers, such as NT-proBNP, and characteristics of adult survivors of pediatric cancer at increased risk of progression to non-ischemic cardiomyopathy (NICM).

Methods: In this retrospective chart review, data was collected for 190 patients at the UT Southwestern After Cancer Experience clinic over the duration of their follow-up care (mean, 4.1 patient yrs, mean of 15 yrs after chemotherapy completion). Patient groups were determined based on absence of NICM (group 1, n=118), those who developed NICM during observation (group 2, n=16), and patients with pre-existing NICM (group 3, n=56). NICM was defined as ejection fraction (EF) <55%. These groups were compared based on demographic data, cardiovascular risk factors, maximum recorded NT-proBNP, and ΔEF ((Max EF-Min EF)/ Max EF). Multivariate regression analysis for ΔEF was performed.

Results: Patients with established NICM were found to have a significantly younger age at diagnosis, greater time from chemotherapy completion, and larger cumulative anthracycline dosage (CAD) as compared to those without NICM (p=0.022, p=0.006, p=0.006). Mean greatest NT-proBNP was 69.4 ng/mL, 206.2 ng/mL, and 302.2 ng/mL for groups 1,2, and 3 respectively. Though group 3 was significantly elevated from group 1 (p=0.043), those who developed NICM (group 2) did not significantly vary from either subgroup. Group 2 did have a significantly elevated ΔEF as compared to group 1 and 3 (p <0.002). Regression analysis of ΔEF yielded 4 variables with limited predictive value (R2=0.35) with NT-proBNP most heavily weighted (partial R2= 0.23).

Conclusions: NT-proBNP was not clearly implicated in early identification of patients at increased risk of progression to NICM. Traditional cardiovascular risk factors, such as HTN, elevated cholesterol, or low HDL were not supported as predictive measures as well. Further prospective data with a larger cohort would be beneficial in clarify the distinguishing characteristics of cancer survivors at elevated risk of developing late-onset NICM.

The Management of Blunt Traumatic Retroperitoneal Hematomas in Children

Pooja Dasari

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Collaborators: Gentry Woods CCRP, RPT & Lorrie Burkhalter MPH, CCRC

Background: Management of blunt traumatic Retroperitoneal Hematomas (RPH) in adults is dependent on anatomical classification. Zone 1 is central, contains the aorta, inferior vena cava, renal vessel origins, partial duodenum/pancreas and requires mandatory exploration. Zone 2 includes the paranephric areas, renal vessels, kidneys, ureters, adrenals/colon and is explored for expanding hematoma. Zone 3 includes iliac vessels, distal ureters, sigmoid/ rectum and may need surgical or radiologic interventional. This strategy has been used in children but has not been studied. The aim of this study is to evaluate the management and outcome of children with retroperitoneal hematomas after blunt trauma.
Methods: With IRB approval, 10 year (2007-2016) retrospective review of all children with RPH from blunt trauma was performed. RPH zone was determined by imaging and/or operative findings. Mechanism of injury, laparotomy, RPH explorations, and outcomes were collected. Descriptive statistics provided mean, standard deviation, median and range. Comparative statistics identified univariate correlations using Fischer's exact test.
Results: We identified 32 patients (84% male, mean age 10±4) with 43 RPH injuries, 14 zone 1, 25 zone 2 and 4 zone 3 injuries (table 1). Mechanisms included motor vehicle collision (75%), struck by object (19%), and pedestrian struck (6%). Nine (28%) patients were unstable on arrival and two expired in the emergency room. Laparotomy was performed in 17 patients, 10 immediately for instability, shock or peritonitis. 13 (30%) RPH zone injuries were explored; two zone 1, nine zone 2 and two zone 3. Four zone explorations required intervention: none in zone 1, four zone 2 (three nephrectomies, one packing) and none in zone 3. RPH exploration had no post-operative surgical complications. Overall mortality was five (16%): two zone 1 before laparotomy (traumatic brain injury, TBI); two zone 1 after laparotomy (TBI and uncontrolled liver hemorrhage); and one zone 2 after laparotomy from chest injury. Mortality was higher in unstable patients (p=0.0006). No mortality occurred from RPH exsanguination and RPH exploration did not impact mortality.
Conclusion: Only a third of pediatric RPH injuries were explored which identified injuries requiring intervention in zone 2 but not zone 1 or 3. RPH injury in children may require a different treatment paradigm compared to adults. Zone 1 injuries in an otherwise stable pediatric patient without peritonitis may benefit from non-operative management. Further larger scale studies will be required to understand the role of surgical intervention in RPH injury in children.

MLT (Microscope Laser Trabeculoplasty) or Not?

Ted Deng

Mentor: Karanjit Kooner MD, MBA, Department of Ophthalmology
Collaborators: Sahar Noorani BA, Alex Yang BS, Munsif Salem MD, Beverley Huet MS, & Xilong Li PHD

Purpose/Relevance: MLT has been shown to be a relatively safe treatment for reducing IOPs in small studies. We wished to determine the efficacy and safety of MLT as an adjunctive therapy in a large diverse patient population with medically uncontrolled mild, moderate, and severe primary open angle glaucoma (POAG) and how patient characteristics may influence outcomes.

Methods: In an IRB-approved single surgeon, retrospective study, 102 patients who received MLT were reviewed. One eye was randomly selected per patient. Patients were excluded if they were <18 years old, had secondary glaucoma, only one functional eye, intraocular surgery three months prior to MLT, or laser trabeculoplasty one year prior to MLT. Over 50 variables were collected including: age, sex, race, BMI, FHx of glaucoma, C/D, visual field defect (VFD), CCT, vision, complications from MLT, additional glaucoma treatments after MLT, pre and post-op IOP, etc. Chi square goodness of fit and one-way ANOVA tests were used to determine any differences in characteristics between patient groups. Multivariate regression analysis was performed amongst candidates who had not failed treatment at six months.

Results: Demographics of the 102 eyes and IOP changes overtime for failure, non-failure, mild, moderate, and severe glaucoma groups are summarized in adjunct Table 1 and Figure 1. Average IOP reduction at 1 year post MLT (n=41) was 17.24% (p<.001). Thirty-six patients (35.3%) failed treatment. Positive family history; increased BMI, age, CCT, pre-op medications; East Indian race; and worse pre-op vision were significantly correlated with lower IOP reductions (respectively, p<.001.) While, mild VFD, female gender, black race, and increased pre-op IOP were significantly correlated with greater IOP reductions (respectively, p<.001.)

Conclusion: Our study has shown MLT at one year is a safe procedure that may offer additional IOP reduction (17.24%) for patients with medically uncontrolled POAG. Predictors for better response are: younger age, lower BMI, black race, female gender, no family history, thin CCT, better vision, and less advanced.

Financial Burden of Recurrent Urinary Tract Infections in Women: A Time-Driven Activity-Based Cost Analysis

Shivani Gaitonde

Mentor: Philippe Zimmern MD, Department of Urology
Collaborator: Rena D. Malik MD

Introduction and Objectives: To apply a Time-Driven Activity-Based Costing (TDABC)1 model to better define the financial burden of long-term management of uncomplicated recurrent urinary tract infections (RUTIs).

Methods: In order to quantify costs for RUTI, a care-delivery value chain was created to delineate each aspect of treatment for RUTI via process maps for: urologic visits, urinalysis and cultures, diagnostic testing, and acute and long-term therapies. RUTI was defined as ≥2 UTIs in 6 mo or ≥3 UTIs in 12 mo2. The treatment pathways included conservative measures (D-mannose, cranberry tablets, estrogens), antibiotic prophylaxis (post-coital, self-start or continuous) and cystoscopy with fulguration of trigonitis3. The practical capacity for each index pathway was derived from the cost summation of all resources utilized, per minute actively spent delivering care. Cost was estimated using the Medicare Physician Fee Schedule, average local pharmacy pricing, and institutional expenses for outpatient cystoscopy under anesthesia with fulguration of trigonitis.

Results Obtained: The baseline cost burden of RUTI, including initial evaluation, imaging, cystoscopy and urine cultures, was $1,100. Acute antibiotic treatment cost ranged widely, from $9 for 7d of oral TMP-SMX to $3,970 for 14d of IV Ertapenem via PICC. Additional yearly cost of long-term management varied considerably among conservative therapies, from $49 for D-mannose to $1,288 for vaginal estradiol ring. Among antibiotic prophylaxis, yearly cost ranged from $40 for self-start antibiotics, $57 for post-coital antibiotics, and $186 for 6-months continuous antibiotics. Cystoscopy with fulguration was costlier than any other pathway, $6,172. Finally, average practical capacity of each stage of care ranged from $0.003/min for urine culture to $80.49/min for estrogen ring.

Conclusion: Using a TDABC approach we found that women with RUTI have significant financial and time investment in the evaluation and treatment of their condition. This information will facilitate the comparison of various treatment pathways in RUTI management.

References: 1Health Policy, 2017; 121(7): 755-763, 2J Urol, 2016;169(2):422-428, 3Urol Science 2015;26(3): 197-201

Deep Venous Thrombosis and Pulmonary Embolism After Lower Extremity Amputation in Patients with Diabetes.

Kathryn Gallaway

Mentor: Dane Wukich MD & Katherine Raspovic DPM, Department of Orthopaedics
Collaborators: Junho Ahn

This study aims to identify risk factors for deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients with diabetes mellitus (DM) undergoing a lower extremity amputation (LEA). A retrospective analysis of 36,445 LEA cases from the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database was performed. 23,380 patients with DM and 13,065 patients without DM were evaluated to determine whether DM is correlated with an increased risk of DVT and PE. Specific risk factors for DVT and PE in this population were also evaluated.

The incidence of DVT in post-LEA patients with DM was 0.94% compared to 1.36% in patients without DM ($p=0.0002$). The incidence of PE in patients with DM was 0.37% compared to 0.54% in patients without DM ($p<0.0001$). Although statistically significant, this small increase in DVT/PE risk appears to be driven by a higher proportion of “completely dependent” patients without DM ($p<0.0001$).

Patients with “completely dependent” pre-op functional status were 2.59 times more likely to develop a DVT (95% CI: 1.81-3.70) and 3.36 times more likely to experience a PE (95% CI: 1.97-5.72), while “independent” patients were significantly less likely to experience either complication. Level of amputation (LOA) was also associated with an increased risk of DVT and PE. Patients who underwent a below knee amputation (BKA) were 2.12 times more likely to experience a DVT/PE (95% CI: 1.40-3.12) and patients with an above knee amputation (AKA) were 1.82 times more likely to experience a DVT/PE (95% CI: 1.40-3.21). Patients who underwent a transmetatarsal amputation (TMA) were significantly less likely to experience either complication.

Other statistically significant risk factors identified in this study include prior myocardial infarction, ASA classification of III-V, and female sex. Patients with a history of dialysis within 2 weeks of surgery had an increased risk of DVT (OR: 1.52, 95% CI: 1.15-2.02); however, no increased risk of DVT/PE in patients with Chronic Kidney Disease (CKD) stage III-V was found (OR: 1.19, 95% CI: 0.97, 1.45).

Although DM is not associated with increased risk of DVT/PE, LOA is a significant predictor of DVT/PE risk. Diabetics with peripheral neuropathy may delay seeking treatment due to lack of pain, potentially resulting in higher LOA. Physicians should emphasize rapid evaluation and management of pressure sores to minimize LOA. Prophylactic antithrombotic protocols should also be considered for patients undergoing a high level amputation and for patients with comorbid risk factors such as cardiovascular disease or dependent functional status.

Outcomes in Two Staged Implant-Based Breast Reconstruction in Patients with Genetic Cancer Risks

Savannah Hampton

Mentor: Nicholas Haddock MD & Sumeet Teotia MD,
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Collaborators: Avi Jayaraman BS, Arya Nair BS, & Chris Venutolo BA

Introduction: Patients with genetic cancer risks (GCR) often undergo therapeutic or prophylactic breast reconstruction. Studies comparing complication rates and number of surgeries within this population are lacking.

Methods: We retrospectively reviewed 542 breast reconstructions, performed by two surgeons (SST,NTH) at one center from January 2012 to February 2016. Patients choosing implants (n=275) were split into 4 groups based on GCR status and mastectomy indication: GCR+, therapeutic (Group1,n=40); GCR+, prophylactic (Group2,n=29); GCR-, therapeutic (Group3,n=189); GCR-, prophylactic (Group4,n=17). GCR included mutations in BRCA, CHEK2, PALB2, Li-Fraumeni Syndrome, and others. Major complications included necrosis requiring surgery, infection requiring IV antibiotics, and hematomas. One-way ANOVA was performed for statistical analysis.

Results: Co-morbidities were equivalent between groups. Average age for each group was: 45.23(Group1), 41.41(Group2), 49.11(Group3), 42.71(Group4), with a significant difference between Group2 and Group3 (p=.003). Percentages of patients with major (p=.415) or minor complications (p=.169) were equivalent. There were no significant differences in the number of complication-related surgeries before (p=.157) or after (p=.604) implant, revision surgeries (p=.589), or total surgeries (p=.672).

Percentages of patients undergoing complication-related surgeries after implant (p=.455) or undergoing revision surgery (p=.192) were equivalent. There was a significant difference between Group2 and Group4 in the proportion of patients undergoing complication-related surgeries before implant (p=0.042).

Discussion: Complication rates and number of surgeries were equivalent between groups. Interestingly, less Group4 women underwent complication-related surgeries before implant compared to Group2 women. The reasons for this difference could be explored. Though more research is needed, it appears overall outcomes between GCR- and GCR+ patients are equivalent. This could be comforting news as more women find out their GCR status.

Impact of Combined Gynecologic Procedures on Two Staged Implant-Based Breast Reconstruction in Patients with Genetic Cancer Risk

Savannah Hampton

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Introduction: Patients sometimes undergo combined mastectomy, gynecologic procedures, and breast reconstruction during one OR visit. We explored this method's impact on surgical outcomes in patients with and without genetic cancer risks (GCR).

Methods: We retrospectively reviewed 542 breast reconstructions, performed by two surgeons (SST,NTH) at one center from January 2012 to February 2016. Patients choosing implants (n=275) were split into 4 groups based on GCR status and combined gynecologic procedures (GYN) status: GCR+, GYN+ (Group1,n=27); GCR+, GYN- (Group2,n=42); GCR-, GYN+ (Group3,n=5); GCR-, GYN- (Group4,n=201). GCR included mutations in BRCA, CHEK2, PALB2, Li-Fraumeni Syndrome, and others. Major complications included necrosis requiring hospital admission, infection requiring IV antibiotics, and hematomas. One-way ANOVA was performed for statistical analysis.

Results: Co-morbidities were equivalent between groups. Average age for each group was: 46.44(Group1), 41.81(Group2), 44.60(Group3), 48.68(Group4) with a significant difference between Group2 and Group4 (p=.012). Percentages of major (p=.686) or minor complications (p=.947) were equivalent. There were no significant differences in the number of complication-related surgeries before (p=.873) or after (p=.894) implant, number of revision surgeries (p=.292), or total number of surgeries (p=.541).

There were no significant differences in the percentages of patients who underwent complication-related surgeries before (p=.546) or after (p=.932) implant or who underwent revision surgeries (p=.308).

Discussion: No significant differences were found in the complication rates or number of surgeries between groups. Though more research is needed, it appears outcomes are equivalent between patients who have combined gynecologic procedures and patients who don't.

More Than Meets the Eye: The Relationship between Dry Eye Disease and Multisystem Exocrinopathy

Waqas Haque

Mentor: Danielle Robertson OD, PhD & Ibtisam Al-Hashimi DDS, PhD, Department of Ophthalmology

Introduction: Sjögren's Syndrome, commonly known to be the disease of "dry eyes and dry mouth", is an autoimmune disease that targets the lacrimal and salivary glands. Sjögren's Syndrome primarily affects women with an estimated prevalence of 1.4% in the United States. Its diagnosis is confirmed via presence of anti-Ro/anti-La antibodies, demonstration of reduced salivary and tear production, and a positive lip biopsy. Patients with Sjögren's Syndrome commonly manifest symptoms of a multisystem exocrinopathy. Currently, over 16 million American adults suffer from dry eye disease and do not meet the diagnostic criteria for Sjögren's Syndrome. For many of these patients, current treatment strategies are not sufficient to eradicate or reduce the chronic symptoms of dry eye, thus decreasing overall quality of life. The objective of this study is to establish whether patients with non-Sjögren's dry eye disease also exhibit symptoms of a multisystem exocrinopathy.

Methods: This was a retrospective chart review of 199 randomly chosen patients who were seen between January 2015 and April 2017 in the Department of Ophthalmology at the Aston Ambulatory Care Center. All patients reviewed had a diagnosis of dry eye disease in their medical chart. Using a validated exocrine dysfunction questionnaire as a template, comprehensive data was collected for ophthalmic findings, patient demographics, oral and topical medications, serology, a review of symptoms for all body systems (such as allergies, congestion, and reflux), and all known diagnoses. A univariate analysis was performed to test for differences between dry eye subtypes. A multivariate analysis is currently underway. Results: 31.2% of patients presented with a diagnosis of evaporative dry eye, 57.5% were aqueous-deficient non-Sjögren's dry eye, and 11.3% were aqueous-deficient Sjogren's dry eye. Analysis of the non-Sjögren's cohorts revealed over 25 symptoms consistent with a multisystem exocrinopathy. 35% of dry eye patients had a diagnosis for rheumatoid arthritis. Exocrine manifestations were significantly different among dry eye subtypes for sinusitis ($p=0.0283$), diarrhea ($p=.0059$), and hypothyroidism ($p=.0291$).

Discussion: This study is the first to indicate a multisystem exocrinopathy disorder in patients with non-Sjögren's dry eye disease. While results from the multivariate analysis are still pending, the identification of specific exocrine symptoms in patients with distinct subtypes of dry eye may lead to the establishment of new, tailored treatment regimens that will enhance patient response to therapy and improve overall quality of life.

Predicting Sub Prophylactic Anti-Factor XA Levels in Trauma Patients Receiving Early Low-Molecular-Weight Heparin

Emily Huang

Mentor: Michael Cripps MD, Department of Surgery
Collaborators: Jonathan Imran, Tarik Madni, Luis Taveras, Audra Clark, & Paul Rizk

Introduction: Standard low-molecular-weight heparin (LMWH) dosing may be suboptimal for venous thromboembolism (VTE) prophylaxis. We aimed to identify independent predictors of sub prophylactic Xa (subXa) levels in trauma patients treated under a new VTE algorithm to start early chemoprophylaxis for high VTE/low bleeding risk.

Methods: A retrospective review was performed of all trauma patients who received Lovenox 40 mg BID and had peak Xa levels drawn from July 2016-June 2017. Cohorts were divided based on having a subXa (< 0.2 IU/mL) or prophylactic (≥ 0.2 IU/mL) Xa level.

Results: 124 patients were included, of which 38 (31 %) had subXa levels and 17 (14%) had Xa levels > 0.4 IU/mL. Of the SubXa cohort, 35 (92%) had their dosage increased. Repeat Xa testing was done in 34 out of 38 patients, with 47% between 0.2- 0.4 IU/mL. The overall median time to initiation of chemoprophylaxis was 21.9 hours [11.45 – 35.07) and in patients at lower risk for bleeding (no ICH or spine fracture) vs. those at higher risk it was shorter (18.39 hours [5.76 – 26.51] vs. 29.5 hours [16.23 – 63.07], $p < 0.01$).

There was no difference in demographics, weight, BMI, creatinine, creatinine clearance, ISS, type of injury, weight-based dose, time to chemoprophylaxis or bleeding complications between the cohorts. Four DVTs and 2 PEs occurred in each group. No independent predictors of a subXa level were identified.

Conclusion: A significant number of trauma patients fail to achieve prophylactic Xa levels. Intrinsic factors may prevent adequate prophylaxis even with earlier administration and higher LMWH dosing.

Effects of SGLT-2 Inhibitors on Visceral Fat and Glucose Metabolism

Connor Hughes

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Collaborators: Ben Bleiberg BS, Colby R. Ayers MS, Craig R. Malloy MD, & Eunsook S. Jin PhD

Introduction: Abdominal obesity and excess visceral adiposity (VAT), have strong associations with insulin resistance, hyperglycemia and type 2 diabetes. A previous pilot study showed that participants with high VAT have less 13C enrichment in glucose reflecting an abundant endogenous substrate pool from adipose turnover for gluconeogenesis, compared with participants with low VAT. This study aims to evaluate the effects of a SGLT-2 inhibitor known to modify markers of VAT on gluconeogenic pathways in the liver.

Methods: Obese adults without diabetes were stratified into high and low VAT groups based on MRI (high n=8, low n=7). After an overnight fast, participants were administered non-radioactive labeled glycerol, and blood samples were collected to calculate glycerol enrichment at sequential time points over 180 minutes. Participants were then randomized to receive empagliflozin 10 mg daily or matching placebo for 3 months and glycerol studies were repeated.

Results: High VAT subjects demonstrated a significantly lower enrichment of ingested glycerol in blood glucose, when compared to low VAT individuals for the 60-180 minute interval ($p < 0.001$). During this same time interval, pentose phosphate pathway activity was significantly decreased in high VAT, compared to low VAT subjects ($p<0.01$). The effects of empagliflozin on these pathways are currently being analyzed.

Discussion: SGLT-2 inhibitors inhibit renal glucose reabsorption in the proximal nephron, inducing weight loss and decreasing systolic blood pressure. This medication has been suggested to reduce CVD event rate and lower hemoglobinA1c levels up to 1%. Observed differences in pathways between high visceral fat subjects on a SGLT-2 inhibitor compared to control high visceral fat subjects could provide insight into the physiologic changes provided by SGLT-2 inhibitors.

Defining Screening Practices for Gestational Diabetes Mellitus in an Urban Indian Community Hospital

Meera Iyengar

Mentor: Iidiko Lingvay MD, Department of Internal Medicine-Endocrinology

Background: The aim of this project was to outline screening practices for gestational diabetes mellitus (GDM) at Apollo General Hospital in Hyderabad, India to understand if GDM was being reliably diagnosed. Current screening guidelines for GDM advocate using an oral glucose challenge test in all high-risk women. Indian women have a 11-fold increased risk of developing GDM, demonstrating the need for a consistent and reliable screening practices.

Hypothesis: If Apollo General Hospital in Hyderabad, India is administering the gold standard screening method for GDM, then pregnant women coming to Apollo should receive an oral glucose tolerance test during their pregnancy.
Methods: A chart review of all deliveries at Apollo General Hospital from its opening in 2012 to 2016 was completed. Information from each chart regarding the hospital's screening practices for GDM including procedures, results, and follow-up practices was collected.

Results: GDM screening rates were high (92%), but not universal. Of the 208 patients reviewed, only 51% received a GTT or GCT sometime during pregnancy. An equal percentage of patients received either an RBS (36%) or GTT or GCT (36%) as their first screening test. The remaining patients received an FBS (21%) or PPBS (0.5%) as their first screening test. 8% were not screened for gestational diabetes mellitus during their pregnancy. 10 out of 208 reviewed patients were diagnosed with GDM, of whom 5 received either a GTT or GCT (45%). The prevalence of GDM at Apollo was 4.8% compared to global prevalence of 6%.

Conclusions: Overall screening for GDM is high at Apollo General hospital. However, the screening practices vary considerably per patient, and only around 50% of women had received the gold standard test during their pregnancy. In addition, the prevalence of GDM at Apollo was lower than the global prevalence of 6%. This combined with the fact that Indian women have a 11-fold increased risk of developing GDM argue that RBS, FBS, PPBS or HbA1c may not be adequate tests to screen for GDM. Inconsistent screening practices prove the need for standardization and inquiry into patient and provider factors that influence the current variability in testing, as undiagnosed GDM can have serious consequences for both the mother and child.

Exploring Compassion Fatigue in Physicians

Aishwarya Iyer

Mentor: Adam Brenner MD, Department of Psychiatry

Compassion fatigue poses a significant threat to the psychological well-being of physicians. Compassion fatigue has severe consequences, not just for those who suffer from it, but for the practice of medicine as well. Physicians experiencing compassion fatigue often suffer from higher levels of depression, anxiety, burnout, and job dissatisfaction. As these physicians continue to practice, they are more likely to commit medical errors and ultimately afford their patients a lower quality of care. These physicians may miss work and have high rates of absenteeism, leading to job turnover and exit from the profession, and costing hospitals roughly $300 billion each year.

Three major factors contribute to the incidence of compassion fatigue in physicians: the culture of medicine, the stigma associated with mental health, and societal perceptions of physicians.

1. Culture of Medicine: Medicine in the United States prioritizes efficiency, such as seeing as many patients as possible within a given timespan, and includes a great deal of administrative tasks, thus making it extremely difficult for physicians to spend enough time with their patients.

2. Stigma: Medical training also socializes physicians, beginning in the very first year of medical school, to believe that it is more appropriate to hide emotions or bottle them up than reflect on and deal with them in an appropriate manner. From students to residents, medical professionals repeatedly express an inability to reach out for emotional support, often for fear of being perceived as weak or incapable.

3. Social Perceptions: Media portrayals of physicians, such as in medical dramas, reflect society's tendency to place physicians on a pedestal, which further contributes to unrealistic expectations of physicians and to the providers' difficulty admitting their struggles.

To combat the negative consequences of compassion fatigue, physicians are encouraged to incorporate self-care into their lifestyles, engage in mindfulness practices, and invest in hobbies and interests outside of medicine. Reflective writing is a strategy that appears to hold great promise, as studies have demonstrated its benefits in improving empathy and providing an appropriate avenue for emotional catharsis. Medical schools are encouraged to consider implementing pass-fail grading and creating more transparency in addressing the realities of what clinical training does to physicians through discussion about the formal and hidden curricula of medical school.

Future research is needed to evaluate the success of these strategies in reducing the incidence of compassion fatigue in physicians.

The Impact of Radiation and Chemotherapy on Outcomes in Two-Staged Implant-Based Breast Reconstruction

Avinash Jayaraman

Mentor: Nicholas T. Haddock MD & Sumeet S. Teotia MD,
Department of Plastic Surgery
Collaborators: Savannah N. Hampton, Lekshmi A. Nair, & Christopher Venutolo

Introduction: Treatments for breast cancer include neoadjuvant chemotherapy (NACT), adjuvant chemotherapy (ACT), radiation (RAD), and combinations of these therapies. Many of these patients will choose to pursue implant-based breast reconstruction concurrently with these treatments. Effects of these therapies on the outcomes of implant-based reconstructions have not been studied fully.
Methods: From January 2012 to December 2016 two surgeons performed 542 breast reconstructions using tissue expanders (TE). The number of patients choosing implants who completed reconstruction was n=272. They were split into 8 groups based on therapy received: Group 1 (no treatment, n=139), Group 2 (NACT, n=32), Group 3 (ACT, n=44), Group 4 (NACT+ACT, n=14), Group 5 (NACT+RAD, n=17), Group 6 (ACT+RAD, n=13), Group 7 (RAD, n=12), Group 8 (ACT+NACT+RAD, n=1). Group 8 was excluded because it had only one patient, leaving n=271. ANOVA (df between groups = 6, df within groups = 264) and Tukey HSD were run to compare differences in the percentages of patients with infections requiring IV antibiotics, necrosis requiring operation, seroma, and TE exchange for new TE. Numbers of different surgeries were also counted.
Results: Comorbidities and age were equivalent across groups, except for Group 7 (55.7 yr) and Group 4 (41.6 yr), p=.03. There were no significant differences in percentages of patients with infection requiring IV antibiotics (p=.32), necrosis requiring operation (p=.09), or seroma (p=.40). For patients who required replacement of TE with another TE due to complication, only Group 1 (1.4%) vs Group 6 (15.4%) had a significant difference, p=.04.
There were no differences in the mean numbers of complication-related surgeries before implant placement (p=.07), complication-related surgeries after implant placement (p=.30), revision surgeries (p=.98), or total surgeries (p=.29). There were no significant differences in the percentages of patients receiving at least one complication-related surgery before implant (p=.16), at least one complication-related surgery after implant (p=.85), or at least one revision surgery (p=.94).
Conclusion: Among most patients who choose to undergo implant-based reconstruction in an academic practice, we found no significant differences in complication rates, mean numbers of surgeries per patient, and percentages of patients undergoing different types of surgeries. Although patients with combined adjuvant chemotherapy and radiation had a higher rate of TE exchange for new TE due to complication, the rates of other complications and surgeries were comparable. Given these results, practice trends in breast reconstruction can remain cautiously optimistic for patients choosing implant-based reconstruction concurrently with cancer treatments.

Multiple Free Flap Breast Reconstruction: An Institutional Experience When 1 Flap for 1 Side is Not Enough

Avinash Jayaraman

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Min-Jeong Cho MD

Background: As breast reconstructive microsurgeons increase their armamentarium of flaps with experience, need for stacked and multiple flaps may generate an improved aesthetic outcome. We present our institutional experience of using single vs. multiple free flap breast reconstruction.

Methods: 769 flaps were performed on 427 patients from 2010-2016 by two senior surgeons (SST, NTH) at a university hospital. 197 of those flaps were either: Stacked PAP flaps, 4-flap (Bilateral PAP+Bilateral DIEP flap), or Double-pedicle DIEP/SIEA flaps. 595 flaps were either: unilateral or bilateral DIEP or PAP flap. Demographic, patient co-morbidities, and flap complications were compared between the 2 groups.

Results: Out of 427 patients, 322 patients (595 breast reconstructions) underwent single DIEP or PAP flap while 105 patients (197 flaps in 113 breasts) underwent multiple free flaps. The multiple flap patient group had statistically lower BMI, longer procedure time, had smaller flaps, and higher DVT compared to single flap group. There were no statistical differences in the rates of flap loss (1.3% in multiple flaps versus 1.7% in single flap), wound complication, hematoma, and pulmonary embolism.

Conclusion: Based on our large experience, stacked/multiple flaps are safe and preferred in properly selected patients with low volume from a unilateral donor site, exhibiting similar complications and success rates compared to single-flap patients. The ability to use multiple donor sites may represent a unique phase of innovation in breast microvascular surgery, with high patient tolerance and aesthetically pleasing results geared towards reconstructing breasts in all subunits. We present our indications and approach for successful multiple flap reconstruction.

Unilateral vs. Bilateral Implant-Based Reconstruction: Complications and Numbers of Surgeries to Completion

Avinash Jayaraman

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Purpose: Reconstruction patients with unilateral breast cancer may opt to undergo bilateral prophylactic mastectomies. Studies comparing outcomes between bilateral and unilateral implant reconstruction patients are lacking.

Methods: From January 2012 to December 2016 two surgeons at one hospital performed 542 tissue expander-based breast reconstructions. There were 232 bilateral implant patients and 39 unilateral implant patients who completed the reconstruction process. T-tests were performed to compare the rates of infection requiring IV antibiotics, necrosis requiring operation, seromas, and tissue expander exchange due to complication. Mean numbers of surgeries, percentage of unilateral patients undergoing latissimus flap procedures, and percentage of unilateral patients undergoing surgery on the contralateral breast were also calculated.

Results: Comorbidities and age were equivalent between groups. There were no significant differences in percentages of patients with infection requiring IV antibiotics (p=.32), necrosis requiring operation (p=.81), seroma (p=.66), or tissue expander exchange due to complication (p=.86). There were no significant differences in the mean numbers of complication-related surgeries before implant (p=.65), complication-related surgeries after implant (p=.12), revision surgeries (p=.30), or total surgeries (p=.27). Percentages of patients undergoing at least one complication-related surgery before implant (p=.86), at least one complication-related surgery after implant (p=.61), and at least one revision surgery (p=.70) were equivalent. Additionally, 24% of unilateral patients underwent latissimus flap surgery and 74% of unilateral patients had surgery on the contralateral breast.

Conclusion: Unilateral patients can expect to face similar complication rates and surgical stresses when compared to bilateral implant- based reconstructions. Therefore, a bilateral prophylactic mastectomy can be safely considered when desired by patients.

Assessing Laboratory Values in Transgender Women Treated with Cross-Sex Hormone Therapy

Rhoda Jiao

Mentor: Nora Gimpel MD, Department of Family & Community Medicine
Collaborators: Emily Gao BSA, Patti Pagels MPAS, & Jeffrey SoRelle MD

Objective: Laboratory results are used to guide clinical decision making, and reference ranges are developed to describe the variation seen in healthy individuals so that pathologic values can be distinguished from normal physiologic values. For transgender individuals taking cross-sex hormone therapy, changes in physiology can be expected to accompany the masculinization or feminization induced by the treatment, but the effect of these changes on laboratory tests is not well defined and cannot be easily predicted. This study seeks to evaluate the response of common laboratory tests to hormone replacement therapy (HRT) in transgender women (male-to-female, MTF), comparing to natal male and female populations.

Methods: We conducted a retrospective chart review for MTF and FTM (female-to-male) patients before initiating HRT and MTF patients after receiving HRT for 6-24 months at transgender-specific clinics in an urban county hospital (Parkland Hospital, Dallas, TX) and a community clinic (Resource Center, Dallas, TX). We collected demographic information, medical history, and laboratory values for CBCs, complete metabolic panels, liver function tests, lipids, and hormone levels taken throughout their course of treatment.

Results: In one of the largest studies of laboratory values in transgender patients, patient charts of 120 transgender women were reviewed, with a median age of 27 years. After initiating HRT, MTF patients showed a significantly increased estrogen and decreased testosterone ($p<0.0001$). Changes in hematologic parameters included decreases in red blood cell count, hemoglobin, and hematocrit ($p<0.0001$) and an increase in platelets ($p=0.0001$). Changes in metabolic parameters include decreases in sodium, creatinine, and alkaline phosphatase ($p<0.0001$).

Conclusion: Better understanding the extent of expected changes in laboratory values can enable clinicians to more accurately evaluate the effects of HRT and choose appropriate treatments for individuals in the transgender population.

Incidence, Risk Factors and Outcomes among Patients with Venous Thromboembolic Events in the Early Post-Transplant Period during the Lung Allocation Score Era.

Rohan Kanade

Mentor: Amit Banga MD, Department of Internal Medicine- Pulmonary
Collaborators: Lauren Smith, Luke Mahan, Srinivas Bollineni, Jessica Mullins, Vaidehi Kaza, Manish Mohanka, Michael Wait, & Fernando Torres

Introduction: With the introduction of lung allocation score (LAS), progressively sicker patients are undergoing lung transplantation (LT) which has the potential to increase the risk of venous thromboembolic (VTE) events during the post-transplant period. This study was conducted to determine the incidence and risk factors for early VTE and its association with 2 year survival.

Methods: All adult patients with single, double or heart LT at the UT Southwestern Medical Center between 2012-14 (n=193) were included in the study. Various demographic, clinical and laboratory variables before and after LT were recorded. Development of any VTE events during the first 30 days after LT was the primary outcome variable. Variables were compared among patients with and without VTE to identify risk factors for VTE. Survival at two years was compared among patients with and without VTE.

Results: Overall incidence of VTE during the first 30 days after LT was 28.5% (n=55) among which, majority were upper extremity thrombosis (48/55). Pulmonary embolism was uncommon (n=3). Majority events (78%) were diagnosed with in the first 15 days after LT. Pre-transplant history of hyperlipidemia (adjusted OR, 95%CI: 2.8, 1.1-7.2; p=0.03) and use of anticoagulants (AC) for at least 72 hours (4.1, 1.8-9.5; p=0.001) were independently associated with a reduced risk of VTE. On the other hand, development of primary graft dysfunction at 72 hours (1.6, 1.1-2.4; p=0.009) and use of >3 central catheters during the post-transplant period (25.9, 2-342.1; p=0.013) were independently associated with increased risk of VTE. Development of VTE was associated with increased risk of 2 year mortality (log rank p=0.036, see figure).

Conclusion: A significant proportion of patients develop VTE early after LT and it is associated with worse survival at 2 yr post-LT. Despite majority being catheter related VTE, the use of AC appears to be protective. Protective effect of hyperlipidemia may be linked to statin use among these patients which needs to be investigated further in future studies.

Potential Impact of the Site-Neutral Payment Policy on Regions and Hospitals with Differential LTAC Utilization: A National Study of Medicare Beneficiaries

Benjamin Kirby

Mentor: Anil Makam MD, MAS, Department of Internal Medicine

Background: Long-term acute care hospitals (LTAC) are the fastest growing and most expensive post-acute care provider. Due to rising LTAC use, beginning in 2018 the site-neutral payment (SNP) policy will reduce reimbursement for Medicare beneficiaries without prolonged mechanical ventilation or ICU stay prior to transfer because these patients are considered less likely to require this level of care. Since half of the variation in LTAC use is explained by differences between regions and hospitals, we sought to examine whether regions and hospitals with more LTAC use transfer patients with lower severity and complexity of illness and how they may be affected by SNP policy.
Methods: We conducted a retrospective cohort study using 5% national Medicare data. We included adults ≥65 years with Medicare parts A and B who were transferred from an acute care hospital to an LTAC in 2012. We compared characteristics of patients transferred to LTACs by tertile of regional LTAC supply (beds per 100,000 residents) and by propensity-score matched hospitals with low (< median of 1.26%) versus high (≥ 1.26%) historical LTAC transfer rates.
Results: We included 3,898 and 1,673 older adults transferred to an LTAC for our regional and hospital-level analyses respectively. For both comparisons, patient demographics, prior healthcare utilization, comorbidities, and functional impairment were similar. Compared to regions with the lowest LTAC supply, patients in the highest supply regions had shorter hospital length of stay (5 fewer days), lower intensity diagnoses (DRG weight of 1.91 vs 3.06), fewer intensive therapies (11% vs 27% for tracheostomy), and were more likely to meet SNP criteria (47% vs. 30%; $p<0.01$ for all comparisons). Similarly, patients from high LTAC transfer hospitals were less sick compared to patients from matched low transfer hospitals. However, the magnitudes of the differences were smaller than those between regions (i.e. length of stay difference of 2 days; 14% vs 22% for tracheostomy; 43% vs. 36% for SNP). Patients who meet SNP criteria were otherwise similar between regions and hospitals with different LTAC supply and use.
Conclusion: High regional LTAC supply and LTAC transfer hospitals were associated with greater LTAC care for patients with lower severity and complexity of illness. The SNP policy will impact LTACs in high supply regions more than those accepting patients from high transfer hospitals, however nearly a third of patients in low supply regions and from low transfer hospitals will also be affected. Further research is warranted to study the impact of SNP policy on LTAC access and how this relates to patient outcomes, recovery, and costs.

Evaluating Telerentinal Imaging Detection of Diabetic Retinopathy in the Dallas County Hospital System

Jessica Lee

Mentor: Lilian Nguyen MD, Department of Ophthalmology

Introduction: Diabetes mellitus (DM) is one of the most prevalent diseases in the United States. Approximately one third of patients with diabetes have diabetic retinopathy, which is the leading cause of new cases of blindness among US adults ages 20-76 years. The American Academy of Ophthalmology recommends annual screenings for diabetic retinopathy beginning 5 years after the onset of DM1 and beginning promptly after diagnosis of DM2. Only 60% of people with DM have yearly screenings, which consist of a dilated eye exam. Nonmydriatic digital retinal imaging with remote image interpretation (teleretinal screening) is a promising new technology because it allows rapid retinal imaging without dilation of the pupil in primary care clinics, with the potential to reach more patients, detect disease earlier, facilitate compliance, and reduce barriers to specialized eye care.

Purpose: To evaluate the effectiveness of a diabetic retinopathy teleretinal screening program and follow-up in a high-risk population.

Methods: Diabetic patients who had teleretinal imaging performed between April 1, 2013 and March 10, 2017 at the community-based primary care clinics of the Parkland Memorial Hospital system were identified through Epic electronic health records. Patient age, sex, screening date and interpretation, completed follow-up eye clinic appointments, and ocular diagnoses were recorded.

Results: 1155 patient charts were reviewed and of those, 399 (34.5%) underwent the screening and had a teleretinal image obtained. Of those screened, 279 (69.9%) were referred to optometry or ophthalmology clinic, and 114 (40.8%) were later seen in clinic. The most common reasons for referral were a yellow report without a specific interpretation (83.5%), mild or moderate non-proliferative diabetic retinopathy (6.8%), nerve-related disease (4.7%), and red report without a specific interpretation (2.2%). The percentage of agreement for all diagnoses was 76.3% and total sensitivity was 72.7%. Diabetic retinopathy was detected for the first time through teleretinal screening in 44 patients (11.0%).

Conclusions: Teleretinal screening is a useful method for detecting diabetic retinopathy. However improvements need to be made in follow up of ordered screenings, image quality and interpretation, and referral follow-up.

Driving Practices of Visually Impaired Patients: Preliminary Findings

Jessica Lee

Mentor: Chan Nguyen MD, PhD, Department of Ophthalmology
Collaborators: Brittany Ransom MD, Peter Clark MD, & Bryan Gallerson BS

Introduction: Motor vehicle accidents (MVAs) are the fourth leading cause of death in the United States. In 2016 there were a total of 55,797 crashes with 315 fatalities in Dallas County. In our clinics, we often encounter patients with impaired vision who are driving despite not meeting the visual acuity requirements for obtaining a Texas driver's license. In Texas there are no requirements for driving restrictions based on visual field or peripheral vision. Furthermore, Texas is not one of the six U.S. states in which physicians are required to report cognitively or medically impaired patients to the Department of Motor Vehicles, and Texas ophthalmologists legally cannot revoke a patient's driver's license. Better understanding of the driving practices of visually impaired patients will improve both patient and public safety.
Purpose: The results of this study are intended to increase physician awareness of visually impaired patients' driving habits in order to better counsel patients, as well as increase patients' awareness of their driving habits in relation to their vision.
Methods: In this ongoing prospective study, 167 patients in the UT Southwestern and Parkland Hospital System Ophthalmology clinics were surveyed regarding their ocular history, awareness of visual impairments, driving status, driving habits, driver's license status, and motor vehicle accident history. Inclusion of subjects was based on best corrected visual acuity of less than 20/40 in each eye during screening examination or defects on confrontational visual field testing. The surveys were then reviewed to establish trends amongst our subjects.
Results: Of the 42.2% of surveyed patients who indicated they currently drive, 54.3% drive frequently, 25.7% drive sometimes, and 20% drive rarely. Of those driving, a significant majority (70%) said they restrict their driving patterns due to their vision (e.g. no nighttime driving) and a majority of the drivers (54.3%) have restrictions on their driver's license. 12.9% of patients indicated they had been in a MVA in which they were at fault as the driver, although only 14.3% attributed their MVAs to poor vision. The average number of MVAs in which they were at fault was 1.1. However 34.2% said they had been in a MVA in which they were not at fault as the driver.
Conclusions: It is concerning that many vision-impaired patients continue to drive frequently. However the large percentage of patients who restrict their driving patterns due their vision shows that they recognize their impairment as a real safety risk, which is reassuring.

Presentation, Treatment, and Outcomes of Patients Diagnosed with uViens Secondary to Ocular Taxoplasmosis

Min Hyung Lee

Mentor: Jennifer Cao MD, Department of Ophthalmology
Collaborator: Yuguang He MD

Introduction: Toxoplasma gondii is an obligate intracellular parasite that is can infiltrate the retina, choroid, and anterior chambers. Its cysts can cause lesions in the retina that can lead to temporary or permanent vision loss. Most physicians prescribe combinations of systemic antibiotics and intravitreal antibiotics to reduce inflammation, scarring, and as a prophylaxis against recurrent infections. However, treatment of ocular toxoplasmosis is an area of debate, with no established standard of care or consensus amongst health providers.
The purpose of this study is to determine whether the addition of intravitreal to systemic antibiotic therapy decreases time to improvement and/or visual outcome.

Methods: This study is a retrospective analysis of treatment regiments and outcomes for patients treated for acute active toxoplasma chorioretinitis UT Southwestern Aston Clinic or Parkland Ophthalmology clinic. The main outcome measured was time to improvement. The secondary outcomes were visual acuity, time to recurrence, and adverse events. Statistically analyses were performed using unpaired and paired t-tests were to compare treatment outcomes of intravitreal injections in combination with systemic antibiotic treatment versus systemic antibiotic treatment only.

Results: A total of 17 patients met inclusion criteria. All 17 cases (100%) were unilateral. There were 7 (41%) females and 10 (59%) males. 14 patients (82%) underwent testing for toxoplasma antibodies and were positive; three were not tested but were diagnosed based on classic exam findings. Eleven (65%) patients were treated with only oral antibiotics, and 6 (35%) were treated with oral antibiotics and intravitreal clindamycin. There was a statistically significant decrease in time to improvement in patients who received intravitreal clindamycin (9.17±2.79 days) compared to patients who received only systemic antibiotics (16.5±8.73 days). The observed P value was 0.034.

Maxillary Growth and Speech Outcomes Following Staged Palatoplasty: A Single-Center Approach

Kurt Leininger

Mentor: James Smartt MD, Department of Plastic Surgery
Collaborators: Jake Alford BS, Richard Ha MD, & Steve Byrd, MD

Introduction: Cleft lip and palate are the most common craniofacial abnormalities in children. However, timing and staging of cleft palate repair remain controversial. Timing of palate repair depends on balancing the speech benefits of early repair with the improved maxillofacial growth of late palate repair. Both single stage and two staged palatoplasty have been proposed for optimizing growth and speech, each to varying success. In this study, we reviewed outcomes of the staged approach at a single center.
Methods: A retrospective chart review was performed for all patients who underwent staged palatoplasty for cleft palate at Children's Medical Center in Dallas between 2006-2012. All patients in the study underwent intra-velar veloplasty at 3 to 6 months and hard palate repair at 18 months. Exclusion criteria included patients undergoing single stage repair, initial treatment at an outside center, secondary surgery at an outside center, and inadequate follow up. 61 patients were eligible for final inclusion. Speech outcomes were evaluated based on Pittsburgh Weighted Speech Scores (PWSS) and rates of secondary operations indicated for correction of VPI. PWSS were collected after completion of staged palatoplasty, postoperatively after any surgical correction of VPI, and at latest available patient follow up. Maxillary growth outcomes were evaluated by rates of oronasal fistula, reoperation indicated for palate repair, Angle class malocclusion, and LeFort I advancement procedures.
Results: For the entire cohort, 26% of patients were determined to have clinical VPI. 28% required corrective VPI surgery. 11% were determined to have residual VPI refractory to corrective surgery. 31% were found to have a persistent oronasal fistula, with 30% requiring surgery. 50% had class III malocclusion. At the time of review, no patients required LeFort I advancement procedures. There were no significant differences when including syndromic patients.
Compared to patient with CLP, patients with isolated CP had higher rates of clinical VPI (33% vs 24%), oronasal fistula (34% to 20%), and class III occlusion (54% to 27%). Compared to patient with complete CP, patients with incomplete CP had higher rates of clinical VPI (36% vs 23%) lower rates of oronasal fistula (14% to 36%), and lower rates of class III occlusion (29% to 53%). Compared to patients with UCLP, patients with bilateral CLP had higher rates of clinical VPI (43% vs 15%), oronasal fistula (57% to 27%), and class III occlusion (64% to 48%).
Conclusion: In our cohort of 61 patients, speech and growth outcomes after staged palatoplasty are similar to what has been previously reported in the literature. Despite the lack of consensus on the appropriate surgical treatment for CP and a trend towards single stage palatoplasty, our data strongly suggests that staged palatoplasty is still a valuable surgical approach to the patient with cleft palate.

Utility of the Clinical Dementia Rating Scale in Detecting Autopsy-Proven Dementia in Patients with Low Education

Chengxi Li

Mentor: Munro Cullum PhD, ABPP, Department of Psychology
Collaborators: Christian LoBue PhD & Jeff Schaffert MS

Background and Objective: The Clinical Dementia Rating scale (CDR) assesses impairment in 6 cognitive and functional domains to stage cognitive decline and dementia. Each domain is scored from 0 (no impairment) to 3 (severe impairment), and these scores are summed to a sum-of-boxes (CDR-SB) score ranging from 0 to 18. The CDR-SB score has shown high reliability in staging dementia. However, no studies have determined whether the CDR remains effective when applied to less-educated individuals. This study investigated the sensitivity and specificity of the CDR-SB score in detecting dementia associated with autopsy-proven AD in patients with less than 12 years of education.
Hypothesis: Using the validated CDR-SB cut score for mild dementia (4.5) to detect autopsy-proven AD in this population was hypothesized to yield low sensitivity and/or specificity (i.e. <70%). A higher cut score was expected to be required for optimal sensitivity/specificity.
Methods: Participants from the National Alzheimer's Coordinating Center Uniform Data Set with less than 12 years of education were divided into two cohorts (autopsy-proven AD and normal age-related brain changes), matched for age and sex, and excluded if other major neurological diseases were present (n = 34; 17 per cohort). Receiver Operating Characteristic (ROC) analysis was performed to determine the sensitivity and specificity of CDR-SB scores in discriminating between subjects with autopsy-proven AD and those with normal age-related brain changes.
Results: The validated CDR-SB cut score for mild dementia (4.5) correctly classified 10 of 17 patients with normal age-related brain changes and 16 of 17 with autopsy-proven AD (sensitivity = .941, specificity = .588). These data reflect the unexpected presence of 7 patients with clinically-diagnosed dementia in the normal cohort and 1 patient without clinically-diagnosed dementia in the autopsy-proven AD cohort. The optimal cut score was found to be 9.5, correctly classifying 15 of 17 patients with normal age-related brain changes and 14 of 17 with autopsy-proven AD (sensitivity = .824, specificity = .882).
Discussion: In patients with <12 years of education, the optimal CDR-SB cut score to detect AD-related dementia (9.5) is in a range associated with moderate dementia, which may be too high for clinical utility. Although numerous neurological syndromes were excluded, factors other than education may have contributed to high CDR-SB scores in the comparison group. Further research in larger samples is needed to validate the results of this preliminary investigation.

Increased Rates of Readmission, Reoperatioin, and Mortality Following Open Reduction and Internal Fixation of Ankle Fractures are Associated with Diabetes Mellitus

Jennifer Liu

Mentor: Dane Wukich MD, Department of Orthopaedic Surgery
Collaborator: Junho Ahn

Background: Ankle fractures are amongst the most common type of fracture injury in adults with an annual incidence of 187 fractures per 100,000 people in the United States. Previous groups have shown that diabetes mellitus is associated with a myriad of complications – including infection, malunion, and impaired wound healing – following open reduction internal fixation (ORIF) surgery for ankle fractures. However, to our knowledge there has not been a large-scale nationwide study on the rate of readmission, reoperation, and mortality associated with diabetes. The purpose of this study was to calculate the increased risk and odds ratios for 30-day postoperative readmission, reoperation, and mortality after ankle fracture ORIF.
Methods: Patients who underwent ORIF for ankle fractures from 2006 to 2015 were identified in the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database using Current Procedural Terminology codes. 30-day postoperative unplanned readmission, unplanned reoperation, and mortality rates were compared in 2,044 patients with diabetes and 15,420 patients without diabetes. Odds ratios (OR) with a 95% confidence interval (CI) were calculated for each parameter.
Results: Out of 17,464 patients that underwent ORIF for ankle fractures, the mean age was 47.9 +/- 17.7 years, obesity (BMI ≥30 kg/m²) was documented in 38.6% of cases, and diabetes that was severe enough to require oral, non-insulin, or insulin therapy was documented in 11.7% of cases. We found that patients with diabetes mellitus had a 2.87 times increased risk of unplanned readmission (OR, 2.87; 95% CI, 2.07-6.23; p = 0.0001) and 3.30 increased risk of unplanned reoperation (OR, 3.30; 95% CI, 2.35-7.54; p = 0.0001) related to the principal operative procedure. Additionally, patients with diabetes had a 2.01 increased risk of mortality (OR, 2.01; 95% CI, 1.08-3.62; p = 0.0377) within 30 days post operation.
Conclusions: Presence of diabetes mellitus increases the risk of unplanned readmission, unplanned reoperation, and mortality after ankle fracture ORIF. Further research in optimization of perioperative care for diabetic patients is crucial to reducing rates of complications and readmission. Large clinical databases including ACS-NSQIP should endeavor to collect more parameters on diabetic patients to facilitate these studies.

Solid Organ Transplantation (SOT) & Data Mining: Bloodstream Infections (BSI) Have a Significant Impact on One-Year Survival, and qSOFA ≥2 Predicts 30-Day Mortality.

Terrence Liu

Mentor: Ricardo La Hoz MD, Department of Internal Medicine
Collaborators: Donglu Xie MS, Beverley Adams-Huet MS, Jade Le MD, Christina Yek MS, Dipti Ranganathan MS, Robert W. Haley MD, FSHEA, & David Greenberg MD, FIDSA

Background: We created a retrospective and prospective database of SOT recipients using innovative data mining tools. This study describing the epidemiology of BSI in SOT serves as a proof of concept of such techniques in clinical research.
Methods: The design of the study was a retrospective single center cohort study. Data mining tools were used to extract information from the electronic medical record and merged it with data from the Scientific Registry of Transplant Recipients (SRTR) national database. First SOT from 1/1/2010-12/31/2015 were included. Charts of subjects with positive blood cultures were manually reviewed and adjudicated using CDC/NHSN and SCCM/ESICM criteria. The 1-year cumulative incidence was calculated using the Kaplan-Meier method. Cox proportional hazards models were used to identify risk factors for BSI and 1 year mortality. BSI was analyzed as a time-dependent covariate in the mortality model. Fisher's exact test and Chi-Square were used to identify risk factors for 30-day mortality and multidrug resistant organisms (MDRO).
Results: 917 SOT recipients met inclusion criteria. 75 patients experienced at least one BSI. The cumulative incidence was 8.4% (95% CI 6.8-10.4). The onset of the 1st BSI episode was: 30 episodes (40%) < 1 month, 33 (44%) 1-6 months and 12 (16%) > 6 months. The most common pathogens were Klebsiella sp. (16%), Vancomycin-resistant E. faecium (12%), E. Coli (12%), CoNS (12%), and Candida sp. (9.3%). Nineteen isolates (25%) were identified as MDRO; the risk of MDRO was highest < 1 month compared to 1-6 and > 6 months (44.8 vs. 12.1 vs. 16.7 p=0.01). The most common source of BSI was CLABSI (29%). In multivariable analysis the risk of BSI was associated with organ type (HR [95%CI] = Multiorgan 3.5 [1.1-11.6], liver 2.5 [1.1-5.4], heart 2.4 [1.1-5.1]) and acquisition of a BSI was associated with a higher 1-year mortality (HR=8.7 [5.1- 14.7]). In univariable analysis, a polymicrobial BSI (14.7 vs. 57.1% p=0.02), qSOFA ≥ 2 (0.0 vs. 25.5% p=0.02) and septic shock (3.9 vs. 52.2% p<0.001) were associated with an increased risk of death at 30 days.
Conclusion: A BSI significantly impacts the 1-year survival of SOT recipients. A qSOFA ≥ 2 can be used at the bedside to identify patients at increased risk for death. Additionally this study illustrates the potential of data mining tools to study infectious complications.

Sleep Quality Disturbance in Patients with Osteoarthritis of the Hip

Jack Riley Martinez

Mentor: Joel Wells MD, MPH, Department of Orthopaedic Surgery

Background: Osteoarthritis is a common chronic condition with the hip being frequently affected. The disease symptoms manifest as pain and loss of function, leading to a diminished quality of life and affecting activities of daily living. Sleep has been well documented as a vital element of our daily function, overall health and well-being. Patients with hip arthritis often report nocturnal pain as the disease progresses yet little is known how hip arthritis affects sleep quality.

Objective: The purpose of this paper was to assess how hip arthritis affects sleep quality.

Methods: Patients that presented to the senior surgeon with a chief complaint of hip pain and were diagnosed with hip arthritis by clinical and radiographic evaluation, were reviewed. Patients completed patient reported outcome scores: WOMAC, Hip Outcome Score and the Modified Harris Hip Score, in addition to the Pittsburgh Sleep Quality Index

Results: A total of 106 adult patients were analyzed, with an average age of 63 years and 59% female. All patients had a Tonnis Grade of two or three. The average ASA Physical Status Classification was 1.94 and 20% had a diagnoses of obstructive sleep apnea. Patients with lower WOMAC scores showed significant sleep quality reduction: Symptoms ($p=0.00036$), Stiffness ($p=0.011$), Pain ($p=0.00080$), Function of daily living ($p=0.00040$), Quality of life ($p=0.000013$) and Function in sports and recreational activities ($p=0.12$). Secondly, patients with lower Hip Outcome Scores, showed a significant decrease in sleep quality ($p=0.0069$). Lastly, a worse Modified Harris Hip Score was significant for a diminished sleep quality ($p=0.0023$).

Conclusion: This study shows that patients with hip osteoarthritis, who endorse a more symptomatic and painful hip, are susceptible to reduced sleep quality. This provides evidence for patients with a higher level of pain to be additionally evaluated for sleep disturbance to ensure they are receiving comprehensive care.

Subcutaneous Fat Thickness as a Risk Factor for Return to OR in Total Knee Arthroplasties

Ajay Narayanan
Pooja Prabhakar

Mentor: Kenneth Estrera MD, Department of Orthopedics
Collaborator: Matthew Swann MD

Background: Total knee arthroplasty (TKA) is an increasingly common procedure performed in the United States. Post-operative complications after TKA, such as unplanned returns to the operating room for an infection or implant failure, can result in high morbidity for patients. Presently, several patient factors are used to identify higher risk patients prior to surgery, such as body mass index (BMI), although these have limitations. However, the amount of subcutaneous tissue at the surgical site affords an objective evaluation of the degree of surgical exposure required at the time of the operation. Increased amounts of subcutaneous tissue may lead to a prolonged dissection, which may increase rates of infection, which could result in unplanned returns to the OR. The aim of this study is to determine whether subcutaneous fat thickness as measured on pre-operative radiographs is a risk factor for return to OR for TKAs.
Methods: This is an IRB-approved, retrospective review of a series of 596 total knee arthroplasties at two hospitals in a large urban setting over a 2-year period (2010-2011). Pre-operative AP knee radiographs were reviewed and measurements were taken using the same imaging software. A medial knee adipose tissue (MKAT) score was calculated using the ratio of the total width of the distal femoral metaphysis perpendicular to the anatomic axis and the width of the medial adipose tissue along the same plane. Additional variables recorded included gender, ethnicity, diagnosis, laterality, pre-operative BMI, date of last follow-up, return to OR, revision, and deceased status.
Results: 596 patients were included in the analysis, of which 24 patients (4%) had an unplanned return to the OR within 3 months of the index operation. In this group, the average pre-op BMI was 32.9 and the average MKAT score was 0.46. The MKAT score was not significantly associated with return to OR
($p = 0.15$). Age and BMI were the only variables that were significantly associated with return to OR ($p = 0.01$ and 0.005).
Conclusions: MKAT scores on pre-operative AP knee radiographs are not significantly associated with increased return to OR after primary TKA. The limitations of this study include its retrospective nature and small study population. Although we did not find a statistically significant difference between the two groups, this data is useful in that it can assist with surgical decision making. This data suggests that patients with increased subcutaneous tissue about the knee are not at increased risk of return to the OR after primary TKA.

How Do Open Distal Tibia Fractures Differ From Open Tibial Shaft Fractures?

Ivy Nguyen

Mentor: Christine A. Ho MD, Department of Orthopaedics

Purpose: The purpose of this study was to compare a cohort of open distal tibia fractures to open tibial shaft fractures in regards to injury severity, method of fixation, and outcomes.
Methods: This is a retrospective review of 49 open distal tibia fractures (group D) with a mean age of 8.7years and 56 open tibia shaft fractures (group S) with a mean age of 8.6years, treated from 2007-May2017 at a single level 1 pediatric trauma center. Mann Whitney test was used to compare means between groups.
Results: Extremely high energy trauma (ATV, GSW, vehicular collision, lawnmower, crush, fall >8 feet) was the mechanism of injury in 90% (44/49) in group D and 77% (43/56) in group S (p=0.119). Mean AIS lower extremity scores were significantly higher in group S compared to group D (2.74 vs 2.55, p=0.043), as were mean Injury Severity Scores (13.10 vs 9.36, p=0.053). There were more Gustilo type II fractures in group S (42% vs. 35%), and more Gustilo type III fractures in group D (51% vs 39%) which trended towards significance (p=0.0622). 88% (43/49) of open distal tibia fractures had ipsilateral fibular involvement, compared to 71% (40/56) of open tibial shaft fractures (p=0.054). Tibial fixation methods were statistically different between the 2 groups (Table 1, p=0.0377), but incidence of fibular fixation was not statistically different (group D-12% vs group S-5%, p=0.4348). While surgical time and fluoroscopy times were not significantly different between the two groups, group D had longer mean length of hospitalization (8.44vs6.36 days, p=0.006), mean duration of immobilization (135vs100 days, p=0.033), and longer mean time to full weight bearing (77vs40 days, p=0.006). Rate of hardware removal (group D-49%, group S-52%) and radiographic angulation at final follow-up were not statistically significantly different between the two groups (p>0.05). Mean time to union was prolonged for both groups (178 days group D-178 days, group S-139 days, p=0.231).
Conclusions: Open distal tibia fractures are significant for extremely high energy of injury. Alternate methods of fixation for open distal tibia fractures such as external fixation, K wires, and ORIF are more likely to be utilized than flexible intramedullary nailing. Open distal tibia fractures have longer hospital stays, immobilization, and time to full weightbearing but radiographic outcomes and time to union are comparable.
Significance: This study increases awareness of the difference in injury severity, fixation methods, and clinical course between open distal tibia and open tibial shaft fractures.

Cataract Surgery and Intraocular Pressure (IOP)

Sahar Noorani

Mentor: Karanjit Kooner MD, Department of Ophthalmology
Collaborators: Ted Deng, Alex Yang, Munsif AlSalem MD, Wayne Bowman MD, Jess Whitson MD, Preston Blomquist MD, Vinod Mootha MD, Beverley Adams-Huet MS, & Xilong Li PhD

Purpose: The effect of cataract surgery on IOP in patients with glaucoma is not well understood. We sought to analyze fluctuations in IOP in controls, glaucoma suspects, and patients with mild, moderate, and severe primary open angle glaucoma (POAG) undergoing cataract surgery in a well-diversified population.

Methods: In an IRB-approved retrospective study, 236 controls (Group A), 37 glaucoma suspects (Group B), and 96 patients with POAG (mild, moderate, severe; Groups C-E) were recruited. One eye was randomly selected per patient. Exclusion criteria included: <18 years, secondary glaucoma, one functional eye, or follow-up <3 months. Data collected included age, race, gender, glaucoma family history, CCT, axial length (AXL), anterior chamber depth (ACD), lens thickness (LT), IOP, and visual acuity (VA). Post-operative IOP and VA were determined at several intervals. Linear trends over groups A-E were made with a Jonckheere-Terpstra test. $\chi 2$ analyses were used to evaluate differences between groups A-E. Wilcoxon Rank-Sum test was used to evaluate postoperative changes. Multiple linear regression was used to evaluate predictors of IOP change at 1 year.

Results: IOP reduction at 1 year in groups A-E were 8.6%, 8.1%, 10.8%, 18.3%, and 9.1%, respectively. Medications at 1 year did not change significantly. In POAG eyes, higher pre-op IOP and more medications were predictive of a higher reduction in IOP at 1 year (β= -0.62, -1.60; $p<0.05$). In control eyes, higher pre-op IOP and higher CCT were predictive of more IOP reduction at 1 year (β= -0.53, -0.02; $p<0.05$).

Discussion: In this population, all groups showed reduction of IOP after cataract surgery. Among the glaucoma groups, severe glaucoma patients had the lowest reduction of IOP (9.1%), most probably due to reduced outflow facility. However, the medication load stayed unchanged in all groups. In the control group, pre-op IOP and thicker CCT determined post-op IOP reduction.

Conclusion: IOP reduction one year after cataract surgery in glaucomatous eyes is dependent on higher pre-op IOP and increased glaucoma medications. In non-glaucomatous eyes, higher pre-op IOP and thick CCT determine the degree of post-operative IOP reduction.

Characterizing Hepatitis C Virus Related Lymphomas in Active and Cleared Viral Infections

Paul Parisot

Mentor: Mamta Jain MD, MPH, Department of Infectious Disease

Introduction: Chronic hepatitis C virus (HCV) infection is a major source of liver cirrhosis and hepatocellular carcinoma. In recent decades clinical data has shown the association between HCV and Non-Hodgkin's Lymphoma (NHL) as well. Prior studies have shown that patients with low-grade lymphomas and HCV infection may be treated successfully with antiviral treatments alone versus being treated with chemotherapy. Our goals were to characterize the type and severity of HCV related lymphomas in our patient population as well as understand the effect of having active infection compared to a previously cleared HCV infection.
Methods: This study was a retrospective chart review of patients at Parkland and UT Southwestern who had a history of HCV confirmed by positive antibody and active lymphoma. Baseline characteristics of initial HCV infection (including genotype, HCV viral load) and lymphoma statuses were collected. The patients' lymphoma and HCV history were then analyzed longitudinally to evaluate treatments and patient outcomes. 41 patients had active HCV at the time of lymphoma diagnosis (HCV RNA-positive), while 7 had a resolved infection (HCV RNA negative).
Results: Patients with active HCV at time of diagnosis most often had Diffuse Large B-Cell lymphoma (DLBCL) (52%) followed by Mantle Cell Lymphoma (17%). At diagnosis, these patients mostly had high stage lymphoma (68%), had extranodal involvement (62.5%), 46% had bone marrow involvement, nearly half (48%) had B-Symptoms, and 70% were treated initially with chemotherapy. Those with resolved HCV most often had DLBCL (57%), 50% had high stage disease, 50% had extranodal involvement, with 20% having bone marrow involvement, and only 33% having B-symptoms. Of those, 43% were treated with chemotherapy as their primary treatment.
Discussion: Overall our patient population had a greater proportion of high stage and aggressive lymphomas necessitating chemotherapy treatments. Despite previous reports of antivirals successfully treating low-grade lymphomas, it is unlikely that most patients with HCV related lymphoma would benefit from such treatments alone, as many had aggressive disease from the outset and required chemotherapy. When evaluating our cohort of 7 patients who had cleared HCV infections prior to lymphoma diagnosis, we noticed a trend of lower stage lymphomas, less extranodal involvement, less bone marrow involvement, and fewer instances of B symptoms. Our current sample size however does not allow us to draw definitive conclusions. The future goal is to expand our sample size in order to evaluate if differences exist.

Safety of Tumor Necrosis Factor Inhibitor Use in Patients with Concomitant Malignancy

Hiep Steve Phan

Mentor: Linda Feagins MD, AGAF, Department of Internal Medicine
Collaborator: Rick Weideman Pharm.D

Background: Tumor necrosis factor (TNF) inhibitors are considered contraindicated in patients with a history of malignancy. However, data to support this notion is limited. We hypothesize TNF inhibitors can be used safely in patients with chronic inflammatory diseases, like IBD, who have concomitant malignancy or develop malignancy while on these agents.

Methods: Retrospective chart review performed 1996-2015 at our local VA. Cases and controls (matched 2:1 for cancer type) were identified using pharmacy and pathology databases and then charts manually reviewed. Cases were patients with inflammatory disease including inflammatory bowel disease (IBD), rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis or spondyloarthropathy (SpA), concomitant malignancy, and TNF inhibitor use while controls were patients with inflammatory disease, concomitant malignancy but no TNF inhibitor use. Data was collected for cases and controls including survival at 1-yr, 2-yrs, 5-yrs after malignancy diagnosis and end of study time points.

Results: 36 cases (3 IBD, 22 RA, 5 PsA, 2 SpA, 1 IBD+SpA, 3 psoriasis) and 70 controls (6 IBD, 44 RA, 12 psoriasis, 6 PsA, 2 SpA) were identified. Age, cancer stage at diagnosis, and Charlson comorbidity index was not significantly different between cases and controls.Treatments with other immunosuppressives at diagnosis were not significantly different between the cases and controls and cancer specific therapies were similar between cases and controls. For cases, survival at 1-yr, 2-yrs, 5-yrs and at end of study follow-ups were 32 (89%), 31(86%), 29 (81%) and 24 (64%), respectively compared to 63 (90%), 61 (87%), 51 (73%) and 45 (64%) for the control group (p=NS for all time points). For cases, recurrence rates at 1-yr, 2-yrs, 5-yrs and at end of study follow-ups were 3 (8%), 5 (14%), 6 (17%), and 8 (22%), respectively compared to 2 (3%), 5 (7%), 7 (10%), 9 (13%) for the control group (p=NS for all time points).

Conclusion: Survival rates and cancer recurrence after a malignancy is diagnosed in patients with inflammatory diseases treated with TNF inhibitors are not different from similar patients not treated with TNF inhibitors. This preliminary data suggests that TNF inhibitors should not be withheld for fear of worsening survival or tumor recurrence after diagnosis with a malignancy if the agent is needed for adequate inflammatory disease control.

Patient Portals: A Potential Source of Disparities in Oncology Practice

Kelvin Pho

Mentor: David Gerber MD, Department of Internal Medicine
Collaborators: Simon Craddock Lee PhD, MPH, Rong Lu PhD, & Donglu Xie, PhD

Background: Healthcare institutions nationwide have implemented patient portal systems. These platforms provide patients with real-time access to their electronic health records, thereby increasing transparency in the medical system. Through this technology, patients may also manage appointments, review test results, provide clinical updates, and pose questions of their providers. Patient portals may have particular considerations in oncology practice, where medical acuity and intensity of data flow may exceed those of most other conditions. To date, how cancer patients receive information through electronic portals has not been well described.
Methods: We identified patients with a cancer diagnosis treated at the UT Southwestern Harold C. Simmons Comprehensive Cancer who enrolled in MyChart, the institution's electronic patient portal (2007-2016). We recorded dates and times that test (laboratory and radiology) results were released and viewed. Associations between patient characteristics and result viewing were determined using ordinal logistic regression and linear mixed effect models.
Results: A total of 19,434 patients who accessed MyChart between January 1, 2007, and December 31, 2016, were included. The median time interval between test result release and viewing on the patient portal decreased significantly from a peak of 17.0 hours in 2009 to 12.4 hours in 2016 (P=0.026). However, after peaking at 61% in 2012, the proportion of released test results ever viewed decreased to 38% in 2015 (P=0.049). This decline coincided with an increase in the volume of released test results. Black, male, and older patients were less likely to view test results, and did so less quickly. At peak result viewing rates in 2012, 47% of results were viewed by black patients, compared to 62% for white patients and 72% for Asian patients (P<0.001). Median time to view results was 15 hours for non-black patients, compared to almost 37 hours for black patients (P<0.001).
Conclusions: Over time, the volume of clinical data released through electronic patient portals has increased substantially. While time between result release and patient viewing has steadily declined, the proportion of released results that are ever viewed by patients has fallen. This unexpected trend may reflect patient information overload and user fatigue. Furthermore, the likelihood and timeliness of result reviewing differ substantially according to patient age, race, and sex, suggesting that electronic communication has varying efficacy across populations. To create best practices for this growing technology, further study of patient use and preferences is warranted.

The Impact of Transversus Abdominis Plane Block on Patients in an Enhanced Recovery Bariatric Surgery Pathway

Sydney Pinch

Mentor: Sara Henessy MD, Department of Surgery
Collaborators: Cynthia Wang MD & Gloria Cheng MD

Introduction: A transversus abdominis plane (TAP) block is an ultrasound-guided injection of local anesthetic in the plane between the internal oblique and transversus abdominis muscles to interrupt innervation to the abdominal skin, muscles, and parietal peritoneum. Currently there are incongruent findings on the benefit of this regional anesthetic to surgical patients, particularly the obese population. We hypothesized the addition of a TAP block in an enhanced recovery pathway (ERAS) for bariatric patients would decrease opioid use and shorten hospital length of stay.
Methods: A retrospective review of all patients who underwent bariatric surgery at a single institution from January to December 2016 was performed. Patients were identified as: no TAP block (No TAP), TAP blocks that were performed after induction either pre-surgery (Pre-TAP) or post-surgery (Post-TAP). The primary outcome was time to first opioid (min) and total morphine (mg) equivalents in PACU. The secondary outcome was hospital length of stay (LOS) and 30-day readmission. Patients were compared on pre-operative and intraoperative factors by univariate analysis using Wilcoxon rank sum, Chi-square, and Fisher's exact tests where appropriate.
Results: A total of 129 bariatric procedures were performed of which 105 underwent a TAP block; with 81 Pre-TAP block patients and 23 Post-TAP block patients. In PACU, average morphine (mg) equivalent was calculated as No TAP of 10.4 ± 8.1, Pre-TAP of 7.4 ± 7.3, Post-TAP of 7.7 ± 8.2mg ($p= 0.33$). There was no significant difference in time (min) to first opioid in PACU (No TAP 29.1 ± 20.9, Pre-TAP 26.8 ± 21.8, Post-TAP 26.1 ± 18.4). Length of stay (days) was not significantly different between No TAP, Pre-TAP and Post-TAP block patients (3.0 ± 2.2 vs. 2.6 ± 5.4 vs. 3.2 ± 5.9). Finally, there was also no difference in 30-day readmission between No-TAP, Pre-TAP and Post-TAP patients (5.9% vs. 4.9% vs. 0%).
Conclusion: The addition of a TAP block to our ERAS pathway for bariatric patients failed to reduce use of opioids or decrease hospital length of stay and 30 day readmission. The failure to show any significant differences may be attributed to our small study population. However, in the TAP block group opioid use was lower by 3mg and with nearly half the number of readmissions. The potential for a positive impact with minimal risk of a TAP block is an important reason to continue to prospectively study the impact of TAP blocks on bariatric surgery patients.

A Prospective Non-Invasive Study Characterizing Facial Skin Aging and Quantifying Sun Damage

Sydney Pinch

Mentor: Jeffrey Kenkel MD, FACS & Fritz Barton MD, FACS,
Department of Plastic Surgery
Collaborator: Xingchen Li

Facial skin undergoes both intrinsic and extrinsic processes that culminate in features of facial aging. To accurately characterize intrinsic facial aging by decade of life, we must correct for sun damage, one of the most significant factors contributing to extrinsic aging. This study aimed to establish a clinical correlation between the subjective Glogau Photodamage Scale and the objective metric scale of the VISIA Complexion Analysis System (Canfield Scientific, Fairfield, NJ). The goal is to eliminate intra- and inter-observer variability when assessing sun damage in an individual subject.

Of the 124 subjects who were enrolled, 109 subjects were deemed eligible for the study. Eligible subjects' ages ranged from 22 to 81, with a median of 54 years, and the ratio of female to male subjects was 3 to 1, which is consistent with the gender demographic seen in a facial aesthetic plastic surgery clinic.

Clinical photography was obtained for each subjects' face and was individually assessed by three independent reviewers. Each photo was rated from 1 to 4, with 4 being the most severe, for spots and wrinkles on the face. These ratings were averaged and rounded to give a final "Glogau spots" and "Glogau wrinkles" score for each subject.

The VISIA spots score strongly correlated with the Glogau spots score. Each group was found to be significantly different than one another (p-value < 0.05) with the exception of Glogau spots groups 1 and 2 using Analysis of Variance (ANOVA). Similarly, the VISIA wrinkles score strongly correlated with the Glogau wrinkles score. Each group was found to be significantly different than one another (p-value < 0.05) using ANOVA. When comparing under eye VISIA wrinkles score with age, there was a positive, exponential correlation with an R^2 value of 0.4845. When the males and females were separated, this correlation increased to an R^2 value of 0.5378 for the males and to an R^2 value of 0.4343 for the females.

This study was able to correlate a subjective scale to objective, non-invasive measurements. In addition, this study suggests that aging is an exponential process, and the way in which males and females age is notably different.

Current Trends of Pilonidal Diesease at a Veteran Administration Hospital: A 12-Year Experience

Oswaldo Renteria

Mentor: Sergio Huerta MD, FACS, Department of Surgery
Collaborators: Holly Cunningham MD, Varun Jain MD, Mohammed Sultany MD, & Maria Ruiz BS

Introduction: Pilonidal Disease (PD) affects primarily young, adult men with highest prevalence in the second decade of life. The Veteran Administration (VA) patient population is composed primarily of older men. The aim of this study was to investigate the incidence and outcomes of veteran patients that underwent surgical treatment of PD.

Methods: A retrospective review of all patients treated for pilonidal Disease at the VA North Texas Health Care System over the past 12 years (2005-2017) was performed. Univariate and multivariate analysis was undertaken to analyze outcomes.

Results: 122 patients were identified with mean age 41.4 ± 17.6 years-old; male = 95.0%; White = 73.8%; BMI = 33.1 ± 7.5 kg/m^2; ASA III-IV = 30.3%. Recurrence and complication rates were 10.7% and 22.1%, respectively. Most patients (65.6%) underwent excision with primary closure. The most common complications were wound dehiscence and infection. No comorbid condition was identified as an independent predictor of complications or recurrence. Longer operative times (OR 1.037, 95% CI: 1.001– 1.075) and older age (OR 1.037, 95% CI: 1.000 – 1.076) emerged as the only independent predictors for complications. No significant difference in complications and recurrence was determined between primary closure and secondary intention healing. There was no difference in the complication rate between colorectal surgeons and general surgeons performing the surgery (p = 0.13), but recurrence was higher for colorectal surgeons (28.0%) compared to general surgeons (6.2%; p = 0.005).

Conclusion: The incidence of PD in Veteran patients is low, but it is associated with substantial morbidity and recurrence. In this small cohort, no comorbid factor revealed to be a predictor for complications or recurrence, but longer operative time and age are predictors of complications. Surgical outcomes were similar to previous studies, however, no surgical method was identified as an optimal standard and management of Veteran patients presenting with PD should be individualized.

Quantifying Differences in Femoral Head and Neck Asphericity in the Common Hip Conditions of Femoroacetabular Impingement and Hip Instability versus Controls Using Radial 3DCT Imaging and Volumetric Segmentation

Natalie Schauwecker

Mentor: Avneesh Chhabra MD, Department of Radiology
Collaborators: Chenelle Slepicka BS, Riham Dessouky MD, Joel Wells MD, & Yin Xi PhD

Aim: 3DCT analysis of femoral head and bump anatomy in quantifying pathology in common hip conditions of FAI and hip dysplasia versus controls.
Material and Methods: Consecutive patients who obtained 3DCT imaging for hip dysplasia or FAI were compared to asymptomatic controls. Alpha angles on radial CT and 3D volumetric femoral head and bump segmentations were obtained by two readers. Inter- and intra-patient comparisons were performed including inter-reader and ROC analyses.

Results: 25 FAI patients, 16 hip dysplasia patients and 38 controls were analyzed. FAI and dysplasia patients exhibited higher alpha angles and higher bump-head volume ratios than the controls ($p<0.05$). FAI patients exhibited larger bumps than dysplasia and the contralateral hips of FAI were also different than the controls. Alpha angle at 2 o'clock and bump to head ratio showed the highest area under the curve for cases versus controls. The reader reliability was better for volumetric segmentation (ICC= 0.35-0.84) as compared to the alpha angles (ICC= 0.11-0.44).

Conclusion: Patients with both FAI and dysplasia exhibit different femoral head anatomy than the asymptomatic controls. Volumetric segmentation of femoral head and bump is more reliable and better demonstrates the bilateral femoral head anatomy differences of cases versus controls

The Association Between Tobacco Use and Intradialytic Hemodynamics in Hemodialysis Patients

Mark Sonderman

Mentor: Peter Van Buren MD, MSCS, Department of Internal Medicine- Nephrology

Background: Intradialytic hypotension is known to be associated with increased mortality in maintenance hemodialysis patients. Smoking is a modifiable risk factor that is more commonly seen in patients with large decreases in intradialytic blood pressure as compared to any other intradialytic blood pressure pattern. However, the mechanisms of this association are unknown. We sought to explore the effect of lifetime tobacco use on vascular hemodynamics during dialysis.
Methods: We used impedance cardiography to measure total peripheral resistance index (TPRI) in 65 hypertensive hemodialysis patients. Additionally, we obtained blood pressure measurements before, during, and after midweek hemodialysis treatments. We then compared intradialytic hemodynamic changes between never smokers (n=35) and current or former smokers (n=30) using simple and multivariable linear regression.
Results: The mean change in TPRI during a single dialysis session was -438 dynes/sec/cm2/m2 in smokers and -105 dynes/sec/cm2/m2 in non-smokers (p=0.1). The intradialytic systolic blood pressure nadir was 115 mmHg in smokers and 123 mmHg in non-smokers (p=0.1). In multivariable linear regression controlling for diabetes, ultrafiltration rate, and other factors associated with intradialytic blood pressure changes, smoking was independently associated with lower nadir SBP (p=0.01) with a trend to also have a greater decrease in TPRI (p=0.08).
Conclusions: Hemodialysis patients with a smoking history demonstrate a tendency towards a greater reduction in intradialytic TPRI as compared to non-smokers, with a significant independent association for lower nadir SBP. Smoking status should be aggressively ascertained in dialysis patients with significant intradialytic hypotension, but further studies are required to determine the effect of smoking cessation on intradialytic hemodynamics.

Results of Multivariate Regression Analysis for Delta TPRI and Intradialytic BP Nadir

	Delta TPRI		Intradialytic BP Nadir	
	β	p-value	β	p-value
Smoker	-461	0.08	-13.3	0.01
Pre SBP	-13.3	0.07	-	-
Delta ADMA	-1060	0.2	-10.8	0.5
Diabetes	-332	0.2	-8.54	0.1
Calcium Phosphate Product	-7.61	0.4	-	-
UF Rate	-9.00	0.8	-0.539	0.5
Delta ET-1	-	-	-10.9	0.07

Alemtuzumab is an Effective Tertiary Treatment vs. Single Agent Gemcitabine and Pralatrexate for Refactory Sezary Syndrome a Systematic Review

Jacob Stewart

Mentor: Heather Wickless MD, MPH, Department of Dermatology

Introduction & Objectives: The efficacy of alemtuzumab for the treatment of refractory Sezary syndrome (SS) versus other third-line agents such as pralatrexate and gemcitabine is poorly characterized. To elucidate the effectiveness of alemtuzumab versus other third-line options for the treatment of refractory SS, we conducted a systematic review of existing data.
Materials & Methods: We performed a literature review in March of 2017 using Ovid-MEDLINE® and OVID-EMBASE®. The following key words were searched: "Sezary Syndrome" crossed-referenced with "alemtuzumab" or "gemcitabine" or "pralatrexate." We excluded all duplicates and all articles not written in English or involving human subjects. We included full-text prospective studies, retrospective analyses, case series, and case reports evaluating single agents alemtuzumab, gemcitabine, and pralatrexate for the treatment of SS and mycosis fungoides (MF).
Results: 433 articles met our search criteria. After individual review, 22 publications fulfilled our inclusion criteria (total n=323 patients, 96 with SS and 154 with MF). The 13 publications examining alemtuzumab included 72 patients with SS and 26 with MF. Across all of these studies, alemtuzumab was found to be significantly more effective to produce a clinical response in patients with SS (overall response rate 82%, complete response rate 39%) than patients with MF (overall response rate 31%, complete response rate 8%). Alemtuzumab was also found to be more effective than gemcitabine or pralatrexate in treating patients with SS, while gemcitabine was more effective in treating MF. When examining the effectiveness of alemtuzumab with different routes of administration (intravenous vs. subcutaneous) or dosing (10 mg vs. 30 mg), no significant differences were found. Adverse events were more with alemtuzumab but route of administration and dose were significant. There was a lower incidence of lymphopenia and other serious adverse events in the patients treated with subcutaneous (15%, compared to intravenous 61%) and lower-dose alemtuzumab regimens (5%, compared to the high-dose 54%).
Conclusions: This review clarifies the role of alemtuzumab as a preferred third-line treatment agent for refractory SS compared to other third line agents and affirms the role of alemtuzumab as an effective agent for SS but ineffective for MF. Additionally, low-dose regimens and subcutaneous administration of alemtuzumab may lead to an improved safety profile, while maintaining effectiveness. Future studies investigating the treatment of refractory SS are warranted.

Subbasal Nerve Plexus Changes in T2DM Correlate with Tear Levels of IGFBP3.

Whitney Stuard

Mentor: Danielle Robertson OD, PhD, Department of Ophthalmology
Collaborators: Bryan Gallerson BS & Rossela Titone PhD

Introduction: Changes in the corneal subbasal nerve plexus have been reported in patients with Type 2 Diabetes Mellitus (T2DM) and suggest that these changes may provide an early, surrogate marker for the onset of peripheral neuropathy. Increasing studies are investigating the use of tear film biomarkers that correlate with corneal nerve changes in diabetic disease. Our prior studies have demonstrated that the primary insulin-like growth factor (IGF)-1 binding protein, IGF-binding protein-3 (IGFBP-3), is elevated in the diabetic tear film. This study examined tear levels of IGFBP-3 in basal tears of patients with T2DM compared to age, sex, and obesity-matched controls; and assessed the relationship between tear levels of IGFBP-3 with morphological changes in the subbasal nerve plexus and corneal epithelial cells.
Methods: This study is a single visit, cross-sectional study comparing two groups: 1) T2DM and 2) healthy controls. A physician diagnosis of T2DM was required for inclusion in this test group. Groups were matched for age, sex, and obesity status. Each volunteer underwent serology testing for Hemoglobin A1c and high sensitivity C-reactive protein, completed the ocular surface disease index (OSDI) questionnaire and clinical measurements of dry eye, assessment of anthropometric parameters, tear analysis, in vivo confocal microscopy to assess corneal nerve morphology, corneal sensitivity testing, and ocular coherence tomography to assess the retinal nerve fiber layer and macula. Anthropometric measurements were used to calculate BMI and waist to height ratio. Human tears were collected for the analysis of tear levels of IGFBP-3 using an IGFBP-3 Quantikine ELISA kit (R&D Systems, Minneapolis, MN). Confocal data was analyzed using ImageJ and MetaMorph Software.
Results: A total of 40 participants were included in this study. There were no differences in corneal sensitivity or dry eye parameters between groups. IGFBP-3 levels in tears of T2DM patients were 3.5 times higher than controls ($P<0.05$). HbA1c was not correlated to IGFBP-3 ($R=0.318$, $P=0.062$). Tear levels of IGFBP-3 were correlated with nerve fiber length ($R=0.522$ $P=0.001$) and nerve branch density ($R=0.481$ $P=0.003$). IGFBP-3 was more tightly correlated with nerve changes than HbA1c. Consistent with our animal models, there was a decrease in corneal basal epithelial cell density in T2DM compared to controls ($P=0.04$).
Discussion: This study demonstrates that IGFBP-3 is higher in patients with T2DM. These studies further suggest that tear levels of IGFBP-3 may be a novel biomarker for monitoring ocular damage in diabetes. Further studies are needed to stratify tear levels of IGFBP-3 with severity of disease.

Creating a Tool to Access the Quality of Life of Patients with Localized Scleroderma: Impact of Surgery on Patient Perception of Facial Features

Nikhitha Thrikutam

Mentor: Christopher Derderian MD, Department of Plastic Surgery
Collaborators: Celia Heppner PsyD & Heidi Jacobe MD

Background: Localized scleroderma (LSc), also called morphea, is a broad diagnosis that encompasses a spectrum of patient presentations due to a localized autoimmune dysfunction. LSc is different from systemic sclerosis in that it almost only involves the skin and underlying muscle/vasculature with absence of internal organ involvement. The disease course typically involves a period of active inflammation that then "burns out" resulting in severe facial asymmetry due to atrophic changes in the skin and subcutaneous tissue, hyperpigmentation of the skin, skeletal asymmetry and alopecia. Treatment of LSc frequently utilizes surgical procedures such as fat grafting and free tissue transfer to restore facial symmetry. No studies to date have addressed the quality of life of patients with LSc nor have studies characterized the aspects of LSc that are most distressing to patients.

Purpose: The purpose of this study is to create a quality of life (QOL) assessment tool to understand the progression of facial deformities commonly seen with LSc, disease course (timing of treatment in relation to "burn out" phase), the physical features that are most distressing to patients with LSc, and to understand how patient quality of life is impacted by surgical intervention. Creating a QOL measure to understand patients' perceptions regarding their appearance and disease progression will help clinicians understand which aspects of facial deformity are most important to address to enhance patients' QOL. This will also allow a threshold of asymmetry that impacts QOL to be determined that will aid in timing intervention.

Methods: The LSc QOL assessment tool has been created by combining pre-existing plastic surgery/dermatology QOL questions and by the addition of novel questions by members of this group. Pre-existing questions have been pulled from plastic surgery FACE-Q tool, plastic surgery CLEFT-Q tool, PedsQL general/rheumatology modules, and Morphea in Adults and Children (MAC) assessment tool. Questions included in the assessment tools evaluate aspects of facial appearance and functionality commonly affected by LSc including patient perception of facial features, functionality, facial volume, skin discoloration, presence of alopecia, and any associated conditions.

Conclusion: The creation of an assessment tool to understand the impact of LSc on patient QOL can greatly help clinicians determine the appropriate course of treatment for patients with LSc.

What Happens to Older Adults Transferred to LTACs?

Thu Tran

Mentor: Anil Makam MD, MAS, Department of Internal Medicine
Collaborators: Oanh Nguyen MD, MAS, Michael Miller MS, Lei Xuan PhD, & Ethan Halm, MD, MPH

Background: Long-term acute care hospitals (LTACs), which were originally designed for the chronic critically ill requiring prolonged mechanical ventilation, provide care for patients with other advanced illness and intensive care needs, including intravenous antibiotics and complex wound care. Hospitalized older adults are increasingly being transferred to LTACs for post-acute care but little is known about the natural history and how many potentially achieve meaningful recovery.
Methods: We conducted a retrospective cohort study using national 5% Medicare data from 2009-2013. We included all adults ≥65 years with Medicare Parts A and B who were transferred from an acute care hospital to an LTAC on the same or next day and no previous LTAC use in the prior year. The main outcomes and analyses were mortality using Kaplan-Meier estimates and the cumulative incidence of achieving a 60-day consecutive window of time without a hospitalization or an institutional post-acute care encounter as a proxy of meaningful recovery using the Fine and Grey method to account for competing risks of death and hospice enrollment.
Results: We included 14,072 older hospitalized adults subsequently transferred to an LTAC. The 1- and 5-year mortality were 55% and 82% respectively. Comparatively, older adults hospitalized for ≤7 days but not transferred to an LTAC had 1- and 5-year mortality of 16% and 44%; and those hospitalized for >14 days and not transferred to an LTAC had 1- and 5-year mortality of 45% and 69% (log rank $p<0.01$). Following LTAC discharge, only half (48%) of older adults achieved a 60-day period without inpatient or post-acute care use (proxy of meaningful recovery) with the cumulative incidence curve plateauing at approximately 12 months, meaning few recovered beyond this point in time.
Conclusions: The mortality rate for hospitalized older adults transferred to an LTAC is extremely high, and is comparable to having advanced cancer (e.g., prostate, lung, colon). Furthermore, only half of patients experience a minimal definition of short-term meaningful recovery. If recovery does not occur within the first year, patients are unlikely to ever recover. In light of this poor prognosis, patients, families, and physicians should begin goals of care discussions earlier on in the clinical course, avoid interventions with sufficiently long time horizons to benefit (i.e., cancer screening, osteoporosis management, and intensive diabetes management), and consider shifting from aggressive treatment to palliative care.

A Retrospective Analysis of Pancreatic Resection Outcomes at a Pediatric Tertiary Care Center

Wei Shan Tsui

Mentor: Joseph Murphy MD, Department of Pediatric Surgery
Collaborator: Shani Harvey MD

Background: Pediatric patients with pancreatic diseases rarely require surgical resection. Our goal is to gain a better understanding of the indications for and outcomes of pancreatic resection surgeries, which are distal pancreatectomy, pancreaticoduodenectomy (Whipple), lateral pancreaticojejunostomy (Puestow Procedure), central pancreatectomy, and total pancreatectomy in the pediatric population.
Methods: With IRB approval, we performed a retrospective review of data of pediatric patients (<18 years) who underwent pancreas operative procedures at Children's Medical Center in Dallas, Texas from January 2005 to July 2017. Data such as demographics, overall mortality, post-op diagnosis, intra-operative complications, post-operative morbidity are collected for all five procedures.
Results: A total of 39 patients were identified to have undergone pancreatic resection surgery. Data for all five procedures are summarized in Table 1. There were no intra-operative complications. Short term post-op complications include pancreatic leak (n=4), acute pancreatitis(n=1), fistula (n=1), abscess (n=3). Both fistula and abscess required IR drainage. 4 patients were readmitted for pancreatitis episode few months after surgery. Only few developed long-term complications, which were pancreatic insufficiency (n=3), and diabetes (n=2). One Whipple patient had metastatic SPT to the liver, and was re-admitted to the hospital for a liver transplant. One patient had a recurrence of the desmoid tumor.
Conclusion: Based on the findings, all five pancreatic resection surgeries show very low mortality rate and relatively low morbidity rate. Therefore, surgical resection of the pancreas is a rare but safe and effective surgical intervention in the treatment of pediatric pancreatic pathology.

Procedure	Gender	Avg Age (yr)	Avg Procedure Length (hr)	Avg LOS (day)	Avg Blood loss (mL)	No. of transfusion	TPN	Avg ICU Days	Avg # of Readmissions per patient (days)	Pathology
Distal Pancreatectomy	11 M, 13 F	13	3.96 (range 1.9-10.52)	10	196	3	7	4 (range 0-13)	1 (range 0-7)	SPT (9), trauma (9), PNET(2), IPMN (1), desmoid (2), Castleman's (1)
Whipple	3M, 5F	10	6.3 (range 3.91-11.1)	13	267	1	3	3 (range 0-5)	2 (range 0-2)	SPT (4), JXG (1), trauma (1), pancreatic islet cell (1), neuroendocrine ampullary tumor(1)
Puestow	3M,2 F	13	3.4 (range 2.65-4.55)	6	80	0	0	0	1	Chronic Pancreatitis (5)
Central Pancreatectomy	1F	13	5.33	10	100	0	0	0	1	SPT
Total Pancreatectomy	1F	6	8.68	29	1300	1	1	8	3	pancreatoblastoma

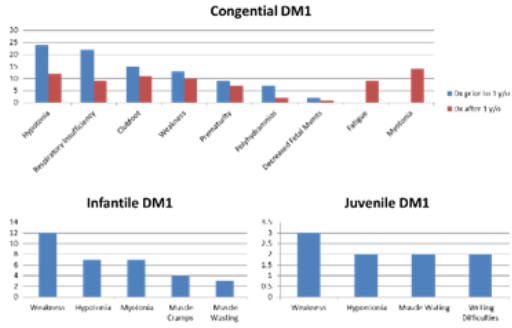
Figure 1 Demographics, surgical, pathology, follow-up data for patients who underwent pancreatic resection (N=39)

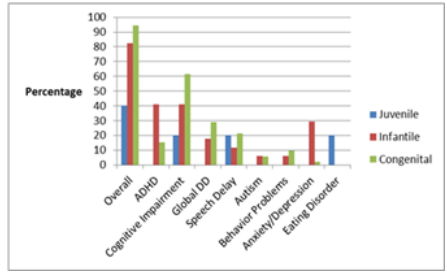
Congenital and Juvenile Myotonic Dystrophy

Natasha Varughese

Mentor: Diana Castro MD, Department of Pediatrics & Neurology
Collaborators: Susan Iannacconne MD & Mat Stokes MD

Myotonic dystrophy type 1 (DM1) is a multi-system autosomal dominant disorder inherited by a trinucleotide (CTG) repeat expansion on the DMPK (dystrophia myotonica protein kinase) gene on chromosome 19q13.3. The adult-onset form is well-characterized, but the disease may also manifest at birth or any age during childhood. Treatment is currently limited to supportive care, but recent developments in small molecule therapies are expected to enter clinical trials in upcoming years, requiring a baseline for the natural progression of this disease on current therapies. This retrospective chart review examined the clinical course and genetics of 74 DM1 patients treated at Children's Medical Center neuromuscular clinics between 1990 and 2017, subdivided by age of symptom onset into congenital (<1 month), infantile (1 month-10 years) and juvenile (10-20 years) forms. From a neuromuscular standpoint, all categories tended to present with weakness, hypotonia, and muscle wasting. Congenital patients also frequently had respiratory difficulty and clubfoot, while childhood-onset patients often had cataracts, cardiac arrhythmias, and GI complaints. The majority of patients had cognitive impairment or other psychiatric manifestations of the disease. The GI and cardiac complaints correlated well with previous guidelines for care of this disease. No patients had thyroid disease or diabetes, unlike their adult counterparts. The onset of the disease correlated roughly with the number of CTG repeats. Results of this study were comparable to a recent retrospective chart review of pediatric DM1 in France, validating our findings. The data strongly suggest that cognitive/behavioral evaluation should be standard of care in this patient population, as well as annual cardiac follow-up and early GI intervention.





Disparities in Follow-up Care for Young Adults with Type 1 Diabetes and Impact on Glycemic Control

Hannah Viroslav

Mentor: Shavani Agarwal MD, MPH, Department of Endocrinology at The University of Pennsylvania
Collaborators: Jesse Hsu, Judith Long, & Jack Eiel

Background: Only 13% of young adults (YA) with type 1 diabetes (T1D), nationally, achieve the American Diabetes Association glycemic target of <7%. YA with T1D of low socioeconomic status (SES) have incrementally worse glycemic control, due to personal, social, and healthcare system factors. Engagement in regular diabetes follow-up has been shown to be beneficial in preventing acute complications and improving glycemic control in YA with T1D, but little is known whether disparities exist in follow-up care based on SES. The purpose of this study was to a) compare differences in diabetes follow-up patterns between low and higher SES YA with T1D and b) evaluate the impact of interrupted care on glycemic control.
Methods: 203 YA with T1D, 18-30 years, were recruited from the adult diabetes clinic at the University of Pennsylvania. Demographic, clinical, and follow-up visit data were extracted from medical charts. Low SES individuals were defined as having medical coverage under a federal or state-sponsored (public) insurance plan while higher SES individuals were defined as having coverage under a commercial (private) insurance plan. Baseline demographic and clinical characteristics were compared by insurance type. Multilevel mixed effects logistic and linear regression models were used to compare differences in follow-up rates and the impact on glycemic control. All models were adjusted for age, sex, race, diabetes duration, insulin regimen, and time in diabetes provider's care.
Results: 203 participants were included for analysis. Mean age was 23.5 years and 55% were female. Forty-six percent (n=95) had public insurance and 53% (n=108) had private insurance; 42% (n=40) of publicly insured YA were black compared to 11% (n=12) of privately insured YA. Mean diabetes duration was 11.8 years with no significant difference between publicly and privately insured. Mean overall HbA1c was 9.0%, with mean HbA1c 9.9% for publicly insured and 8.8% for privately insured ($p<0.001$). Publicly insured YA were 1.5 times more likely to no show for scheduled visits (OR=1.53, $p=0.009$) and were 2.3 times more likely to be lost to diabetes follow-up after 6 months (OR 2.3, $p<0.001$), compared to privately insured YA. Glycemic control worsened substantially with each successive no show to a scheduled visit (HbA1c +1.10% per no show, $p=0.001$).
Conclusion: Low SES YA with T1D are less likely to consistently follow up in diabetes care, are more likely to be completely lost to diabetes care after 6 months, and have worse glycemic control as a result of inconsistent follow-up, compared to higher SES YA. Further research needs to explore why disparities in follow-up exist, as well as innovative healthcare delivery modalities.

Cocaine Use and General Anesthesia:
A Prospective Study of Cardiovascular Effects

Kevin Vu

Mentor: Tiffany Moon MD, Department of Anesthesiology
Collaborators: Agnes Kim, Rachael Lu, Eve Sharifi

Background: Cocaine usage in surgical patients is a concern for many hospitals. In large urban hospitals, up to 1.0% of elective surgical patients and 38% of major trauma victims may test positive for cocaine preoperatively. Previous retrospective studies have shown that cocaine positive surgical patients do NOT have an increase in adverse hemodynamic events, length of stay, or mortality compared to cocaine negative controls. However, prospective studies evaluating the impact of recent cocaine use on intraoperative hemodynamics plus inflammatory and cardiac biomarkers have not been undertaken.
Hypothesis: This study will test the hypothesis that patients who have 1) a preoperative toxicity screen that demonstrates recent cocaine use, are 2) undergoing non-emergent surgery with general anesthesia, and 3) have normal vital signs will NOT experience an increased incidence of adverse perioperative cardiovascular events compared to similar control patients with a negative toxicity screen.
Methods: This prospective study stratifies patients into cocaine positive and cocaine negative cohorts. Cocaine positive patients were non-toxic with positive urine toxicology, while cocaine negative patients were defined as having used cocaine in the past year with negative urine toxicology. Anesthesia protocol was standardized. The primary outcomes measured were intraoperative hemodynamics and vasoactive medications, with a secondary outcome of pre- vs. post-operative troponin levels.
Data: Preliminary outcome analysis of cocaine positive (N = 59) and cocaine negative patients (N = 40) are shown in the table below:

Primary Hemodynamic Outcomes as Percentage of Anesthesia Duration		
Hemodynamic Events	Cocaine Negative	Cocaine Positive
MAP <55 or >110 mmHG	1.8	1.4
HR <50 or >100 BPM	3.2	2.7
Perioperative Change in Troponin T		
No Change	95.0%	100.0%
Decrease	2.5%	0.0%
Increase	2.5%	0.0%

Conclusion: The data supports the idea that positive cocaine urine toxicology tests in non-toxic individuals are not associated with increased cardiovascular instability or troponin elevation. Thus, automatic cancellation of these patients may not be warranted. Further analysis of the full study cohort (N = 300) will be completed at the end of 2017.

Comparisons of Anterior Vaginal Wall Indentation Parameters in Age-Matched Control and Prolapse Patients using an Operator Independent Artificial Finger

Connie Wang

Mentor: Philippe Zimmern MD, Department of Urology
Collaborators: Panos Shiakolas PhD, Michael Abraham BS, & Christopher Abrego BS

Goal: To compare reaction forces of the human anterior vaginal wall in control (C) and prolapsed (P) women in response to pressure applied at different angles of indentation through an automated artificial finger equipped with a distal sensor.

Methods: Following IRB approval, a tripod-mounted, artificial finger equipped with a calibrated, piezoresistive sensor at its tip and automated by NI LabView 2015 software for motion control via an actuator was used to create anterior vaginal wall deformations at 10, 15 and 20 degree angles. Age-matched women in the C and P groups were compared. All measurements were performed in the supine position in the operating room, with patients under general anesthesia prior to the start of the operation and after the bladder was drained. Each deformation included a 1 second upwards indentation, a 1 second maintenance "hold", and a 1 second return of the fingertip to the baseline. Measurements were done in triplicate with a 3 second interval between each deformation sequence. Real-time voltages, equivalent to reaction forces sensed by the sensor during each indentation, were modeled as function of motion profiles and analyzed in Excel. The motion profile of each indentation was used to calculate baseline voltage, amplitude change over the 1 second interval of upwards indentation, and slope of the upwards indentation curve in its median 0.5 second range.

Results: Five women of similar age group (mean 64, 51-73) were studied in each group. A significant difference was observed between all degrees of indentation in baseline voltage in P and C groups ($p<0.05$). At 10 and 20 degrees of indentation, there was a significant difference in amplitude change between P and C groups, while there was a significant difference in slope of indentation at 15 degrees between P and C groups.

Conclusion: The biomechanical properties of the human anterior vaginal wall can be objectively determined by a new device resembling the human finger. This mounted, free-standing artificial finger can apply a predictable and reproducible deformation to the anterior vaginal wall to compare the indentation properties of vaginal tissue in prolapsed and non-prolapsed conditions.

Complications: Evolution of Presenting Symptoms Over Time

Connie Wang

Mentor: Philippe Zimmern MD, Department of Urology
Collaborator: Alana L. Christie MS

Introduction: To study the evolution of type of presenting symptoms after mid-urethral sling (MUS) placement relative to the time course between this placement and subsequent removal for complication(s).

Methods: An IRB-approved, prospectively maintained database of women who underwent synthetic sling removal (SSR) was retrospectively reviewed. Demographic information, history of chronic pain syndromes and recurrent urinary tract infection (RUTI), history of prior anti-incontinence surgeries and prolapse repairs, and interval between MUS placement and SSR were recorded. Patient's presenting symptoms for MUS-related complications included storage dysfunction, voiding dysfunction, RUTI, vaginal pain, non-vaginal pain, mesh exposure, and urinary incontinence (UI) and were tallied from an electronic medical record (EPIC). Number and nature of these presenting symptoms were compared between patients divided into 2 and 4- year intervals between MUS placement and presentation for SSR. We tested the hypothesis that early presentation groups would have higher rates of mesh exposure and pain and/or dyspareunia complaints whereas late presentation groups would have higher rates of UTI and UI complaints.

Results: Between 2005 and 2017, 278/435 women met study criteria. Overall, mean number of presenting symptoms per patient was 3.8 ± 1.4. Mean number of presenting symptoms per patient increased significantly over time since MUS placement (p= 0.0010). Amongst the 2-year interval groups, there was a significant difference over time between number of patients presenting with RUTI (p= 0.0095), vaginal pain (p= 0.0289), and UI (p=0.0327) (See Table). Between the 4-year interval groups, there was a significant difference over time between number of patients presenting with RUTI (p= 0.0039), non-vaginal pain (p= 0.0106) and vaginal pain (p= 0.0463).

Conclusions: In our tertiary care center, women with MUS-related complications presented with multiple symptoms that increased in number over time and evolved in relation to interval between MUS placement and presentation. A higher rate of pain complaints was noted earlier whereas a higher rate of UI and RUTI was observed in the later groups.

The Subdomain Question 6 on Pain of the Urogenital Distress Inventory Short Form is Sensitive to Change

Connie Wang

Mentor: Philippe Zimmern, Department of Urology
Collaborator: Alana L. Christie MS

Introduction: To determine the validity of question six (Q6) of the modified short form version of the Urogenital Distress Inventory (UDI-6) to measure post-operative presence and severity of pain in women after mid-urethral sling (MUS) placement.
Methods: Following IRB approval, a prospectively maintained database of non-neurogenic women was used to identify women with UDI-6 Q6 data before and after synthetic sling removal (SSR). Demographics and baseline and post-operative self-report of pain and Q6 scores were recorded. Q6 scores were compared pre-and post-operatively and against patient self-report of pain for women whose SSR was indicated for pain (SSR-P) and for indications other than pain (SSR-C). Three hypotheses were tested: 1) higher baseline Q6 scores in the SSR-P than in the SSR-C group 2) decrease in Q6 scores after SSR indicated for pain relief and 3) correlation of baseline and follow-up Q6 scores with patients' self-reported pain.
Results: Between 2005-2017, 116/435 women met study criteria. We found: 1) mean baseline Q6 scores in the SSR-C group was 0.95 ± 1.2 and 2.3 ± 1.1 (69% none or mild) in the SSR-P group (19% none or mild) 2) mean improvement in Q6 score after SSR was -0.19 ± 1.2 in the SSR-C group and -0.88 ± 1.4 in the SSR-P group and 3) Q6 scores were significantly ($p<0.0001$) associated with self-reported pain, with increasing likelihood of self-reporting pain as Q6 scores increased (See Table).
Conclusion: In women undergoing SSR for MUS-related complications, Q6 of the UDI-6 is a valid and sensitive measure of lower urinary tract associated pain.

Table 1. UDI6 Q6 score vs. self-report of pain

	Self-report pain = No	**Self-report pain = Yes**	***p***
UDI6 Q6	**(n = 42)**	**(n = 74)**	
0	23 (55%)	9 (12%)	<0.0001
1	6 (14%)	5 (7%)	
2	5 (12%)	12 (16%)	
3	8 (19%)	48 (65%)	<0.0001

Upgrading Pathology of MRI Targeted vs Standard Prostate Biopsy

Daniel Wong

Mentor: Nabeel Shakir MD, Department of Urology
Collaborators: Niccolo Passoni MD & Jon Bloom MD

Importance: The majority of new prostate cancer (PCa) diagnoses made in the United States occur via transrectal ultrasound (TRUS) guided systematic template prostate biopsy ("standard biopsy"). Since this modality depends on random sampling of the organ, which may lead to undersampling of aggressive disease in addition to detection of low-risk PCa with concomitant harms of overtreatment, there is a demand for more reliable and accurate diagnostic methods. Multiparametric magnetic resonance imaging (MP-MRI) of the prostate can identify lesions suspicious for PCa, and platforms using software fusion of pre-acquired MRI with real-time TRUS ("MRI-targeted biopsy") are now FDA-approved.
Objective: To assess whether MRI-targeted biopsy detects a significantly greater proportion of higher-grade, clinically-significant disease as compared to standard biopsy ("upgrading") in patients who underwent both approaches.
Design: Prospective cohort study of men undergoing both MRI-targeted and standard biopsy from the National Cancer Institute (NCI) and UT Southwestern from 2007 to 2017. Pathology was categorized by the International Society of Urological Pathology grading scheme and compared between targeted biopsy and concurrent standard biopsy with McNemar's test. Parameters associated with upgrading, determined by threshold $p<0.15$, were evaluated in multivariable logistic regression models where significance was defined as $p<0.05$.
Interventions: Following referral for elevated serum prostate-specific antigen (PSA), patients underwent MP-MRI. Men with lesions suspicious for PCa on MRI underwent a single biopsy session during which targeted biopsy and standard biopsy were performed concurrently.
Results: Of 1913 men in the study, 1235 were diagnosed with PCa by either standard or targeted biopsy. Patients between the two centers were matched by age and PSA (Table 1) but differed by history of previous biopsy, MRI prostate volume, and racial distribution. 408 patients had intermediate to high grade prostate cancer diagnosed by either targeted or standard biopsy (Table 2), of whom 194 (47%) had concordant targeted and standard biopsy results. 151 (37%) men had intermediate to high grade disease missed or downgraded relative to targeted biopsy by standard biopsy, and 63 men (15%) were missed or downgraded relative to standard biopsy by targeted biopsy ($p<0.0001$). On multivariable analysis of upgrading by targeted biopsy, when controlling for potentially confounding factors, increasing age, MRI prostate volume, number of targets and PSA remained significantly associated, whereas the performing center was not predictive.
Conclusions: MRI-targeted prostate biopsy results in greater detection of clinically significant higher-grade PCa as compared to standard biopsy. Whether MRI-targeted biopsy can be performed instead of standard biopsy, versus being performed in selected risk-stratified populations or as a supplemental technique, requires additional study.

Power of OCT-A (Optical Coherence Tomogrphy Angiography) in Glaucoma

Alex Yang

Mentor: Karanjit Kooner MD, MBA, Department of Ophthalmology
Collaborators: Ted Deng BS, Sahar Noorani BS, Xilong Li PhD, Munsif AlSalem MD, & Beverley Adams-Huet MS

Purpose/Relevance: OCT-A is a new non-invasive, motion contrast micro-vascular imaging modality. Using OCT-A, we analyzed vessel density measurements and structural properties in controls, glaucoma suspects and patients with mild, moderate and severe glaucoma.
Methods: In an IRB approved retrospective study, 69 controls, 36 glaucoma suspects, 54 mild glaucoma, 25 moderate glaucoma, and 12 severe glaucoma patients were studied. One eye was randomly selected per patient. Collected data included: age, race, gender, family history of glaucoma, CCT, IOP, visual field (VF) MD and PSD, cup/disc ratio (C/D), and OCT-A scanning parameters: global and sectoral optic nerve fiber thickness, ganglion cell complex thickness, disc vessel densities, retinal vessel densities, and the foveal avascular zone area. A Jonckheere-Terpstra, chi-square, independent t-test, and correlation matrix were used to determine differences between controls and glaucoma groups.
Results: Optic disc and retinal vessel densities showed a significant decrease as the glaucoma progressed, from mild to severe form, 52.9% to 43.1% and 48.1% to 43.4%, respectively ($p<0.01$). Nerve fiber layer thickness decreased from 83.0μm to 60.1μm, respectively ($p<0.01$). Both structural properties and vessel densities were effective at determining glaucoma stage, but neither variable was superior to the other ($p=0.21$). Between controls and glaucoma suspects, we noticed structural property differences, but not vessel density differences ($p\leq0.05$).
Discussion: The vessel densities and structural properties from OCT-A have a significant decreasing trend as glaucoma progresses and they support the clinical diagnosis of glaucoma based on VF damage. However, in glaucoma suspects, the structural properties were reduced compared to controls, while vessel densities remained unchanged. This could suggest that structural damage may occur before vessel damage in glaucoma suspects when there is no VF defect.
Conclusion: Optic disc and retinal vessel densities and structural properties assessed by OCT-A can provide an objective measure of glaucoma damage in the eye. Our study has shown that structural damage may occur before vessel density damage in glaucoma suspects.

Reduced Physical Activity Level and Cardiorespiratory Fitness in Children after Acute Venous Thromboembolism

Zhuo Yang

Mentor: Ayesha Zia MD, Department of Pediatrics-Hematology Oncology
Collaborator: Kendra Malone MPH

Introduction: Venous thromboembolism (VTE), accompanied by its chronic sequelae such as post-thrombotic syndrome, has reached epidemic proportions. Early identification may offer an opportunity for effective intervention and reduction of long-term morbidity. Currently, no data is available regarding physical activity post-VTE in children and its relation to adverse post-VTE sequelae over time. Therefore, we sought to: (1) assess self-reported physical activity levels in children 6 months post-VTE and change over time from acute diagnosis, (2) compare activity levels of patients with and without adverse post-VTE sequelae, and (3) determine predictors of activity limitations after VTE and assess its association with health related quality of life (HRQoL).

Methods: Data on 50 children ages 2-21 years were extracted from our ongoing TOP study, with 36 diagnosed with lower extremity DVT and PE. We assessed pre-, 3, and 6 months post-VTE physical activity, using the Godin activity questionnaire. Age, race, ethnicity, gender, BMI, site of VTE, clot burden at diagnosis and follow-up, coagulation activation, dyspnea score, 6-minute walk distance (6MWD), and HRQoL were measured during follow-up.

Results: Out of 36 subjects, 20 had DVT, 16 had PE, and 3 had both DVT and PE. Of those followed for 12 months, 65% were active at 6 months post-diagnosis compared to 80% before. 36% of subjects had evidence of post-thrombotic sequelae – a composite of post-thrombotic syndrome per the Manco-Johnson Instrument and post-PE impairment at 12 months post-diagnosis. In multivariate analysis, age, race, ethnicity, gender, BMI, site of VTE, baseline or residual clot burden, and type of anticoagulant were not predictive of activity limitations at 6 months post-VTE. Decreased activity level at 6 months was not associated with a decreased HRQoL at this time. Insufficient activity compared with high activity, reduced 6MWD at 6 months, and coagulation activation (defined by D-dimer > 500 ng/mL at 3 months post-diagnosis) were predictive of increased short-term risk for post-thrombotic sequelae when assessed at 12 months post-diagnosis (OR 1.55, $p < 0.001$; OR 2.7, $p = 0.02$; OR 4.2, $p = 0.02$ respectively).

Conclusion: 35% of children with DVT and PE had activity limitations post-VTE that adversely influenced short-term post-VTE sequelae. Only 65% of children had resumed their usual activity within 6 months after VTE, highlighting this as a critical time period for interventions aimed at preventing post-VTE disease. Continual data accrual from our ongoing, prospective study may offer further insight to predict risk factors for decreased activity levels and walking distance in children after VTE.

Influence of Post-Treatment PET/CT on Patient Outcomes and Management After Definitive Chemoradiation Therapy in Oropharyngeal Squamous Cell Carcinoma

Helena You

Mentor: Rathan Subramaniam MD, PhD, MPH, Department of Radiology
Collaborators: Yin Xi PhD & Yasemin Sanli MD

Background/Objective: Oropharyngeal squamous cell carcinoma (OPSCC) is one of the most common subtypes of head and neck cancer. PET/CT is useful in staging OPSCC, assessing treatment response, and detecting recurrence and metastases. The National Comprehensive Cancer Network recommends post-treatment imaging within six months of treatment. However, there is a lack of detailed imaging recommendation past the first six months. This study aims to evaluate the utility of PET/CT in the two-year period following definitive chemoradiation for OPSCC, particularly the impact of PET/CT after the first six months on patient outcomes and changes in management.
Methods: We identified 149 patients from our PET center database diagnosed with OPSCC between 2006 and 2015 who met inclusion criteria of stage III, IVA, or IVB; completion of definitive chemoradiation therapy; and at least two years of post-treatment follow up at our institution. Patients who had at least one PET/CT in the last 18 months of the two-year follow up were placed in one group (experimental), while patients who had no PET/CTs in the 18 months were placed in the other group (control). Hazard ratios were calculated using univariate Cox proportional hazards model. Chi-square analysis was used to test association between positive PET/CT and change in patient management. Kaplan-Meier analysis was used to generate survival curves. $P<0.05$ was considered significant.
Results: All 149 patients had at least 1 PET/CT in the two-year follow up period. Patients had 1.01 ± 0.39 PET/CTs in the first 6 months and 0.97 ± 1.04 PET/CTs in the next 18 months. Patients with at least 1 positive PET/CT or change in management during the last 18 months of the period had higher hazard ratios for overall survival ($P<0.0001$) and progression free survival ($P<0.0001$). Older patients had higher hazard ratios for overall survival ($P=0.03$) but not progression free survival ($P=0.82$). Positive PET/CT in the last 18 months was positively associated with change in patient management ($P=0.02$).
Conclusion: In patients with stage III, IVA, or IVB OPSCC treated with definitive chemoradiotherapy, positive follow-up PET/CT and change in management were associated with worse overall and progression free survival. Positive PET/CT in the last 18 months of the two-year follow up was positively associated with change in patient management.

Description of Bleeding and ROTEM Use in Patients Undergoing Transjuglar Portosystemic Shunt Procedures

Sarah Yuen

Mentor: Michael Cripps MD, Department of Surgery
Collaborator: Evan Barrios, BS

The placement of Transjugular Intrahepatic Portosystemic Shunts (TIPS) is a procedure performed by Interventional Radiology (IR) which can lead to bleeding. TIPS procedures are performed in patients with portal hypertension and liver disease, a population in which coagulopathies are especially prevalent. In bleeding patients, identification of the causes of bleeding and appropriate resuscitation is paramount for the survival of the patient. However, traditional laboratory tests such as INR and PTT, which are most commonly used to analyze bleeding, fail to predict bleeding, identify coagulopathies, or provide specific characteristics of the bleeding. However, viscoelastic analysis can provide specific information about clotting characteristics and dynamics, including time to clot formation, strength of the clot formed, as well as clot lysis. The potential to identify patient-specific coagulopathies at the outset and provide targeted correction for bleeding patients makes viscoelastic analysis a viable, powerful tool for the treatment of bleeding patients. This study compares bleeding characteristics and the use of viscoelastic analysis among patients treated by IR undergoing TIPS procedures in two time periods: 2012-2014, before the introduction of viscoelastic analysis, and 2014-2016, in which viscoelastic analysis was available for use. No significant difference was found in the number of coagulation labs or transfusions per patients classified as bleeding between the 2012-2014 cohort and the 2014-2016 cohort. Viscoelastic analysis appears to currently be used in IR as a post-transfusion analysis rather than as for the identification of potential coagulopathies and prevention of bleeding in patients, thus failing to utilize viscoelastic analysis to its true potential. Further analysis and education about the current and potential application of viscoelastic analysis is needed to expand the use and efficacy of this tool.

Outcomes of Multi-Focal Electroretinography (mfERG) Studies for Hydroxychloroquine Screening

Alice Zhang

Mentor: Chan Nguyen MD, PhD, Department of Ophthalmology
Collaborator: Ashish Singh MD

Background: Many patients in the United States are treated with hydroxychloroquine (HCQ) for rheumatologic diseases such as Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA). The risk of toxicity with HCQ increases with increasing dosage and duration of therapy. Screening is of major importance because retinal toxicity is irreversible and untreatable. There are multiple diagnostic modalities used to screen for retinal toxicity with no consensus on the primary modality of choice. The aim of this study was to better understand the efficacy of multifocal ERG (mfERG) in detecting HCQ toxicity and its influence on physician intervention. In addition, mfERG was analyzed for its potential as a first line diagnostic modality.
Methods: A retrospective chart review of patients at Parkland Memorial Hospital from 2012 to 2016 who were screened for HCQ toxicity with mfERG was performed. The data analyzed consisted of percentage of abnormal mfERG results, interpretation of the result, clinical response to result, and the final patient outcome. Other pertinent data that was extracted from the medical records included patient name, gender, date of birth, ethnicity, race, ocular findings including visual acuity, mfERG reports, posterior segment examination findings, current medications, and any medical or ocular disease process.
Results: Of the 670 patients screened with mfERG to look for evidence of HCQ toxicity, 169 (25.2%) received an abnormal test result. 76 patients (11.3%) from this group showed possible evidence of early or frank toxicity. Of the 76 patients, 48 presented for follow-up after mfERG testing. 46 of the patients who presented for follow-up (96%) had their medication either reduced or completely stopped, and 2 of those patients (4%) had repeat testing. There was no evidence of clinical toxicity in any of these 48 patients. These patients either had stable visual acuity, or their decrease in visual acuity was adequately explained by another ocular abnormality. 28 patients were lost to follow-up and final visual outcomes were unable to be determined.
Conclusions: A large number of patients had test results showing possible early or frank retinal toxicity, and the vast majority of these patients had the medication stopped or dosages lowered based on these findings. This led to no patients with evidence of clinical toxicity, not accounting for the significant number that were lost to follow-up during this time. Regardless, the use of mfERG in screening patients for HCQ toxicity is a very helpful adjunct tool for ophthalmologists.

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Ω Oral Presenter - UT Southwestern Medical Student Research Forum
Δ Dean's Research Scholar, τ T35 NHLBI Training Grant Funded
∗ Poster Presenter

Wrinkles, Brown Spots, and Cancer: Appearance and Health Motivate Sunscreen Use

Hongjing Cao

Mentor: Heather Wickless MD, MPH, Department of Dermatology
Collaborators: Mary Brehm MD & Linda Hynan PhD

Background: There is increasing evidence that appearance-based messages are more effective than health-based messages in promoting daily sunscreen use. It is unclear if most know about photoaging and sunscreen's utility in preventing it. We hypothesized that more people associate deleterious effects of UV exposure with health than aging, and those with more comprehensive understanding of photoaging use sunscreen more consistently.

Methods: We conducted a cross-sectional survey of local adult population assessing the extent to which they knew about the health versus appearance benefits of sunscreen and how this knowledge correlates with sunscreen usage.

Results: 88% of respondents strongly associated sun exposure with skin cancer while fewer associated it with signs of aging. Avoiding sunburn and skin cancer were the two strongest motivating factors for sunscreen use. Over half reported they would consider using sunscreen if anticipating sun exposure lasting 1 or 2 hours, but 30% reported using sunscreen daily. Knowledge about the role of sun exposure in skin aging was positively associated with sunscreen adherence (at least $p<0.05$). Those with darker complexions or skin less likely to burn reported less knowledge in the risks and benefits ($rho=-0.219$, $p =<0.001$) and lower sunscreen adherence ($rho=-0.301$, $p< 0.001$).

Conclusion: Health-based information has reached more people than appearance-based information. More comprehensive appearance knowledge corresponded to greater sunscreen adherence. There may be misconceptions that short-interval sun exposure that do not result in sunburn is less harmful than extended exposure.

Sources of Sun Protection Information Among US Adults: A Cross-Sectional Studty

Hongjing Cao

Mentor: Heather Wickless MD, MPH, Department of Dermatology
Collaborators: Mary Brehm MD & Linda Hynan PhD

Background: Despite widely available sunscreen information, skin cancer is still the most prevalent form of cancer in the United States, and its incidence is increasing. In recent years, there has been evidence suggesting appearance-based sun protection messages are more effective than traditional health-based messages in promoting sunscreen use. Currently, little is known about where individuals obtain their photoaging (premature aging of the skin due to UV exposure) and sun protection knowledge.

Aim: Our aim was to define respondent's sources and quantity of information regarding sunscreens and their correlation with frequency of sunscreen use. Methods: We conducted a cross-sectional survey of local adult population assessing their sources of photoaging and sun protection knowledge.

Results: Family, TV, and friends were the most influential sources of sun protection information. Those reporting hearing about the importance of sun protection from multiple sources reported greater sunscreen adherence (rho=0.236, $p<0.001$). Having a facialist information source was associated with greater sunscreen adherence (facialist median=10 versus non-facialist median=6, $p<0.001$). Having at least one physician (dermatologist or primary care physician) as an information source was associated with greater sunscreen adherence as well (at least 1 physician median=8 versus no physicians median=5, $p<0.001$).

Conclusion: Our data indicate that most people are not adequately using sunscreen. The sheer quantity of sunscreen messages can influence its use, particularly those coming from family, friends, and television. Our findings support those of previous studies indicating that physicians are an important source of this information. Overall, physicians, family and friends, as well as media play an important role in providing sun protection information and helping patients understand how daily sun exposure leads to skin damage and can influence health protective behavior in this instance, use of sunscreen.

Optimizing Oral Chemotherapy and Efficacy Through Closed Loop Systems and Financial Assistance

Tina Chu

Mentor: Jason Fish MD, Department of Internal Medicine &
Christine Hong PharmD
Collaborators: Rohit Srivastava BS & Patty Brown RN, MBA, CPC

Introduction: The increasing use of oral chemotherapy presents both adherence and financial challenges for patients. Non-adherence leads to premature discontinuation of treatment and progression of disease. Pharmacist counseling is essential to ensure proper medication use, monitor for adverse events, and promote adherence. We investigated the local incidence of verbal counseling for oral chemotherapy at the UT Southwestern Simmons Comprehensive Cancer Center (SCCC). We aim to have 90% of patients prescribed capecitabine for the treatment of oncology indication verbally counseled by a SCCC pharmacist prior to their first dose from May 2017-2020.

Methods: We conducted a retrospective review of medication therapy management telephonic counseling for the oral oncolytic capecitabine at the SCCC during January-May 2017. We measured the 1) number of new prescriptions for capecitabine, 2) number of prescriptions filled at SCCC vs. a non-SCCC pharmacy, 3) time between verbal counseling by a pharmacist and medication start date, and 4) turnaround time (time between the date medication was ordered and date it was filled). There are two interventions: an electronic medical record notification for pharmacists and an educational brochure for patients.

Baseline Data: Of the 27 SCCC patients who started capecitabine between January-May 2017, 59% (n=16/27) were not verbally counseled by an UTSW pharmacist prior to their first dose and the majority received counseling more than a week afterwards. More than half (63%) of prescriptions were filled outside of SCCC whereas 37% were filled at the SCCC. The average turnaround time was 24 days.

Conclusions: Implementing planned interventions may improve use of the SCCC pharmacy, verbal counseling and patient outcomes.

Development and Implentation of Patient Knowledge Assessment in the Emergency Department

Charisma DeSai

Mentor: Andra Blomkalns MD, Department of Emergency Medicine

Introduction: Improving health literacy is a national goal endorsed by the U.S. Department of Health and Human Services. Lack of patient knowledge may lead to adverse outcomes such as decreased compliance, decreased patient safety, increased Emergency Department return rate, and lower patient satisfaction. Despite this, studies have shown that many patients leave the Emergency Department with partial comprehension of their visit and discharge instructions. This study's objective was to develop and implement a method to assess current patient knowledge of treatment and discharge plan at the Clements University Hospital Emergency Department.

Methods: The questionnaire was developed using CMS OP-19 Transfer Record and Joint Commission recommendations. Project team included nurses, techs, nurse practitioners, physician assistants, and physicians who provided input and approved the relevance and importance of questions included. Responses from patient interviews was then scored against the medical record, including the after visit summary, in Epic. Scoring system was created to measure degree of knowledge. Final scores were calculated per patient and demographic criteria (age, patient education level, whether patients read their discharge papers).

Results: Only one of the 50 patients analyzed had complete comprehension of their ED visit and discharge instructions, although most patients stated they understood their discharge instructions. Average total score was 69.73%. Patient understanding is lowest in the domain of post-ED care, with the lowest categories being medication knowledge and return to ED instructions.

Discussion: This study highlights the importance of clear communication with patients. Although providers may put time into educating their patients, opportunities remain for further studies to assess effectiveness of teaching and areas in which we may improve health literacy. We have identified specific areas (medication and return instructions) in the ED that will be targeted in future projects.

Barriers to Continuity of Care at a Community Based Free Clinic

Emmanuella Egbonim

Mentor: Nora Gimpel MD, Department of Family and Community Medicine
Collaborators: Sabrina Vizzini PA, Teagan Batts, & Tiffany Kindratt MPH

Context: Chronic uncontrolled diabetes and hypertension continue to place a substantial burden on health care in the United States. Chronic conditions such as these are especially hard to treat in underserved populations, where continuity of care is challenging. Identifying barriers to continued care for underserved patients is essential to improving the quality and delivery of care in health care delivery centers. Objective: To identify barriers and facilitators to care among patients attending a community-based free clinic. Design: Cross sectional study.

Setting: Community-based free clinic in Dallas, TX. Participants: Adult patients (N=50) receiving treatment for hypertension and/or diabetes. Instrument: Survey (21 item) evaluating perceived barriers, fears, and severity, along with demographic information (including age, race, gender, level of education, average monthly income, marital status, household size, etc.). Survey data was collected face-to-face and over the phone with the use of translator when needed. Main Outcome: Perceived barriers to care from survey responses.

Results: The majority (75%) of the diabetic patients were uncontrolled (Hb1Ac < 7%) and 27% of the hypertensive patients were uncontrolled (blood pressure > 140/90 mmHg). Reported barriers included work (32%), time (30%), and transportation (16%). There were no significant differences across barriers and overall control status, age, or gender. There were also no significant differences in barriers across age and gender when looking at solely hypertensives or solely diabetics. The majority of uncontrolled diabetic patients feel they are controlled (70%). The vast majority of uncontrolled hypertensive patients feel they are controlled (83.3%). Two patients denied being diagnosed with hypertension.

Conclusion: Preliminary data points to appointment availability as a potential barrier to continuity of care. The data also show a disparity between the patients control status and their perception of their own health. Potential strategies to meet the identified barriers include increased appointment availability and health education interventions.

The Vitiligo Experience of the South Asian Patient: Exploring the Impact of Culture on Psychosocial Burden

Amrita Hans

Mentor: Amit Pandya MD, Department of Dermatology

Background: Vitiligo patients struggle with low self-esteem, social stigmatization, and frustration due to unpredictable disease course and variable treatment response. South Asian patients specifically are subjected to a distinct type of intolerance, social exclusion, and set of modern day struggles, which are deeply rooted in traditional historical and religious beliefs. No prior study has examined both the DLQI and SF-36 in the U.S. There is no published information about South Asians who have acculturated to American culture.

Design and methodology: This is a prospective, comparative survey study that was conducted at the dermatology clinic at UTSW. The Dermatology Life Quality Index (DLQI) and SF-36 Health Survey Mental Component Summary (MCS) were used as the primary outcome measures for assessing quality of life (QoL). Acculturation status was determined with a study specific questionnaire, which asked about use of native language, consumption of native food, observation of native cultural/religious holidays, and contact with family/friends in home country.

Results: Nineteen South Asian patients above the age of eighteen were enrolled in this study. Each patient participated in an in depth interview and physical exam. Acculturated South Asians residing in the United States had a mean DLQI score of 3.67 ± 3.72 and a mean SF-36 MCS score of 47.3 ± 11.79 while their non-acculturated counterparts had a mean DLQI score of 5.38 ± 5.45, a mean SF-36 MCS of 51.22 ± 10.16, and reported feeling significantly more embarrassed and self-conscious.

Conclusion: South Asians with vitiligo residing in the United States who are acculturated to American culture were found to have better quality of life when compared to non-acculturated South Asian vitiligo patients. Patients who feel more disabled by their vitiligo tend to experience feelings of low self-esteem and embarrassment. These attitudes pervade into the patient's view of himself/herself as well as opinions of disease course and treatment response. Dermatologic conditions and mental health are associated with unique stigmas in South Asian culture; therefore, it is vital to to address these issues in vulnerable patient populations.

Conflicts of Interest of Editors of Opthalmology Journals

Waqas Haque

Mentor: Deepak Agrawal MD, MPH, MBA, Department of Gastroenterology
Collaborator: Kadam Patel MD, MPH

Introduction: Financial conflicts of interest (FCOI) between medical publishing personnel (authors, reviewers and editors) and the biomedical industry raise concerns about publishing bias and the transparency of financial disclosures. Authors are mandated to publicly disclose FCOI, but despite explicit guidelines, the same standard and scrutiny is rarely employed for the journal's editors. The National Institutes of Health (NIH) considers financial interests above $5000 significant and mandates disclosure. We sought to determine – for the first time - the magnitude and disclosure of FCOI of editors of ophthalmology, a specialty with significant ties to biomedical industry.
Methods: We noted names of Chief and Associate Editors of 12 top-ranked ophthalmology journals and cross-matched them with the Centers of Medicare Services Open Payments 2016 database, which contains information on all reported industry payments to physicians. We performed a descriptive analysis to observe the relation between FCOI and payment type (food & beverage, travel, consulting, and royalties) and stratified the results based on the role of editors and impact factor of the journal. We also determined which drugs/devices are associated with the most payments. The websites of the journals were reviewed to determine public disclosure of FCOI of the editors.
Results: We analyzed 143 physician editors licensed to practice in the US. Overall, 81.8% (117/143) of editors received industry payments. The mean payments received by Chief Editors ($86,640) was significantly higher as compared to Associate Editors ($20,494). In the entire period, the greatest value of payments was for consulting ($3.85 million) followed by speaking fees ($869,144) and travel/lodging ($628,373). The products associated with highest payments included Xiidra ($130,868), OCT ($57,586), and Lucentis ($43,644). Disclosure of FCOI of the editors was available for only 1/12 (8%) journals.
Discussion: FCOI are common among editors of ophthalmology journals but rarely disclosed. The payments received by the editors of ophthalmology exceed the threshold considered significant by the NIH and are significantly more than the payments reportedly received by editors of other specialties. Chief Editors had significantly more FCOI compared to other editors, contrary to the expectation that Chief Editors hold themselves to more FCOI standards.
Recommendations: FCOI of ophthalmology journal editors need greater scrutiny, transparency and compliance with recommendations and established guidelines.

Assessing Medication Adherence in Patients with Diabetes at UT Southwestern

Shailavi Jain

Mentor: Chanhaeng Rhee MD, MBA, Department of Internal Medicine
Collaborators: Vedang Kulkarni, Connor Hughes, Laura Gammon, Eleanor Phelps, Chaofan Yuan, & Jerzy Lysikowski

Background: On average, only 50% of patients with chronic conditions adhere to their prescribed treatments. Increasing adherence to medication regimens will improve health outcomes and decrease healthcare costs, thus the NIH has stated it is a top priority. Patients with diabetes struggle to take their medications as prescribed due to various factors and the most important factors from the patient perspective have not been previously described in the literature.
Aim: The overall aim of this project is to improve the percentage of patients with diabetes at UT Southwestern who adhere to prescribed medications from 54% to 70% during the period of June 2017- May 2020. To improve medication adherence, it was first important to determine what the major barriers to adherence are from both the patient and provider perspectives and to identify any demographics associated with poorer adherence.
Methods: A driver diagram and fishbone analysis were used to analyze information on the most important barriers to adherence from both patient and provider interviews. Data on prescription refills, HgbA1c, number of ER visits, number of hospitalizations, and demographics was extracted from the EMR and analyzed. Finally, potential interventions were researched and rated using a prioritization matrix.
Discussion/Results: Improving medication adherence is vital as patients with MPR <80% at UTSW have 1.35x greater risk of having HgBA1c ≥7%. Data from 9058 UTSW patients with diabetes showed that 1) women are 10% less adherent than men, 2) as age increases adherence improves significantly with a 24.3% gap between patients 18-29yo and 80+yo, and 3) African Americans and Hispanics are over 10% less adherent to medication regimens than whites and Asians. Physicians, pharmacists and patients all agreed that cost, complicated medication regimens, and fear of side effects are the most important factors/barriers to address. However, it was found that providers did not realize how pivotal patients' routines and occupations are in leading to poor adherence. This could be a major opportunity for improvement in the care provided in the future.
Recommendations: Given the demographics and barriers data, the best methods to improve adherence will be to: 1) Develop a form where individual patients mark specific hours they are willing/able to take their medications and have providers prescribe treatment regimens accordingly, 2) Develop an insurance flowsheet for patients to follow to ensure all patients have proper coverage, and 3) Create a list of stores with the best prices for each medication that is kept in each exam room.

The Utility of Waveform Capnography in the Termination of Out-of-Hospital Cardiac Arrest (OHCA) Resuscitation Efforts

Alysha Joseph

Mentor: Ray Fowler MD, Department of Emergency Medicine
Collaborator: Brandon Morshedi MD

Purpose: The administration of sodium bicarbonate (SB) during out-of-hospital cardiac arrests (OHCA) has been shown to produce increased end-tidal capnography ($EtCO_2$) during resuscitations. Traditionally, EMS systems may authorize termination of resuscitation (TOR) efforts after prolonged periods where the $EtCO_2$ remains <10 mmHg. However, if SB has been administered, the $EtCO_2$ may be elevated, possibly resulting in prolonged resuscitation efforts. This study aimed to determine the effects of the administration of SB during OHCA on $EtCO_2$. We hypothesized that there would be no observable difference in $EtCO_2$ readings between OHCA TOR patients who received SB and those who did not.

Methods: A retrospective analysis was performed on all OHCA TOR patients in a large, urban EMS system between January 2013 and December 2016. The off-line and on-line medical control databases were queried to identify all patients for whom the Provider Impression was “Cardiac Arrest”. The records were individually examined to determine the $EtCO_2$ readings and whether these patients received SB.

Results: The authors found that there was a significant difference in the level of EtCO2 when SB had been administered, especially when the absolute levels of EtCO2 were higher than approximately 20 mmHg. Thus, the utility of interpreting EtCO2 levels as part of the TOR decision is significantly decreased in high levels of EtCO2, especially in the setting of the administration of SB. The significance of the administration of bicarbonate effect on EtCO2 levels was lost with measurements under approximately 20 mmHg. This indicates that when EtCO2 levels are low, the utility of waveform capnography in making TOR decisions is not complicated by SB administration. It is the hope of the authors that this study adds insight into the utility of EtCO2 both in the setting of very high absolute levels of EtCO2 with and without the administration of SB.

Conclusion: Administering SB during OHCA will significantly elevate the $EtCO_2$, and SB administration complicates the utility of EtCO2 when levels are above 20 mmHg.

Educational Implications of the Emergency Medicine Residency Interview Process

Matthew Siebert

Mentor: Jeffrey Van Dermark MD, Department of Emergency Medicine
Collaborators: David A. Wald DO, John Robert Corker MD, & David Godley Reid DO

Background: Emergency Medicine (EM) residency interviews may impact the educational choices for applicants. Students select educational opportunities based on the length and unpredictability of the EM interview season. Allowing more freedom educational choices during the important M4 year needs to occur by modifying the current EM interview process.

Objectives: We sought to determine if applicants could accurately predict the time burden of the interview season. We also sought to ascertain if the predicted time burden influenced educational decisions by the senior medical students. Finally, we reviewed decisions on electives by senior medical students.

Methods: IRB-approved, piloted email surveys were sent to student members of the Emergency Medicine Resident/Student Association (EMRA) in the fall of 2015 and Spring 2016. Results were reported using descriptive statistics, ranking and percentage answers.

Results: 180/1425 EM applicants in 2016 completed the survey. Students accurately predicted the numbers of interviews they would attend (pre-season average 14.8, post season average 12.3). Vacation time, flexible-schedule clinical electives and choosing an elective in which they had no interest, were the top 3 methods to attend interviews. Students declined an average of 7.21 interviews.32.8% cut interviews due to their clinical schedule. 43% selected, changed, or cancelled an elective due to interviews. 28% felt they missed out on a clinical opportunity due to interviews.

Conclusions: EM applicants appear to be able to accurately predict the time burden of the EM interview season and make choices accordingly. Shortening the interview season, interviewing multiple programs simultaneously in a fixed location or using video interviews may reduce both uncertainty and time spent away, in lieu of education priorities. EM, other specialties and organized medicine need to reform their systems so that education is not sacrificed in the final year of medical school.

Analysis of Neurologic Injuries Sustained by Motorcyclists Involved in Road Traffic Accidents in the Dominican Republic

Maura Walsh

Mentor: Abier Abdelnaby MD, Department of Surgery
Collaborators: Sumanth Reddy BS, Robert Paulino-Ramírez MD, Jaime Fernández MD, Jomar Florenzán MD, & Abier Abdelnaby MD

Background & Objectives: The Dominican Republic had the most road traffic fatalities per capita worldwide in 2013. Motorcycle-related deaths constituted the majority of these fatalities. This study aims to characterize the neurologic injuries suffered by motorcyclists admitted to Hospital Traumatologico Ney Arias Lora (HTNAL) in Santo Domingo.

Methods: Information regarding the nature of the accident, helmet usage, and the injuries sustained was collected from the medical records of 117 patients who were admitted to HTNAL following a road traffic accident.

Results: The most common injuries sustained by motorcyclists were definite moderate/severe traumatic brain injuries (TBI, 32.5%). Among these patients, the most common intracerebral hemorrhage was subdural hemorrhage (10.3%) and subarachnoid hemorrhage (7.7%). Each of the patients who died in the hospital sustained a moderate/severe TBI.

Only 22.4% of patients were wearing a helmet at the time of the accident. Non-helmet users were 5.2 times more likely to present with a TBI than those who wore a helmet (OR = 5.2, 95%CI: 1.7, 16.4). On average, they also had an initial Glasgow Coma Scale (GCS) score that was 1.63 points lower, (95% CI: 0.6, 2.7). None of the patients who wore a helmet died from their injuries while in the hospital.

A stepwise multiple linear regression using various neurologic injuries, type of collision, alcohol use, 911 use, age, gender, helmet use, and initial GCS was created to demonstrate which variables correlated with an increased risk of death. The results indicated that initial GCS ($\beta = -0.95$, $p < 0.01$) was the only statistically significant predictor of mortality.

Conclusion: In the Dominican Republic, as in other developing countries, a motorcycle provides an economical mode of transportation, often equating to the ability to make a living. Accordingly, increasing helmet usage may be the most effective way to decrease injury on the road.