2016 Student Research Forum Abstracts

(Alphabetical By Student Last Name)
EVALUATING THE BENEFITS AND HARMS OF RISK-BASED VERSUS AGE-BASED MAMMOGRAPHY SCREENING IN WOMEN AGED < 50 YEARS

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Mentor: Elizabeth S. Burnside, MD, MPH, MS

Support: Shapiro Summer Research Program; Department of Radiology

Background: Risk-based screening in women <50 years old has been promoted to increase benefits and decrease harms of a mammography screening program, but has not been evaluated in practice. We set out to quantify the benefits and harms of risk-based screening versus traditional age-based screening using publicly available risk tools and data from an academic breast imaging practice. Methods: We analyzed a database of 72,220 consecutive screening mammograms (1/1/2006-12/31/2013) from an academic practice of women ages 40 to 74. To evaluate only “average risk” women, we excluded those with a personal history of breast cancer or with a documented BRCA mutation. In women <50 we estimated their breast cancer risk at the time of each mammogram using the BCSC risk calculator (https://tools.bcscc.org/bc5yearrisk/calculator.htm) Starting with a screened population, we compared two hypothetical groups of women: women who would have been included in the given screening strategy and women who would have been excluded based on age or risk. We emulated age-based screening similar to the American Cancer Society guidelines by excluding all women <45. We emulated risk-based screening by excluding women <50 whose 5-year breast cancer risk was less than the average risk for a 50-year old (≤ 1.578%). For included women, we defined cancers detected as benefits and recalls and biopsies as harms. For excluded women, we defined recalls and biopsies saved as benefits and cancers not detected as harms. To compare benefits/harms ratios for the screening strategies, we conducted bootstrapped mediation analyses, where a 95% confidence interval (CI) around the difference that does not cross zero indicates statistical significance. Results: For women who would be screened, risk-based screening detected 1.2 more cancers per 100 recalls (95% CI 0.790, 1.526) and 3.3 more cancers per 100 biopsies (95% CI 1.567, 5.194) compared to age-based screening at 45. For women who would be excluded from screening, risk-based screening did not detect 0.4 more cancers per 100 recalls avoided (95% CI -0.394, 1.103) and did not detect 2.9 more cancers per 100 biopsies avoided (95% CI -0.704, 6.284) compared to age-based screening at 45. Conclusion: Risk-based screening in women <50 results in greater benefits/harms ratio for women who would meet the screening threshold but no significant difference in benefits/harms ratio for women who would not, compared to women who start screening at age 45.
BUILDING HUMAN EMBRYONIC STEM CELLS WITH INDUCIBLE NOTCH ACTIVATION

Authors: Sekani Allen, Yunlong Tao, Su-Chun Zhang

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Mentors: Su-Chun Zhang, MD, PhD; Yunlong Tao, PhD

Support: Shapiro Summer Research Program; Mentor funds

Background: Notch receptor and its ligands are single pass transmembrane proteins important in development. Activated Notch is cleaved and its intracellular domain translocates into the nucleus to activate downstream transcription factors that play a role in the neuron-glial switch of neural progenitor cells\textsuperscript{1,2,3}. Higher Notch activity drives the progenitor cells to glial lineage and accelerate the astroglial differentiation. By utilizing CRISPR-Cas9, we hope to insert Notch Intracellular Domain (NICD) into the AAVS1 site of Chrom. 19 in human embryonic stem cells (hESCs). We would be able to induce NICD expression by incubating the transfected hESCs with Dox, a drug that activates the NICD upstream promoter, allowing us to examine the function and role of Notch in the neuron-to-glia switch and how it helps with neural progenitor self-renewal. Methods: We created donor plasmids that contained the gene of interest, NICD, and the sg-RNA recognition site for CRISPR-Cas9. The NICD Tet-on donor plasmid quantity was amplified by transforming E. coli with the plasmid and growing the bacteria on ampicillin plates for 24 hrs. Colonies were picked and resuspended in 5 mL of Luria broth for further overnight growth. After gel electrophoresis to look at plasmid inserts and gene sequencing to look for mutations, we took the extracted NICD Tet-on plasmid, gRNA plasmid and CRISPR-Cas9 endonuclease and incubated with electroporated H9 hESCs and plated on mouse embryonic fibroblast (mEF) plates. The H9 hESCs were fed once a day with hES media and Fibroblast growth factor (FGF) until confluent and ready for passage. After 1 week, the cells were passaged and incubated in hES media + FGF + G418, a neomycin analog used to select for transfected H9 cells that integrated the NICD and neomycin resistance gene. After 1 week, colonies that grew were selected for expansion, DNA gel electrophoresis, qPCR, and incubation with Dox. Results: Using DNA primers for both the NICD and Neo insert (neomycin resistance gene) we were able to determine if the selected H9 colonies were homozygous, heterozygous or WT (no inserts). The H9 colonies that had both the Neo and NICD inserts were expanded and incubated with Dox to induce NICD expression. Dex conc. Ranged from 1:350K to 1:50K in 50K increments. After a 24 hr. incubation period, cells were harvested for qPCR to look at cDNA levels of NICD, GAPDH (control), HES1 and GFAP (neural progenitor cell markers). qPCR showed that at lower concentration of Dox (1:350K), there was a higher induction of NICD gene expression in comparison to GAPDH. Conclusion: Results demonstrate a successful creation of a new inducible H9 cell line to look at Notch activation and its role in the neuron-glial switch. Future studies include examining the glia lineage markers (GFAP, S100B, NF1A and CD44) by immunostaining and qPCR at different time points to compare with normal H9 hESCs. By doing this experiment, we will find out if Notch promotes glia fate.

Citations:
THE USE OF TRADITIONAL AND COMPLEMENTARY MEDICINE FOR DIABETES IN RURAL GUATEMALA

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Mentor: James Svenson, MD, MS

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

Background: The global burden of type 2 diabetes mellitus is increasing, especially in Central America. Little is known about treatment for diabetes in limited-resource settings where there are significant barriers to care such as Guatemala. Without consistent access to medications, many Guatemalans use plants to treat their diabetes. The purpose of this study is to understand the use of medicinal plants in a diabetic population in rural Guatemala. 

Methods: Semi-structured interviews were conducted in communities around San Lucas Tolimán, Guatemala with three groups: diabetics, health promoters, and traditional healers. Participants were asked about medicinal plants used to treat diabetes and knowledge of the disease. 

Results: Of the 55 diabetics interviewed, 35 (63.6%) had used medicinal plants to treat their disease. Most diabetics received recommendations for plants from other community members. The most frequently used plants among diabetics were Artemisia absinthium, Moringa oleifera, Carica papaya, and Neurolaena lobata. Out of the 18 species identified by diabetics, 11 have evidence of hypoglycemic effects. The majority of diabetics cited lack of access to prescription medications as the reason for their use of medicinal plants. Although health promoters had a good knowledge of diabetes, diabetics showed limited understanding of their disease and resistance to behavior change.

Conclusion: Although there are some traditional healers in the area, more diabetics relied on word-of-mouth recommendations for medicinal plants. Since the majority of plants identified by diabetics have some hypoglycemic properties, future research is necessary to determine their potential as diabetic treatments. Most diabetics cite low income and lack of access to care for their inconsistent adherence to medications and their use of medicinal plants. In order to improve access to diabetic care, it is important to understand the use of medicinal plants in the San Lucas Tolimán area.
IDENTIFICATION OF HIGH-RISK GLAUCOMA CHARACTERISTICS IN OLDER WOMEN

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Mentor: Yao Liu, MD

Support: Dan and Ellie Albert Student Vision Award; Shapiro Summer Research Program

Introduction: Glaucoma is the leading cause of irreversible blindness in the world. Women carry a larger burden of blindness from this condition. Prior epidemiologic studies to assess glaucoma prevalence have not incorporated retinal nerve fiber layer optical coherence tomography (RNFL OCT) for identifying subjects at high risk of glaucoma. This project assesses the literature to identify subjects with high-risk glaucoma characteristics, including RNFL OCT measurements, in an observational prospective cohort of older women in the Carotenoids in Age-Related Eye Disease Study 2 (CAREDS2), a multi-center ancillary study to the Women’s Health Initiative (WHI). In CAREDS2, identification of subjects with high-risk glaucoma characteristics will allow for the subsequent confirmation of glaucoma diagnoses. This information will be used to assess whether lower baseline macular pigment levels may be associated with a higher risk of glaucoma among older women. Methods: A literature search was conducted to determine appropriate criteria for identifying high-risk glaucoma characteristics among CAREDS2 participants. Intraocular pressure and stereoscopic disc photograph risk factor criteria were based on prior epidemiologic studies. RNFL OCT criteria were based on recent clinical studies that tested its sensitivity and specificity for glaucoma diagnosis. A flow chart incorporating these criteria was developed to identify subjects with high-risk glaucoma characteristics among study participants. Results: Data from the literature search resulted in the following high-risk glaucoma criteria: intraocular pressure ≥ 22 mm Hg, cup-to-disc ratio ≥ 0.6, cup-to-disc asymmetry ≥ 0.2, and presence of disc hemorrhages or rim notching. RNFL OCT measurement ≤ 5th percentile was selected as the cutoff for high-risk glaucoma. We chose the more lenient 5th percentile instead of the 1st percentile because of the gain in sensitivity and the limited literature available on the utility of RNFL OCT in glaucoma screening. In addition to any subject who meets these high-risk glaucoma criteria, those with a self-reported diagnosis of glaucoma or self-reported use of any glaucoma medication will have her ophthalmic medical records reviewed to confirm a diagnosis of manifest glaucoma as defined by specific patterns of visual field loss. If the medical records are inconclusive regarding glaucoma diagnosis, the subject will be invited back for a second study visit to perform confirmatory visual field testing. Visual field tests are expected to confirm glaucoma diagnoses in approximately 72 of the 1,043 women expected to attend CAREDS2 visits. Conclusion: This is the first large scale epidemiologic study utilizing RNFL OCT as a selection criterion for identification of subjects with high-risk glaucoma characteristics. Further data analysis will evaluate the relationships between RNFL OCT and other glaucoma risk factors. This study offers a unique opportunity to make recommendations on how to incorporate RNFL OCT measurements into other epidemiologic glaucoma studies as well as for glaucoma screening.
EFFECTS OF LOCAL RADIATION AND IMMUNOCYTOKINE ON ENDOGENOUS ANTI-TUMOR ANTIBODY QUANTITY AND DIVERSITY

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Mentors: Jacquelyn Hank, PhD; Zach Morris, MD, PhD; Paul Sondel, MD, PhD

Support: Shapiro Summer Research Program; UW Carbone Cancer Center; Department of Pediatrics

Background: Despite the continuing efforts of doctors and scientists around the world, cancer mortality rates remain high. Combinatorial therapies utilizing low-dose radiation therapy (RT), anti-CTLA4 antibody (anti-CTLA4), and intratumoral immunocytokine (IT-IC), which is a tumor specific antibody conjugated to interleukin-2 (IL2), provide an efficacious means of treating melanoma tumors in mice with little systemic toxicity. Clinical translation is being planned. While the efficacy and cell mediated mechanisms involved with this treatment have been explored, little work has been done thus far in elucidating the role of the humoral arm in RT+IT-IC combination therapy. Herein, we present the initial findings characterizing the long term endogenous anti-tumor antibody response in mice treated with this combinatorial therapy.

Methods: In the treatment group, 5 C57BL/6 mice that had previously been cured of a prior, established, B78 melanoma by receipt of RT+IT-IC+anti-CTLA4 combined treatment (given 378 to 511 days earlier) were subcutaneously re-challenged with a lethal dose of 2 million B78 melanoma cells. Likewise, 4 naïve C57BL/6 mice were injected with 2 million B78 cells as a control. Serum was collected before and after these injections of B78 tumors and analyzed for quality and quantity of anti-tumor antibodies using flow cytometry. Anti-IC antibodies were also detected using ELISA. Results: All 4 naïve mice showed progressive tumor growth, requiring euthanasia (on day 56). In contrast, all mice that were previously successfully treated for their B78 tumors with immunocytokine+RT+anti-CTLA4 showed rapid rejection (complete elimination) of the rechallenge tumor cells. These previously treated mice displayed humoral immunological memory both before and after re-challenge with an otherwise lethal dose of B78 tumor cells. IgG antibodies were observed that bound selectively to B78 tumor cells. These anti-tumor antibodies displayed B78 tumor antigen specificity; in contrast, no appreciable difference between naïve and treatment serum binding was noted when exposed to unrelated tumor Panc02 or Panc02-GD2+ cell targets. Analyses of serum samples collected from the control mice on day 35 after tumor implantation (when their growing tumors were ~ 200mm³ in volume) revealed an increased anti-tumor antibody response relative to the naïve serum samples, yet this response was still less than that of the pre-tumor rechallenge serum for the previously cured mice. Data also suggest that after re-challenge with B78 tumor cells, there was no significant increase in circulating anti-tumor antibody levels; however a strong initial (pre-challenge) circulating level of endogenous antibody was observed. Conclusions: Endogenous anti-tumor antibody responses have been observed up to 511 days after administration of combinatorial therapy in these tumor-challenged mice. These antibodies are B78 tumor specific and are present at high levels even prior to tumor re-challenge. Further studies should continue to explore the potential involvement of these antibodies in mediating tumor destruction, both in the initial tumor response as well as in the prevention of relapse.
NOVEL KCNJ13 MUTATION AND LOSS OF KIR7.1 CHANNEL FUNCTION CAUSES LEBER CONGENITAL AMAUROSIS

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Mentor: Bikash Pattnaik, PhD

Support: Dan and Ellie Albert Student Research Vision Award; Shapiro Summer Research Program

Background: Leber congenital amaurosis (LCA) is the most common cause of congenital autosomal-recessive retinal blindness and is characterized by severe vision impairment and nystagmus at birth. The KCNJ13 gene, which codes for Kir7.1, the inwardly rectifying K+ channel of the retinal pigmented epithelium (RPE), is one of 19 genes associated with the LCA clinical phenotype. By facilitating K+ efflux from the RPE into the sub-retinal space to offset local K+ decreases in response to light exposure, Kir7.1 plays a critical role in maintaining the ionic microenvironment between the RPE and juxtaposed photoreceptors. However, relatively little is known about the mechanisms by which Kir7.1 channel dysfunction leads to photoreceptor degeneration and the LCA phenotype. Methods: We identified a novel nonsense homozygous KCNJ13 gene mutation (T153I) in several LCA patients, ages 5 to 19. The identified mutation is located at nucleotide position 458 at amino acid 153 of the Kir7.1 protein, and results in threonine substitution for isoleucine. Using site-directed mutagenesis, we generated the novel T153I mutation in an eGFP-containing plasmid. The plasmid was transfected into CHO-K1 mammalian cells using a Lonza 4-D nucleofector system and both mutant and control Kir7.1 protein expression and localization were determined using a Nikon FN1 epifluorescence microscope and NIS elements. Preliminary whole-cell patch clamp recordings were also obtained for both sets of cells. Results: Live cell imaging of CHO-K1 cells expressing the mutant eGFP-T153I plasmid demonstrated robust protein expression and localization to the plasma membrane. Preliminary whole-cell patch clamp data showed decreased K+ current through the mutant T153I channel, indicating a loss-of-function mutation. Conclusions: Our results showed that the T153I mutation in the KCNJ13 gene is a novel Kir7.1 mutation that causes a variation of LCA. Replacement of the polar threonine with the non-polar isoleucine likely results in a structural alteration of Kir7.1, which affects channel closure, severely decreases inward K+ current, and compromises the integrity of the sub-retinal space. These findings provide further insight into the mechanisms of LCA pathobiology.
‘INACTIONABLE’ MUTATIONS IN LONG-TERM SURVIVORS WITH METASTATIC BREAST CANCER, A DESCRIPTIVE AND GENOMIC ANALYSIS STUDY

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Department: Medicine, University of Wisconsin School of Medicine and Public Health

Mentor: Mark Burkard, MD, PhD

Support: Shapiro Summer Research Program; Department of Medicine

Background: Breast cancer has highly variable clinical course. For untreated breast cancer of all types, half of individuals die within 2.7 years, yet 3.6% live >10 years (Bloom et al). Today, effective therapies have increased the likelihood of surviving with incurable cancer over long periods of time, yet there remains significant diversity in clinical outcomes amongst patients with similar treatment (Yardley et al). If the specific determinants of long-term survivorship were known, these individuals could be identified at diagnosis and a personalized treatment regimen could be devised. The purpose of this study is to identify unique genetic features of cancer patient who experience long-term survival with incurable cancer. We will assess the impact of patient characteristics, disease characteristics, therapies, and supportive care of patient outcomes.

Methods: Patients with metastatic breast cancer with longer survival than expected for their tumor type and receptor profile were identified using the University of Wisconsin Carbone Cancer Center (UWCCC) tumor registry from 1/1/1970 through present and/or querying current medical oncologists at University of Wisconsin Health. From the UWCCC tumor registry, we looked at the time from patient’s diagnosis with cancer to now and where the existence of metastatic cancer came into place. The factors used in determining the cohort of patients included how unusual the metastatic disease is to cancer experts and whether or not the patient’s tumor is accessible for biopsy. Results: We searched for long term-survivors with incurable breast cancer at our institution. Of the >350 individuals identified with metastatic cancer that survived for five years, 46 had hormone receptor (HR) positive breast cancer whereas 7 had HR negative breast cancer. At initial diagnosis of these 53 individuals 72% were diagnosed Stage II or less. The range of cancer burden for patients selected as part of the cohort to be sequenced was 216-464 months. Conclusion: From the data collected on the cohort of patients a sample of 15 patients were selected to be a part of the study and will have either fresh or archived biopsies of their tumor sequenced. After the patient’s tumor is biopsied, we plan to compare them with the database from The Cancer Genome Atlas in order to identify genetic patterns of similarity and/or differences that characterize these long-term survivors.

Citations:
THE MOLECULAR GENETICS OF PRIMARY CONGENITAL GLAUCOMA

Authors: Weeden Bauman, Terri Young, Stuart Tompson, Kristina Whisenhunt, Bethany Kloss

Department: Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health

Mentors: Terri Young, MD, MBA; Stuart Tompson, PhD; Kristina Whisenhunt, BS; Bethany Kloss, PhD

Support: Shapiro Summer Research Program; Department of Ophthalmology and Visual Sciences; Mentor funds

Introduction: Glaucoma is a disease that can cause vision loss when abnormally high pressure within the eye leads to optic nerve damage. Primary congenital glaucoma (PCG) is a severe inherited form of infantile glaucoma that can also present with an unusually large appearance of the eyes (buphthalmos). PCG is a major contributor to childhood blindness worldwide, but the molecular defects underlying the disease are only partially understood. The key risk factor contributing to glaucoma, and more specifically PCG, is elevated intraocular pressure (IOP), which is believed to result from defects in the aqueous humor outflow (AHO) pathway, including the ciliary body, trabecular meshwork, and Schlemm’s Canal. A deficiency in this pathway can create an imbalance in fluid homeostasis, leading to elevated IOP, increased eye size and optic nerve damage – the hallmarks of PCG. The principal goal of this research was to utilize data from exome sequencing technology to identify novel candidate genes that may be mutated in individuals with PCG.

Methods: The family proband and both parents were recruited and consented at UW Health University Station Clinic, Madison, WI. DNA samples were extracted from saliva, and exome sequencing was performed using a Nimblegen EZ v3 capture kit (Roche) and 100bp paired-end sequencing on a HiSeq2000 platform (Illumina). Exome sequence variants unrelated to the disease were filtered using Golden Helix’s SNP & Variation Suite (SVS) software. Candidate PCG-causing variants were prioritized by frequency, evolutionary conservation, relevant tissue expression of the gene and additional information from the literature.

Results: A list of 400 rare, conserved gene variants was identified in family 40016 through SVS filtering. 16 rare gene variants were prioritized based on literature searches in VarElect yielding a possible link to glaucoma. We further investigated two of these gene variants: a heterozygous non-synonymous missense mutation in the Inositol 1,4,5-Triphosphate Receptor Type 1 gene (ITPR1), and a heterozygous nonsynonymous missense mutation in the NOTCH1 gene (NOTCH1). The ITPR1 gene variant was harbored by the proband and the mother, while the NOTCH1 gene variant was found in the proband and the father. ITPR1 encodes an intracellular calcium channel, while NOTCH1 is an important signaling molecule involved in several processes such as angiogenesis, embryogenesis, and apoptosis. Conclusion: We identified rare gene variants in 16 candidate genes that may be causal for PCG. Two of these genes, ITPR1 and NOTCH1, were further investigated because they were both highly conserved, involved in apoptosis, and expressed in the trabecular meshwork of the eye.

Conclusions: We propose a possible digenic interaction between these two genes, with the proband inheriting a heterozygous variant in ITPR1 from his mother and NOTCH1 from his father. ITPR1 is differentially expressed in the trabecular meshwork, and a gain-of-function mutation causes increased intracellular Ca2+ which is a signal for apoptosis. Normally a molecule called BCL2 lowers this Ca2+ and aids in cell survival, but a mutation in NOTCH1 lowers levels of BCL2. Therefore, the trabecular meshwork cells with mutations in ITPR1 and NOTCH1 may succumb to apoptosis, damaging the drainage pathway for aqueous humor and raising IOP. The next steps will be to confirm the variants in these two genes by Sanger sequencing, to look for these same variants in other PCG families, and ultimately to make an animal model. If results are negative, other genes in the list of 400 rare, conserved variants may be further investigated.

Citations:
3. Ocular Tissue Database - https://genome.uiowa.edu/otdb/
MENISCUS T2 RELAXATION TIME AT VARIOUS STAGES OF KNEE JOINT DEGENERATION

Authors: Ben Beduhn, Fang Liu, Kaitlin Woo, Richard Kijowski

Department: Radiology, University of Wisconsin School of Medicine and Public Health

Mentor: Richard Kijowski, MD

Support: Shapiro Summer Research Program; Department of Radiology

Background: The T2 relaxation time of musculoskeletal tissue is a property of its composition and ultrastructure. This study was performed to investigate changes in meniscus T2 at various stages of knee joint degeneration. It is our hypothesis that subjects with more advanced joint degeneration will have higher meniscus T2 indicating greater disease-related changes in meniscus composition and ultra-structure.

Methods: An MRI sequence used to measure T2 relaxation time was performed on the knees of 121 patients with meniscus tears who underwent subsequent arthroscopic meniscus surgery. Regions of interest were placed around the medial and lateral meniscus to measure T2 of the torn and untorn portions of the meniscus with a tear and the T2 of the contralateral untorn meniscus. Radiographs were reviewed to determine the severity of knee joint degeneration using the Kellgren-Lawrence osteoarthritis grading scale (KL0=no osteoarthritis, KL1=minimal osteoarthritis, KL2=established osteoarthritis). The severity of cartilage loss within the medial and lateral compartments of the knee joint at arthroscopy was numerically scored. Kruskal-Wallis tests were used to compare meniscus T2 between KL0, KL1, and KL2 subjects, while Spearman correlation coefficients were used to correlate T2 of the medial and lateral meniscus and the severity of cartilage loss in the same compartment of the knee joint. Results: There was a significant difference (p<0.001) in meniscus T2 between KL0, KL1, and KL2 subjects in the torn and untorn portions of the meniscus with a tear and within the untorn contralateral meniscus with KL2 subjects having highest T2 and KL0 subjects having lowest T2. There was a significant direct moderate correlation (rho=0.535, p<0.001) between meniscus T2 and the severity of adjacent cartilage loss.

Conclusions: Meniscus T2 is progressively higher in individuals with worsening knee joint degeneration indicating that joint degeneration leads to changes in the composition and ultra-structure of both torn and untorn meniscus. The direct correlation between meniscus T2 and the severity of adjacent cartilage loss indicates the important inter-relationship between changes in the meniscus and cartilage that occur during the process of joint degeneration. Our results suggest that measurement of meniscus T2 with MRI may provide a new non-invasive method to assess changes in meniscus composition and ultrastructure in osteoarthritis research studies.
PREVALENCE OF PRESERVATIVES ACROSS ALL PRODUCT TYPES IN THE CONTACT ALLERGEN MANAGEMENT PROGRAM

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Mentor: Margo Reeder, MD

Support: Shapiro Summer Research Program; Department of Dermatology

Background: Preservatives in personal care products, topical medications, household products and industrial products are known causes of allergic contact dermatitis (ACD). The Contact Allergen Management Program (CAMP) is an American Contact Dermatitis Society (ACDS) database that providers can use to generate a list of safe products for patients with ACD to better assist them with allergen avoidance. The present study involved mapping preservative usage in all CAMP product categories to determine the prevalence of preservatives in each product category and in different product types. As sensitization rates for preservatives change over time, it is important for dermatologists and industry alike to compare the frequency of their use in the market with their current positive reaction rates.

Methods: CAMP product information was queried based on the 53 European Union and Association of Southeast Asian Nations approved preservatives in cosmetic products plus 5 additional preservatives used in U.S. products. The CAMP data was extracted and collated in Microsoft® Excel for further sorting and analysis. The prevalence of preservatives in CAMP was then compared with sensitization data published by the North American Contact Dermatitis Group (NACDG).

Results: Phenoxethanol (PE) and parabens were the most common preservatives found in CAMP with 23.9% of products containing PE and 20.75% of products containing parabens. PE and parabens were also the most common preservatives in the skin care, makeup, and nail care product categories. Methylisothiazolinone (MI) was found in 12.9% of products, most commonly in hair care and household products. Nearly 10% of CAMP products contained at least one of the five most common formaldehyde-releasing preservatives (FRPs). Preservatives that are both common in products and have a high incidence of ACD, like MI and methylchloroisothiazolinone (MCI), are of greatest concern as contact allergy hazards. PE and parabens are common, highly efficacious, and have weak sensitizing power, making them preferred preservatives.

Conclusion: Evaluating the prevalence of preservatives provides important information on allergen exposures in various topical products. By comparing the prevalence of preservatives with their current positive reaction rates, the risk of sensitization to a given preservative can be more accurately estimated and may affect the use of certain preservatives by industry in the future.
AN ANALYSIS OF AMBULATION IN TRAUMA PATIENTS

Authors: Ashok Bhattarai, Tiffany Zens, Megan Beems, Timothy Xiong, Suresh Agarwal

Department: Surgery, University of Wisconsin School of Medicine and Public Health

Mentors: Suresh Agarwal, MD; Tiffany Zens, MD; Megan Beems, MD

Support: Shapiro Summer Research Program; Department of Surgery

Introduction: Traumatic injuries often lead to prolonged bed rest and immobilization in patients. Early ambulation is essential in these patients to avoid complications of immobility including blood clots, muscle atrophy, and pneumonia. Unfortunately, there are many perceived and actual barriers to ambulation in the trauma patient population, and research is lacking to understand these. The aim of this study was to examine current health care provider attitudes towards ambulation, as well as, perceived and actual barriers to ambulation in UW trauma patients which could be targets for future interventions for quality improvement initiatives. Methods: A survey was developed and distributed to UW trauma faculty, trauma residents, trauma nurse practitioners, trauma nurses, and trauma physical therapists (PT) and occupational therapists (OT) in order to assess their attitudes towards patient ambulation, and perceived barriers to ambulation. Next, Fitbit devices were applied to trauma patients to assess post-injury ambulation. Data was compared between perceived and actual barriers to ambulation. Results: Of the 69 survey respondents (response rate of 54%), 8 were trauma faculty, 20 were residents, 4 were nurse practitioners, 16 were nurses, and 21 were PT/OT. 55% of providers (n=69) thought nursing was primarily responsible for walking trauma patients but only 40% of RNs (n=15) felt comfortable walking trauma patients without PT seeing them first. The more years of experience a provider had, the more likely they were to think the responsibility of patient ambulation fell within the domain of their practice, and the less likely they were to think that nursing was primarily responsible for ambulating patients. Interestingly, 67% of PTs believed patient ambulation was the responsibility of the entire care team. When evaluating the timing of ambulation, 49% of providers (n=69) thought trauma patients started walking on hospital day 1, and 32% thought they started walking on hospital day 2; Fitbit data showed on average, patients (n=11) started walking on hospital day 1. In addition, 38% of the providers (n=63) believed counting walks was an accurate way of assessing patient activity but Fitbit data showed the number of steps per walk ranged from 80 to 4246. When assessing barriers to ambulation, the top three perceived barriers were 1) waiting for radiology clearance, 2) waiting for clearance from a consulting service, and 3) awaiting brace placement. Analysis of our trauma patients demonstrated the most common actual barriers were 1) waiting for clearance from a consulting service, 2) waiting for radiology clearance, and 3) delay in MD placing an order. Conclusion: There are discrepancies between views surrounding patient ambulation among interdisciplinary team members. Quality improvement initiatives to formalize a plan for patient ambulation, as well as, expediting the hospital services would improve our patients’ ability to ambulate early.
PROCESS EVALUATION OF THE RESOURCE NAVIGATOR PROGRAM AT WINGRA FAMILY MEDICAL CENTER: FINDINGS, RECOMMENDATIONS, AND CONSIDERATIONS

Authors: Casey Birschbach, Rachel Grob

Department: Center for Patient Partnerships, University of Wisconsin-Madison

Mentor: Rachel Grob, MA, PhD

Support: Shapiro Summer Research Program; Center for Patient Partnerships

Background: For children living with stressful social factors related to poverty, poor behavioral and developmental outcomes are more common than for the population at large.1 Informed by programs such as HealthLeads, the Resource Navigator Program was developed to address inequities in child health and development in Wisconsin. Implemented in spring of 2016 at Wingra Family Medical Center, the program screens for un-met needs related to social determinants of health (SDOH). Pre-health University of Wisconsin-Madison undergraduate students trained as Resource Navigators then review the screening forms and connect patients with relevant resources in the community. Methods: A subset of the program’s implementation team conducted a process evaluation of the program in order to assess progress toward the goals of the program and to inform ongoing program development in the following areas: patient interactions and resources provided, workflow and implementation, Navigator learning and experience, and community needs and strengths. For this process evaluation, we analyzed Navigator reflections, interviews with Wingra clinic staff members, and documentation from 151 patient cases opened from March 31, 2016 through July 15, 2016. Results: Based on staff interviews, the program increased the capacity of the clinic to talk to patients about SDOH. The areas with the highest number of positive screens were “utility/bills assistance” and “skills training”, and documentation indicated that Navigators were able to find reliable resources to address needs in these areas. Although the majority of patients received resources (70.2%), Navigators were unable to address all of the needs of most patients. Navigators valued patient interaction and began to understand structural barriers and the limitations of the program, but Navigators were not familiar with self-care as a way to maintain wellness. Staff members thought that the program fit the mission of Wingra clinic but suggested a better introduction to the program, improved collaboration with clinic staff, and changes to the program’s workflow. Conclusion: Based on the findings of this process evaluation, we suggest that the implementation team considers greater collaboration with the Community Resource Specialists (CRSs) in the clinic, along with a re-introduction to the program and an update on the success of the program for the clinic staff. We also recommend incorporating exercises on self-care and recognizing personal biases into Navigator training. We see potential for this program in a subsequent phase or in replication to gain from greater integration into the healthcare team, and patients may benefit from extended models of patient interaction, such as “warm hand-offs”, as seen in other clinical navigator programs.2,3 Future formal evaluations of program impact may include patients’ perspectives on the program’s efficacy, along with the effects of the program on patients’ utilization of healthcare, patients’ health-related behaviors, and providers’ delivery of care.

Citations:
PERSONALIZING IRON DEFICIENCY SCREENING IN PEDIATRIC PRIMARY CARE

Authors: Nicholas Bohrer, Carol Diamond, Jeffrey Sleeth, Caroline Paul, Scott Hebbring, and Pamela Kling

Department: Pediatrics, University of Wisconsin School of Medicine and Public Health

Mentors: Pamela Kling, MD; Carol Diamond, MD

Support: University of Wisconsin Cardiovascular Research Center

Introduction: Untreated iron deficiency and iron deficiency anemia (ID/IDA) in infancy can impair neurocognitive development. Universal screening of hemoglobin (Hb) is recommended at one year of age, or earlier with risk factors. Initiation of a best practice alert in 2014 improved UW Health screening with Hb at one year of age. Hb is neither sensitive nor specific as a sole marker of body iron status, but is easy to obtain. This project has two aims. The Enhanced Screening aim assessed need for and then created an ID learning module for pediatric nurses and providers, to improve screening of high-risk infants. The Familial Hemoglobin aim utilized a dataset to further define the limitation of Hb as a sole iron screen by characterizing familial and environmental influences on Hb. Methods: Enhanced Screening: qualitative data was collected from observation of infant health supervision visits at five UW Health pediatric clinics, and a verbal needs assessment of clinic nurses. An online learning module was developed based on the American Academy of Pediatrics 2010 iron screening guidelines covering iron deficiency risk factors and nutrition/supplementation. Familial Hemoglobin: patient Hb/hematocrit data from two population-based datasets from the Marshfield Clinic are being analyzed at 9 months-3 years and 16-18 years of age, comparing Hb between twin-twin and parent-child pairs, to assess the relative influences of heritable and environmental factors on Hb over time. Results: Enhanced Screening: variability exists between nurses’ and providers’ attention to both ID screening and nutrition in general, and between UW Health pediatric clinics, are not evaluated earlier than 1 year. Familial Hemoglobin: initial data show that the distribution of Hb values are similar between male and female twins at 9 months-3 years, and gender differences emerge at 16-18 years of age, with non-normal distributions, especially for males. Values between twins are strongly related in early life and relationships continue into adolescence, even with twins of the opposite sex. Conclusion: Despite improvements in screening rates for identification of ID/IDA, the need exists to further improve and standardize screening practices, especially earlier screening in high-risk infants. We will continue to improve the learning module, and analyze screening data. Awareness that familial Hb pattern may predict Hb values, independent of iron status, supports using additional iron status indicators rather than solely Hb.
THE IMPACT OF PRE-SIMULATION ORIENTATION ON ANXIETY AND PERFORMANCE DURING A SURGERY INTERN PREPARATORY BOOT CAMP

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Support: Shapiro Summer Research Program; Department of Surgery

Background: Each July, recently graduated medical students become interns, a transition often associated with anxiety and lack of confidence. The positive impact of “boot camp” style surgical pre-residency preparatory courses has been documented, but no research addresses the role of orientation prior to simulation. A 2015 pilot study found that pre-simulation orientation decreased anxiety, increased confidence, and improved performance. The current study attempts to gather additional support for the hypothesis that orientation to this simulation environment improves clinical decision making during simulation while lowering anxiety and improving confidence. Methods: Fifteen fourth year medical students who matched into an accredited surgery internship participated in the two-week preparatory curriculum. Two weeks prior to the course, learners completed a survey assessing anxiety related to the surgical intern year. Baseline trait anxiety was also assessed via a six-question form of the 4-point Likert scale State-Trait Anxiety Index (STAI). Prior to the first simulation on day two of the course, participants were randomly divided into two groups with one group receiving an orientation to the simulation environment and the other group receiving no orientation prior to simulation. An attending/resident team evaluated each participant’s performance during the simulation. Learners participated in two additional clinical simulations on day nine of the course. Prior to the second simulation session, all students received orientation to the simulation environment. To measure simulation-specific anxiety, participants completed a six-question state portion of the STAI immediately preceding and following each simulation. Learners also completed a simulation-specific confidence survey adapted from Cato immediately following each simulation. Upon completion of the course, participants completed a course evaluation that reassessed anxiety levels surrounding intern year. Statistics were performed using non-parametric tests. One participant was excluded as an outlier. Results: The average trait score for the cohort was 2.12±0.23, suggesting that the learners did not tend to experience anxiety day-to-day. The cohort reported heightened anxiety immediately preceding the first simulation (state: 2.52±0.44, p=0.013). The oriented group experienced a significant decrease in state anxiety following their first simulation (2.48±0.46 vs. 1.90±0.47, p=0.034) while the control group did not. The oriented group had a significantly higher confidence level compared to the control group following both the second (3.20±0.58 vs. 2.14±0.32, p=0.004) and third (3.35±0.43 vs. 2.16±0.46, p=0.002) simulations. The oriented group also significantly outperformed the control group on both the second (4.10±0.47 vs. 1.98±0.68, p=0.001) and third (4.38±0.34 vs. 2.93±1.13, p=0.001) simulations. The cohort reported an overall decrease in anxiety related to the start of intern year (2.93±0.83 vs. 2.64±0.63); however, the result was not significant (p=0.157). Conclusion: Results from this year’s surgery intern prep course again support the use of pre-simulation orientation.
Background: The widespread use of sentinel lymph node biopsy has led to an increase in the diagnosis of breast cancer micrometastases. Although lymph node micrometastases have been shown to carry intermediate risk between node negative disease and macrometastatic disease, the optimal local treatment for women with micrometastatic breast cancer remains unclear. The purpose of this study was to analyze the care patterns and risk factors for recurrence for breast cancer patients with lymph node micrometastatic disease to help patients and physicians make more informed treatment decisions.

Methods: Data was collected from the records of 147 women with T1-3, pN1mi, M0 breast cancer treated at the UW Hospitals and Clinics between 2002 and 2015. The Kaplan-Meier method was used to compute overall survival (OS), disease-free survival (DFS), and recurrence rates. The multivariate Cox proportional hazards model was utilized to estimate risk associated with disease characteristics.

Results: The median follow-up time for all patients was 3.2 years (38.7 mos). The actuarial OS and DFS at 5 years were 87.7% ± 3.5% and 87.5% ± 3.2%, respectively. The 5-year locoregional control rate was 93.2% ± 2.3%. Multivariate analysis demonstrated that negative ER status, amplified HER2 status, and the absence of adjuvant radiation treatment were correlated to lower disease-free survival. Conclusions: ER status, HER2 status, and the receipt of radiation treatment affect the risk for recurrence in women with micrometastatic breast cancer. Women with lymph node micrometastases who are ER negative and/or HER2 positive should strongly consider adjuvant radiation treatment. Additional research directed at assessing the risk associated with molecular subtypes of breast cancer would help to further elucidate recurrence risk in this patient population.
EVIDENCE OF COGNITIVE IMPAIRMENT AMONG CONTINENCE-PROMOTION WORKSHOP PARTICIPANTS

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Support: Wisconsin Academy of Rural Medicine (WARM); Department of Obstetrics and Gynecology; Mentor funds

Introduction: Incontinence affects more than half of older adults and is even more prevalent in those with dementia. Incontinence contributes significantly to caregiver burden and is a driving force towards institutionalization for those individuals with cognitive impairment. During pilot testing of a non-pharmacological intervention promoting self-management of incontinence for older women, it became apparent that some workshop participants showed possible signs of early cognitive impairment that may have affected their participation in and benefits from the workshop. The objective of this study is to characterize cognitive impairment among workshop participants. Methods: We used conventional content analysis to perform a secondary analysis of data collected from a community-based continence promotion program pilot tested in five senior centers in four rural and urban counties in Wisconsin. Data included transcripts of five participant focus groups, following the final workshop session, and exit interviews with all of the workshop leaders. Quotes suggesting the possible presence of cognitive impairment were grouped into themes. Results: Emergent themes across the focus groups and workshop leader interviews included impairments with learning and memory, “I don’t remember seeing the video,” complex attention, “I don’t think I ever really understood the exercise itself,” and potentially executive function, “We’re not all twenty years old, that makes a difference, so our brain doesn’t work as fast.” Conclusion: The analysis of the pilot data is still underway, however our preliminary analysis suggests that some older women attending the workshops had memory impairment, difficulty with complex attention and potential problems with executive function. One limitation of this study is that we did not conduct formal cognitive testing. Another limitation is that the secondary analysis precluded our asking questions to specifically probe for cognitive impairment and its effects on participation and how we could improve the program. Given these limitations and in light of these preliminary findings, further research is needed to identify individuals with early cognitive impairment and understand how best to adapt the current continence promotion program to better meet their learning needs.
EVALUATING THE EFFECTS OF ETHNICITY AND LEGAL STATUS ON CHILDHOOD VACCINATIONS IN CHIANG MAI PROVINCE, THAILAND

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Background: Social disparities have a large impact on child health in Thailand. The origins of these disparities vary, and among them, displaced populations and those considered to be economic migrant groups are incredibly vulnerable. Being a migrant, particularly an undocumented migrant, presents acute barriers to receiving public healthcare services in many nation states, including Thailand. One of the largest population groups that have resettled in Thailand from Myanmar in the past 50 years are the Shan, mostly displaced from the Shan state. Upon arrival in Thailand, the Shan people often face insurmountable challenges to obtaining critical and affordable public health interventions. Particular interest lies in re-emerging infectious diseases, which disproportionately affect child health, due to Myanmar's inadequate surveillance and control of treatable infectious disease. Due to recent outbreaks of formerly controlled diseases on the Myanmar border of Thailand, a timely examination of childhood immunization rates in the region and the most important factors for determining receipt of these immunizations is extremely crucial.

Methods: This research project looks at childhood vaccination status in children sampled from northern Chiang Mai village communities, which is part of a larger, ongoing research study being conducted in the area. Data was collected through face-to-face interviews conducted by Thai and Shan research assistants throughout 2016 and is still ongoing. Interviews are recorded on paper questionnaires, including questions on demographics and childhood vaccinations. Results: Databases were created for the child health data and demographic information. Currently, child health data from 452 surveys have been entered. Data analysis has not yet started but a plan has been created for moving forward with the project. Conclusion: Next steps for this research project are to do preliminary data analysis, looking at the different vaccinations children in the study have or have not received and whether they were received according to the WHO childhood vaccination timeline. With a general idea of the vaccines children in the population have received, an in-depth analysis of important factors determining the receipt of vaccinations can be completed, such as ethnic minority status, birth documentation and registration, maternal education, and maternal language abilities.
SPECTRAL DOMAIN-OPTICAL COHERENCE TOMOGRAPHY (SD-OCT) IN TRACKING PROGRESSION OF GEOGRAPHIC ATROPHY IN INDIVIDUALS WITH LATE-STAGE DRY AMD

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Background: Age-related macular degeneration (AMD) is the leading cause of vision loss in individuals over 50 years old. AMD is a degenerative retinal disease with environmental and genetic causes, which progresses through early, intermediate, and late stages. Geographic atrophy (GA), the clinical appearance of a region with nearly complete loss of retinal pigment epithelium (RPE) surrounded by relatively healthy RPE, is diagnostic of late-stage AMD. GA area and growth is a common metric to evaluate the progression of late AMD. Current methods for measuring GA area include color fundus photography and fundus autofluorescence (FAF), however, both of these methods have limitations, especially accessibility [1]. SD-OCT is a widely available high resolution cross-sectional retinal imaging technique. Using novel software, it is now possible to measure GA using SD-OCT.

Methods: 42 participants with GA underwent FAF, color fundus photography, and SD-OCT imaging at baseline and subsequently at 6 and 12 months. Graders were instructed to follow established criteria [2] for color fundus photography and FAF to determine GA area in square millimeters. SD-OCT graders used two distinct criteria: 1) complete absence of RPE or 2) presence of hyper-reflective (‘waterfall’) area in choriocapillaris; to compute GA width on each B-scan, which are cross-sectional images of the retina. GA width measurements were transcribed to en face infrared reflectance images, which were used to manually trace the GA area in square millimeters. ANOVA was used to compare measurements of the three modalities and a Bland Altman plot was used to identify trends in measurement bias. Results: 7 participants were excluded from GA area measurements due to poor SD-OCT quality. Data collection is complete and is currently undergoing statistical analysis.

Conclusion: If SD-OCT proves to be an effective and reliable method to measure GA it will vastly expand the number of patients who can be monitored for GA size and growth, which is a critical component of recruiting participants for GA clinical trials. By increasing accessibility to GA monitoring using SD-OCT, we can accelerate GA research until we find a cure.

Citations:
THE EFFICACY AND SAFETY OF IMAGE-GUIDED PERCUTANEOUS MICROWAVE ABLATION IN TREATING METASTATIC TUMORS

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Background: Thermal ablation can provide a highly effective yet minimally invasive treatment for select patients with oligometastatic disease. Radiofrequency and cryoablation have historically been the preferred thermal ablation techniques. However, the drawbacks of long procedure times and susceptibility to heat sink, which increases risk for local tumor progression, have warranted the adoption of modern microwave ablation (MWA) systems. **Objective:** Our goal was to assess the safety and oncologic efficacy of MWA at a single center. **Methods:** A retrospective review of 97 patients with 203 metastatic tumors treated with percutaneous MWA using a high-powered, gas-cooled system (Certus 140, Neuwave Medical, Madison, WI) between January 2011 and February 2016 was conducted. Colorectal metastases (CRM) were treated in 40 patients (69 hepatic tumors, 13 extrahepatic tumors) and non-colorectal metastases (NCRM) treated in 57 patients (90 hepatic tumors, 31 extrahepatic tumors). Patients with NCRM included 13 with carcinoid/neuroendocrine, 10 gynecologic, 10 renal, 5 melanoma, 4 sarcoma, 3 breast, 3 pancreatic, 2 lung, 1 anal, 1 hepatocellular carcinoma, 2 esophageal, 1 pheochromocytoma, 1 thyroid, and 1 gastrointestinal stromal tumor. Procedural data was comprised of tumor size, antenna type and number, treatment time and power, and technical success. Following the procedure, complications, survival, local tumor progression, and extra and intra-organ progression were assessed by chart review and on follow-up imaging. **Results:** All procedures were technically successful. Mean power was 67 and mean treatment time was 7 minutes. Average CRM were 1.9 cm (range 0.6-5.0 cm) and NCRM 2.0 cm (range 0.3-6.0 cm). Local tumor progression occurred for 10.1% of hepatic CRM, 7.7% of extrahepatic CRM, 7.8% of extrahepatic CRM, and 6.4% of EH. There were 2 major complications (1.6%) which included femoral nerve injury following treatment of an iliopsoas sarcoma metastasis and hepatic abscess following treatment of a hepatic pancreatic metastasis. There was no procedure-related mortality. Overall survival is 69% at median 17.5 month follow-up. **Conclusions:** Image-guided percutaneous MWA for oligometastatic disease is safe with effective local tumor control when compared with predicate ablative modalities.
TRENDS IN PEDIATRIC PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH MENTAL HEALTH COMPLAINTS

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Background: The number of pediatric patients presenting to the Emergency department (ED) with mental health complaints is on the rise. While there is strong evidence that evaluation and treatment of these children utilizes substantial ancillary resources, national trends in ED treatment of these patients are unknown. This study aimed to determine national trends in treatment and disposition of pediatric patients presenting to the ED with mental health chief complaints. Methods: Data from 2005-2012 was extracted from the NHAMCS database. Patients ages 5-18 with a chief complaint of anxiety and nervousness, depression, psychosis, general psychiatric symptoms, other mental problems, intentional overdose or attempted suicide were analyzed. Statistics depicting trends over time as well as the frequency and median number of diagnostic tests based on chief complaint and disposition were determined. Results: Weighted total of 2,924,456 visits were identified from 2005 to 2012, which comprised 2% of total ED visits. General mental health and ‘other’ comprised 18.8% and 39.7% of the complaints, depression (16.3%), anxiety (11.4%), overdose (6.9%), psychosis (3.3%), and suicide attempt (3.6%). The median number of diagnostic tests performed and the median length of stay (LOS) rose from 0 tests and 161.82 minutes in 2005 to 3 tests and 208.97 minutes in 2012. The percent of patients who received at least 1 diagnostic test ranged from 60% to 75% without notable trend with the exception of 2005 (36.4%). The three most common tests were CBC (41%), UA (36.2%) and BMP (26.3%). Based on chief complaint, the median number of tests in decreasing order were intentional overdose (8), Suicide Attempt (5.2), Psychosis (3), Depression (2), Other (2), anxiety and nervousness (1), and general (1). Approximately 40% of visits resulted in admission without notable trend. The median number of tests varied by dispositions other than discharge: transferred to a psychiatric facility (4 tests), transferred to another hospital (6 tests), admit to hospital (3 tests) and admit for observation (4.14). These dispositions had longer LOS than those who were discharged. Conclusion: While our findings show that the number and proportion of children with mental health complaints have remained stable, the LOS and number of diagnostic tests performed have sharply increased. Approximately 40% of these visits result in admission and are associated with more diagnostic tests and increased ED LOS.
ETHICAL CONSIDERATIONS SURROUNDING MINOR KIDNEY DONATION AND CONCEPTION FOR SOLID ORGAN DONATION: A CASE STUDY

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Support: Shapiro Summer Research Program; Department of Medical History and Bioethics mentor funds

Background: Three decades ago at the University of Wisconsin, “RT,” a young man suffering from renal failure, received a kidney transplant from his 14-year-old sister, “KT.” RT had undergone two unsuccessful cadaver transplants 14 and 12 years prior to this third transplant, and had survived the intervening years on dialysis despite his worsening condition. While evaluating KT as a potential donor, it came to the attention of the transplant team and the UW Hospital Ethics Committee that she may have been conceived in the hope of someday serving as a donor to her brother. The possibility that KT had been conceived to act as a donor was a unique ethical issue at the time, as the earliest cases of conception for the donation were yet to be reported. While children have since been conceived to act as cord blood or bone marrow donors, there have been no documented cases of a child being conceived to act as a living solid organ donor. Prior analyses of conception for donation have declared the practice of conceiving solid organ donors as unethical on the basis that the transplantation procedure would place the donor at too great a risk. The circumstances surrounding KT’s conception, and her status as a minor kidney donor, sheds new light on the problems surrounding minor organ donation and conception for donation. This project reports the events of the case and analyzes relevant ethical issues. Methods: Literature review, review of medical records, interviews with the providers and administrative personnel involved in the case, and interviews with the organ recipient and his family. Results: Review of records revealed that KT—who at the time of donation was believed to have been born nine months after the onset of RT’s illness—was born nine months before he fell ill. However, the circumstances surrounding the case of RT and KT demonstrate that there may be circumstances wherein a child conceived to act as a solid organ donor may be an appropriate candidate for donating an organ, even if they are a minor at the time of donation. Conclusion: Despite the decreased willingness to consider minors as living kidney donors, there is a potential that a family may attempt to utilize new reproductive technologies like preimplantation genetic diagnosis in order to conceive a potential living solid organ donor in the future. Contrary to previous analyses, the case of RT and KT demonstrates that conception for donation may be permissible in certain limited circumstances.
THE EFFECT OF SPORT SPECIALIZATION ON LOWER EXTREMITY INJURY RATES IN HIGH SCHOOL ATHLETES

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Background: Sport specialization has been shown to be associated with increased risk of musculoskeletal lower extremity injuries (LEI) in adolescent athletes presenting in clinical settings. However, the association of sport specialization and incidence of LEI has not been studied prospectively in a large population of adolescent athletes. Purpose: To compare the incidence of LEI in high school athletes who are classified as being specialized (SPEC) or not specialized (NoSPEC). Methods: Subjects (male and female, interscholastic athletes in grades 9-12) were recruited from 29 Wisconsin high schools during the 2015/16 school year. Subjects reported all of the interscholastic and club sports they participated in during the previous year and current school year, their primary sport and whether they specialized in their primary sport. Sport specialization was determined using the total score on a previously used 7 point scale (score: 0 - 3 = NoSPEC, score 4 - 6 = SPEC). Licensed athletic trainers at each school reported all athletic exposures and LEI that occurred for each subject for each interscholastic sport season they participated in during the school year. Analyses included group proportions, Odds Ratios (OR, [95%CI]) and median days lost due to injury (Med [IQR 25th,75th]). Multivariate Cox Proportional Hazards Ratios (HR, [95%CI]) were calculated to investigate association the incidence of LEI and sport specialization level while controlling for gender, grade, history of previous LEI, primary sport and number of primary sport competitions. Results: A total of N =1,525 subjects (Female = 50%, Age =16.1+1.1 yrs.) enrolled in the study. Subjects participated in 2,843 athletic seasons and 167,349 athletic exposures during the school year. Females (41%) were more likely to SPEC than Males (28%) (OR = 1.72 [1.39 – 2.13], p<0.001). The percentage of SPEC athletes was highest in soccer (46%) volleyball (43%), and basketball (37%) players. SPEC athletes (76%) were more likely to compete in a sports league outside of their high school setting than NoSPEC (35%) (OR = 3.22 [2.51 - 5.42], p<0.001) and more likely (OR = 2.50 [2.06 - 3.22], p<0.001) to report a previous time loss LEI (SPEC = 46%, NoSPEC = 24%). Two hundred thirty five (15%) subjects sustained a total of n = 276 new LEI that caused them to miss a median of 7.0 [2, 22.5] days. Injuries occurred most often to the ankle (34%) knee (25%) and upper leg (13%). Common injuries included ligament sprains (41%), muscle / tendon strains (25%) and tendonitis / tenosynovitis (20%). LEI were acute (66%) or gradual/ recurrent (34%) onset. Surgical treatment was required for 8% of the LEI. The rate of LEI for SPEC subjects (20%) was higher than NoSPEC subjects (13%) (HR= 1.52, [1.11 – 2.06] p=0.008). The percentage of recurrent / gradual onset LEI in SPEC subjects (42%) was higher than NoSPEC (20%) (OR = 2.83, [1.54 – 5.30] p < 0.001). Conclusion: Interscholastic athletes who specialized in a sport were more likely to sustain a LEI than athletes who did not specialize. This increased risk for LEI was present even when controlling for gender, grade, previous injury status, primary sport and competition volume. Sports medicine providers need to educate interscholastic athletes, parents and coaches regarding the increased risk of LEI for athletes who specialize in a single sport in high school.
ANATOMY OF FAMILY PHYSICIANS’ CLINICAL CARE WORK DAYS THROUGH DIRECT OBSERVATION

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Mentor: Brian Arndt, MD

Support: Student Summer Research and Clinical Assistantship, Department of Family Medicine and Community Health

Background: There is growing evidence related to electronic health record (EHR) system impact on quality and safety of healthcare services. However, it is unclear how primary care physician (PCP) workload is impacted by EHR use based on evolving provision of non-face-to-face patient care tasks such as electronic communication with patients. The objective of this study is to assess time and usage patterns of PCPs interacting with an EHR system via direct observation. Design: Time and motion study. Setting: Family Medicine residency clinics and community clinics. Participants: 14 family physicians with a diversity of age, FTE, self-reported EHR efficiency, gender, and clinical settings. Instrument: Direct observation with physicians scheduled in clinic between work hours 8a-6p Monday through Friday. The WorkStudy+ application was used on an iPad to track all face-to-face and non-face-to-face patient care activities to help validate previously obtained EHR system physician access logs from an enterprise data warehouse. Outcome measures: Time spent on various face-to-face and non-face-to-face EHR and non-EHR tasks between 8a-6p Monday through Friday. Results: Non-EHR activities accounted for 60% of physicians’ clinical care workdays with direct clinical care accounting for 63% of that time with the remaining time for staff interactions, email, and other non-EHR administrative work. Physicians spent 40% of their clinical workday interacting with the EHR. The largest EHR time components were documentation (37%), chart review of notes (13%), and order entry (11%). These results were similar to results obtained from EHR system access logs. Conclusions: Physicians spend a large portion of their clinical days interacting with the EHR, and EHR system access logs provide a useful tool for analyzing physician time usage. These findings have implications for physician satisfaction, primary care workflow design, and policy.
BEST PRACTICE FOR TOBACCO CESSIONATION IN MEDIC CLINICS

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Support: Shapiro Summer Research Program; Prevention Innovations in Medical Education (PRIME-Madison)

Background: Tobacco use is the leading preventable cause of death in the United States. In Wisconsin, approximately 20% of the adult population are current cigarette smokers. Populations with low educational attainment and high rates of poverty are more likely to use tobacco; the same populations are likely to seek care at free clinics. MEDiC student-run free clinics operate around Madison, WI providing free acute care to patients. The purpose of this study was to evaluate current tobacco use screening and intervention practices within MEDiC clinics. Methods: Data from the electronic health record database (PED) was reviewed to determine the proportion of patients screened for tobacco use; descriptive statistics were performed to characterize those screened, with regard to demographics, chief complaint, and clinic attended. Logistic regression was performed to identify predictors to screening. Observational data on screening and intervention was collected by in-person visits to three MEDiC clinics. Key informant interviews were conducted with thirteen individuals involved with MEDiC then analyzed for themes. Results: Tobacco use was screened in 56.2% of encounters (N=2302). Clinic and chief complaint were found to be significant predictors of being screened. Patients at Salvation Army were most frequently screened (66.3%) and were more likely to be screened than those at Safe Haven (OR 13.5, CI 5.6-32.6). Patients with a respiratory chief complaint were most likely to be screened (78.8%), and were significantly more likely to be screened than those with chief complaints that were cardiovascular (OR 1.9, CI 1.1-3.5), dental (OR 2.0, CI 1.0-3.9), musculoskeletal (OR 2.4, CI 1.5-4.0), or dermatologic (OR 2.8, CI 1.7-4.8). Observational data showed that inconsistent assessment and handling of tobacco use by the student volunteers. Key informant interviews highlighted limited time and prioritization as barriers and increased volunteer education and PED changes as possible facilitators to tobacco use screening and intervention. Conclusion: The current rate of tobacco use screening falls short of clinical guidelines. Potential improvements to screening that should be explored include the following: 1) emphasize tobacco screening as a priority during pre-clinic orientation, 2) modify the PED to incorporate tobacco screening protocols into the workflow; and 3) educate MEDiC volunteers on community cessation resources that can provide long-term follow-up.
EVALUATION OF INJURY PREVENTION PROGRAMS AT AMERICAN FAMILY CHILDREN’S HOSPITAL

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Support: Shapiro Summer Research Program; Prevention Innovations in Medical Education (PRIME-Madison)

Background: Unintentional injuries are the leading cause of death each year among children in the United States and disproportionately impact minority and low-income families. The American Family Children’s Hospital (AFCH) offers unique services to reduce injuries throughout Dane County, including the Kohl’s Safety Center (KSC) and Safe Kids Madison Area (SKMA) program. Objective: We aimed to 1) determine if the AFCH programs are sufficient to meet the needs of low-income families and children in Dane County and 2) examine barriers to the AFCH injury prevention programs. Methods: A paper survey was completed by 50 randomly selected customers at the KSC. The survey collected demographic information, KSC-specific questions, and asked parents/caregivers to rate their knowledge of safety topics. Descriptive statistics were used to describe the collected data. Additionally, in-person or phone interviews were conducted with key informants at 8 Dane County community agencies. Current relationships with KSC and SKMA, barriers to working with the injury prevention program, and opportunities for program improvement were discussed. Interview notes were then coded to identify recurring themes. Results: Of those surveyed, 98% identified as White and 71% had an annual household income ≥$75,000. Approximately 80% of individuals surveyed learned about the KSC through family or friends, and there was broad distribution of child ages for whom parents/caregivers were shopping. For those surveyed, there was minimal concern with transportation or language barriers but 32% found the hours inconvenient. Additionally, nearly all surveyed customers were pleased with the selection and prices of products and services and education offered at the Safety Center. The key informant interview highlighted the following major themes about the KSC and SKMA: income and transportation as barriers, lack of outreach in the community, and the KSC being inconvenient due to hours and location. Conclusions: While customers coming to the KSC are pleased with the products and services that are provided and note limited barrier, these individuals do not seem representative of the Dane County population. Numerous opportunities exist to improve KSC and SKMA service to reach a broader population in Dane County and better address injury disparities. Evidence-based best practices should be used to expand outreach of programs to low income areas in Dane County.
MORCELLATION DURING HYSTERECTOMY OR MYOMECTOMY AT THE UNIVERSITY OF WISCONSIN HOSPITAL AND CLINICS AND MERITER HOSPITAL

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Mentor: Dobie Giles, MD

Support: Shapiro Summer Research Program, Department of Obstetrics and Gynecology

Background: Uterine morcellation is a surgical method used during minimally invasive hysterectomy or myomectomy that allows for fragmentation of the uterine tissue before removal via laparoscopic ports. Benefits of morcellation include decreased recovery time, pain, complications, and risk of surgical site infections. However, morcellation is controversial because if used on an unsuspected uterine cancer, may spread the cancer and result in poorer prognosis. Leiomyosarcoma (LMS) is a uterine smooth muscle tumor that is of concern with morcellation because once metastasized, LMS has a 5-year survival rate of 14%. The Food and Drug Administration (FDA) estimates the rate of unsuspected LMS during hysterectomy or myomectomy to be 1 in 4983 and has banned the use of power morcellation. Other studies estimate occult LMS to occur in 1 in 2,000 and 1 in 8,300 cases. There is a need to correctly estimate the number of unsuspected LMS during hysterectomy or myomectomy in order to weigh the risks of tumor spread versus the benefits of minimally invasive surgery. This study is multi-institutional and the large, diverse sample will allow for a better understanding of the risks associated with LMS and uterine morcellation. This interim analysis looks at characteristics of cases at UWHC and Meriter that did and did not involve morcellation.

Methods: A retrospective chart review of 270 cases was performed. Females aged 18-90 who received a hysterectomy or myomectomy at UWHC or Meriter between January 2004 and August 2014 were included. Information was extracted from electronic medical records and descriptive data analysis was performed.

Results: The prevalence of unsuspected LMS in the sample was 1 in 270 and this case was in the non-morcellated group. Women in the morcellated group tended to be younger with an average age of 47 compared to 57 for women in the non-morcellated group. Women receiving morcellation had higher rates of prior uterine surgery (61.7% vs. 50.5%), history of abnormal uterine bleeding (72.3% vs. 52.5%), history of smoking (48.9% vs. 34.7%), and preoperative reports of pain (51.1% vs. 32.9%). Compared to women in the non-morcellated group, women in the morcellated group were more likely to have a laparoscopic (17.0% vs. 9.4%) or vaginal (83.0% vs. 70.4%) surgery. Pathology showed that women in the morcellated group had larger uteri (260.95 g vs. 153.72 g) and a higher rate of uterine fibroids (83.0% vs. 58.3%).

Conclusion: More cases need to be reviewed to determine the prevalence of LMS in women receiving hysterectomy or myomectomy. This study will continue at the University of Wisconsin, with a total of 8,064 charts needing review. With this information and data from the other institutions, we will be better equipped to assess the risk posed by morcellation during uterine surgery.

Citations:
   http://doi.org/10.1007/s10397-015-0894-4
PATIENT PERSPECTIVES ON ACCESSING ACUTE ILLNESS CARE

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Mentors: Manish N. Shah, MD, MPH; Nicole E. Werner, PhD

Support: Wisconsin Academy of Rural Medicine (WARM); BerbeeWalsh Department of Emergency Medicine; University of Rochester Provost’s Multidisciplinary Award

Background: Rather than consulting with primary care providers (PCPs), older adults frequently utilize emergency departments (EDs) for minor acute illness care; due to the chaotic environment and potentially dangerous effects of EDs on the health of an older adult, the reasons for their common use by this demographic are not clear. This hypothesis-generating study explored older adults’ perspectives on the factors that influence whether they obtain care for acute illnesses in the ED or from their PCP. We aimed to measure older adults’ views to inform the optimal structure of the healthcare system. Methods: We performed a qualitative study of community-dwelling older adults (age ≥65 years) presenting to an academic medical center ED for care. A convenient sample of 27 subjects were enrolled, 12 of whom returned to the ED within 30 days, and 15 of whom did not. Semi-structured interviews were conducted during the ED visit and over the subsequent weeks. Interviews were recorded, transcribed, coded, and analyzed using a directed content analysis approach. Subjects were enrolled until the study team felt saturation had been reached. Results: Five themes were identified that influence where older adults obtain care for acute illnesses: 1) care availability, 2) transport availability, 3) burden on friends/family, 4) interactions with healthcare providers and systems, and 5) personal experience with and reaction to illness. These themes were further categorized as individual-level or systems-level factors. Themes 3, 4, and 5 fell under individual-level factors, while themes 1, 2, and 4 fell under systems-level factors. Some individual-level factors (e.g. strong relationship with their PCP, variable ED experiences) supported PCP use, yet others (e.g. fear of burdening family, loved ones’ advice, previous experiences with similar illness) supported ED use. Systems-level factors (e.g. variable access to PCP appointments, lack of public transport to PCP offices, frequent referral by PCPs to the ED) all tended to support ED use. Conclusion: Many individual- and systems-level factors influence older adults’ decisions regarding where to obtain acute illness care for minor conditions. This decision-making process integrates their experiences, personality, resources, and relationships with caregivers, healthcare providers, and the healthcare system. Additionally, this decision-making is person-centered, rather than dependent on medical symptoms. Our findings will be utilized to design larger, multi-centered trials on acute care decision-making in older adults, and need to be considered when developing innovative models to provide older adults acute illness care.
RELATIONSHIP OF ATHEROSCLEROTIC RISK WITH ALZHEIMER’S DISEASE CEREBROSPINAL FLUID BIOMARKERS OF INFLAMMATION IN AT-RISK ADULTS


Department: Medicine, University of Wisconsin School of Medicine and Public Health; Wisconsin Alzheimer’s Disease Research Center (ADRC); Madison VA Geriatric Research, Education & Clinical Center (GRECC), Madison, Wisconsin, USA; Sahlgrenska Academy at the University of Gothenburg, Mölndal, Sweden; University College London, UK.

Mentor: Cynthia Carlsson, MD, MS

Support: Shapiro Summer Research Program; Department of Medicine

Introduction: Epidemiological studies show adults with hypercholesterolemia in midlife are at increased risk of developing Alzheimer’s disease (AD) as they age. Statins have been proposed as a potential primary preventive strategy for AD in people at risk for developing the disease. The purpose of this study is to determine if measures of baseline atherosclerotic risk correlate with biomarkers of brain inflammation or cognition, and if simvastatin treatment lowers levels of these biomarkers and improves cognition in a clinical study of at risk adults. Methods: Eighty-eight non-demented, middle aged adults with a parental history of AD were randomized in a 1:1 ratio to simvastatin 40 mg daily (n=44) vs matching placebo (n=44) in the 18-month, double blind clinical study. 10-year atherosclerotic cardiovascular disease (ASCVD) risk scores were calculated using the American Heart Association risk estimator. Cerebrospinal fluid (CSF) biomarkers neurofilament light chain protein (NFL), monocyte chemoattractant protein (MCP-1), and chitinase-3-like protein 1 (YKL-40) were analyzed using standardized assays. The cognitive battery in this analysis consisted of seven tests measuring performance in learning, memory, processing speed, and executive function. Results: NFL, MCP-1, and YKL-40 were all correlated to baseline ASCVD risk (p < 0.02), but in regression models adjusted for age, only NFL was predicted by baseline ASCVD risk (p = 0.004). Of the seven cognitive tests, higher baseline ASCVD risk and NFL levels were correlated with lower Digit Symbol and Stroop Color Word Interference scores (all p < 0.05). Higher CSF NFL was correlated with longer Trail Making B times, and this association held true in regression models adjusted for age and education (p = 0.026). Subjects treated with simvastatin had similar changes in CSF biomarkers and cognitive test scores as subjects treated with matching placebo (all p > 0.10). Conclusion: The relationship observed between increased 10-year ASCVD risk and CSF NFL levels supports vascular health being important for neuronal health, as increased NFL is indicative of white matter damage in the brain. However, in this population of healthy adults at risk for developing AD, simvastatin treatment did not decrease levels of CSF biomarkers nor improve cognitive measures compared to matching placebo treatment. Future studies with larger sample sizes and longer durations will help to determine if simvastatin has a role in the prevention of AD in at-risk adults.
HIGH-RESOLUTION MANOMETRY OF PHARYNGEAL SWALLOWING PRESSURE EVENTS AND RELATED HYOID MOVEMENTS IN NORMAL SWALLOWING

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Department: Surgery, Division of Otolaryngology-Head & Neck Surgery, University of Wisconsin School of Medicine and Public Health

Mentors: Timothy M. McCulloch, MD; Corinne Jones, MS, CCC-SLP; Sarah Rosen, MD; Chelsea Walczack, BS

Support: Department of Surgery NIH T32-DC009401 grant

Introduction: Hyoid bone movement, following activation of suprahyoid muscles (stylohyoid, anterior and posterior digastic, geniohyoid, and mylohyoid), is important in the swallowing process contributing to laryngeal elevation, laryngeal vestibule closure, and upper esophageal sphincter (UES) opening. High-resolution manometry (HRM), in conjunction with videofluoroscopic studies, can help identify the relationship between hyoid kinematics and swallowing pressures in regions of interest, a relationship we do not currently have a clear understanding of. We hypothesized that maximum pharyngeal pressures would be positively related to hyoid movement while nadir UES pressures would be negatively related. We also hypothesized that taller individuals (those with greater C2 to C4 cervical spine length) would have increased maximal pharyngeal and decreased nadir UES pressures.

Methods: Simultaneous HRM and videofluoroscopy were recorded in 67 (aged 50.7 ± 2.6 years, 28 M) healthy volunteers while swallowing 10 mL thin liquid barium boluses 10 times. Hyoid displacement was measured in anterior and superior directions, as well as anterior-superior displacement from the starting position and from the spine. Distance data were normalized to the length of the C2 to C4 cervical spine height. Manometric data were extracted via a custom Matlab program. Statistical analysis compared hyoid displacements to velopharyngeal, mesopharyngeal, and UES pressures via multiple regression. The relationship between UES opening duration and nadir UES pressure duration with the duration of hyoid movement was calculated via Pearson correlation.

Results: Maximum velopharyngeal pressure was positively related to maximum superior hyoid displacement (p=0.05) while maximum mesopharyngeal pressure was negatively related to maximum superior (p=0.016), and anterior-superior hyoid displacement from both the starting position (p=0.03) and the spine (p=0.018). There was a weak positive correlation between UES opening duration and duration of hyoid excursion (r = 0.264; p=0.031). Nadir UES pressure was negatively related to cervical length (p=0.044).

Conclusions: Increases in hyoid bone excursion may be related to increased positive pressure in the velopharynx important for bolus propulsion. Increases in hyoid bone excursion may result in diminished pressure in the UES, reducing the need for bolus clearance pressure in the mesopharyngeal region. A larger pharynx appears to have capacity for increased UES opening and thus lower nadir pressures during swallow. With future study we hope to confirm the temporal association between the kinematic measurements and the pressure events recorded. This type of information can be used to identify therapeutic targets to treat swallowing disorders.
IDENTIFYING INDEPENDENT RISK FACTORS FOR INJURY IN FEMALE YOUTH ATHLETES

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Mentors: Andrew Watson, MD, MS; Stacey Brickson, PhD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

Background: Sports participation is associated with increased risk of injury. Recent studies suggest that acute:chronic training load (TL) ratio may be a useful predictor of injury risk in adult athletes. The purpose of this study was to determine if TL is an independent risk factor for injury in adolescent female athletes.

Methods: A cohort of 75 female soccer players (13-18 years old) were followed for a 12-month training period. Participants recorded TL for all activity, calculated as exercise duration (minutes) multiplied by subjective intensity (1-10). Injuries resulting in time loss were self-reported throughout the season. TL was expressed as daily, weekly, monthly, and acute:chronic (ratio of daily divided by monthly). TL variables were aggregated by day and compared between days with and without an injury. Poisson regression was used with acute:chronic TL as a predictor to predict the number of injuries per day.

Results: Forty-eight injuries were recorded. Days on which injuries occurred had higher daily TL (16769±9177 v 9805±7690, p<0.001, Cohen's d = -0.88), weekly TL (12441±4049 v 10514±3550, p=0.005, Cohen's d = -0.53), and acute:chronic TL (1.39±0.62 v 0.88±0.59, p<0.001, Cohen's d = -0.84), but not monthly TL (11285±2978 v 10581±2885, p=0.21, Cohen's d = -0.24). Daily TL (odds ratio [OR]=1.0001 [95% CI 1.000-1.001], p<0.001), weekly TL ([OR]=1.0001 [95% CI 1.000-1.001], p=0.001), and monthly TL ([OR]=1.0001 [95% CI 1.000-1.001], p<0.001) were significant predictors of injury. Acute:chronic TL was also a significant, independent predictor of injury ([OR]=2.8 [95% CI 1.8-4.5], p<0.001).

Conclusion: Among youth female soccer players, higher daily, weekly, and acute:chronic TL ratios are associated with increased risk of injury, while chronic TL is not. A half-unit increase in the acute:chronic TL ratio (50% increase in TL relative to the preceding month) was shown to predict a 90% increase in injury within the group. Our results suggest that real-time monitoring of daily TL among female youth athletes can potentially guide training prescription to reduce in-season injury. Future studies should account for the influences of other potential risk factors such as sport specialization, age, fitness, and subjective-wellbeing to identify independent, modifiable risk factors for injury.
A CLINICAL APPROACH TO ASSESSING HIGH RISK HERBAL-DRUG INTERACTIONS

Author: Julie Friedman

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Mentor: David Kiefer, MD

Support: Summer Student Research and Clinical Assistantship, Department of Family Medicine and Community Health

Background: Herbal medicine use is common among patients in the United States with recent estimates ranging from 18-30% and increasing across demographics. Nonetheless, in contrast to widespread media coverage on the risks of herb-drug interactions (HDI), there remain many unknowns about the specifics of HDI such as which HDI are clinically relevant and who is most at risk of HDI. Objective: To determine whether clinical diagnosis can be used to predict the presence of HDI and severity of risk. Methods: A literature search was used to gather qualitative data on themes of herbal drug use including high user populations, common types of herbals purchased, purpose of use, and studies on herbal-drug interactions. Additional basic statistical analysis was performed using SPSS to analyze the national survey of Midlife Development in the United States (MIDUS) 2 Project 4 database that collected biomarker assessments on a subsample of respondents. Results: Clinical diagnoses did not significantly alter the kinds of herbal medicines patients were taking nor the reasons for taking them. Certain clinical diagnoses and number of chronic conditions did, however, alter the propensity to take herbal medicines and the number taken. Decreased herbal use was associated with diabetes, trouble sleeping, and fewer chronic conditions. Increased use was seen in patients with cancer, anemia, thyroid disease, trouble staying awake, and increased number of chronic diseases. Few HDIs were found possibly due to limited generalizability of the sample population and high incidence of non-herbal alternative medicine use. Conclusion: This study elucidates a clinical approach that may be needed to assess herbal-drug interactions not only based on the kinds of herbals patients are taking, but importantly the number of herbals they are using. Most of the current research in the herbal medicine field is based on in vitro or animal models and has minimal clinical applicability. Standard of care among physicians commonly involves discontinuing their patients’ use of herbal medicine or reducing doses to inefficacious levels, but this may not be the most effective method to counsel patients. Providing clinicians with pertinent information about herbal use can facilitate better disclosure rates and hopefully more efficient and accurate identification of unsafe herbal-drug interactions.
ALTERNATIVE PROVIDERS’ CONTRIBUTION TO THE RISE OF ANTIBIOTIC RESISTANCE IN RURAL INDIA

Authors: Youhi Ghouse

Department: Pediatrics, University of Wisconsin School of Medicine and Public Health

Mentors: James Conway, MD

Support: Shapiro Summer Research Program; Department of Pediatrics; Medanta the Medicity Hospital; Clinical Research Department

Background: Antibiotic resistance is a rapidly growing problem throughout today's world. There is significant research being conducted to find solutions for this increasingly global problem; however, developing countries are still lagging behind in regards to research and management of antibiotics. In India specifically, their massive population density, lack of antibiotic knowledge on the prescriber’s part, mass production and cheap prices, make it a hotspot for the growth of antibiotic resistance. Much of India’s population also practices a variety of medicines in addition to allopathy, such as ayurvedic, unani, and homeopathy. There is little research that has studied if these alternative providers who practice different forms of medicine prescribe and dispense antibiotics, and if so, how often, correctly, etc. Methods: We conducted a qualitative study in the villages and rural areas surrounding Gurgaon, Haryana, India. We created two surveys: one survey focusing on the knowledge, attitude, and dispensing habits of alternative providers and the other focusing on knowledge and seeking habits of community members. For the purpose of this study, alternative providers were defined as healthcare providers who did not have an M.D or M.B.B.S. Community members were those who were seen at the alternative providers’ offices. 19 alternative providers and 17 community members were identified and interviewed in Hindi with the help of Medanta Hospital research staff. The survey included scenarios, multiple choice questions, and open-ended questions. Results: We found that the majority of alternative providers in India, regardless of the specific form of medicine they studied or practiced, prescribed antibiotics despite not being legally allowed to. Many community members said they trusted their local provider with what they prescribed. Several factors seemed to contribute to inappropriate antibiotic use, from convenience, education, location, reputation, to cost of travel and services. Furthermore, majority of alternative providers felt very confident when prescribing or dispensing antibiotics, however, many of these providers were unable to give a correct definition of antibiotics or antibiotic resistance. In general, alternative providers and community members agreed that antibiotics were used too often. Conclusion: This was a small-scale study with several limitations. To better understand which steps to take next, a similar study on a much larger scale in rural and urban areas in India should be done. Based on this study’s findings, there needs to be tighter control of antibiotic dispensing and/or more formal training regarding antibiotic use. Just this year, India passed another law reinforcing that only M.D or M.B.B.S providers can prescribe antibiotics so steps are being taken to regulate how antibiotics are used in this country.
IDENTIFYING BARRIERS TO MRI AND ULTRASOUND USE IN THE EMERGENCY DEPARTMENT

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Mentor: Michael D. Repplinger, MD, PhD

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine; NIH National Center for Advancing Translational Sciences, grants UL1TR000427 and NIH KL2TR000428

Introduction: National imaging guidelines have been created in order to balance diagnostic accuracy with radiation exposure. Despite guidelines that suggest the use of ultrasound (US) or MRI rather than CT, such as in the case of pediatric appendicitis, CT use in the ED remains high for these cases. What is not fully understood is what barriers exist to adherence to these guidelines. The purpose of this study is to identify barriers and facilitators to guideline-adherent use of MRI and US in the ED. Methods: This was a prospective, qualitative study utilizing semi-structured focus group discussions. Groups were composed of emergency physicians as well as radiologists, and conducted at two large urban hospitals. Discussions were scheduled for 60 minutes, and moderated using a guide with open ended questions. All discussions were recorded, transcribed, and analyzed using conventional content analysis. Results: Barriers identified to guideline-adherent use of MRI and US in the ED included lack of guideline awareness due to the volume and ever-changing nature of guidelines, access and availability of technology, concerns over time in the department, patient factors, and lack of acceptance by other specialties. Facilitators identified included having a specific guideline-adherent protocol in place, having necessary technology available 24/7, and having experienced and proficient technicians. Overall, physician attitudes regarding using national imaging guidelines was found to be very positive. Conclusion: In order to take steps to improve adherence to national imaging guidelines, and to limit radiation exposure to patients, barriers to radiation-free imaging use must be fully understood. This study found that physicians want to follow these guidelines, but a number of external and environmental factors exist. Additionally, it is difficult for physicians to keep up to date with each specific guideline. In order to gain additional perspectives, and a fuller understanding of barriers, we plan on conducting future focus groups with imaging technicians and administrators as well as additional focus groups at smaller hospitals in suburban and rural areas.
ARE HOSPITALIZATIONS AMONG CHILDREN WITH MEDICAL COMPLEXITY SENSITIVE TO AMBULATORY CARE?

Authors: Evan Goyette, Mary Ehlenbach, Ryan Coller

Department: Pediatrics, University of Wisconsin School of Medicine and Public Health

Mentors: Ryan Coller, MD, MPH; Mary Ehlenbach, MD

Support: Shapiro Summer Research Program; Department of Pediatrics

Background: Hospitalizations for ambulatory-care sensitive conditions (ACSCs) are considered potentially preventable in general populations because they are thought to respond well to prompt, effective ambulatory care. The involvement of multiple severe chronic conditions, as seen in children with medical complexity (CMC), may impact the validity of this classification. Objective: To identify differences in ambulatory care between ACSC and non-ACSC hospitalizations for CMC and children with non-complex chronic diseases (NC-CD).

Methods: Retrospective cohort study including a 20% random sample of all hospitalizations to the pediatric hospital medicine service at American Family Children’s Hospital during 2007-2014. Hospitalizations for children with primary care providers outside UW Health were excluded to avoid missing continuity ambulatory care information. The Pediatric Medical Complexity Algorithm (PMCA) categorized children into CMC or NC-CD groups. Standard Agency for Healthcare Research and Quality definitions were used to identify ACSCs. Measures of ambulatory care quality which could be abstracted by chart review were identified from existing literature. Differences in ambulatory care quality measures were compared between ACSC and non-ACSC hospitalizations using logistic regression clustered by patient, stratified by PMCA category.

Results: Patient demographics (age, race/ethnicity, primarily language) were similar for discharges of CMC (n=180) and NC-CD (n=120); however, CMC discharges were more often publicly insured (36.7% vs 22.5%, P=0.01). Discharges were over 4 times more likely to be for ACSCs among patients with non-complex chronic conditions (P<0.001). Among NC-CD, discharges were also more likely to be for ACSCs than non-ACSCs when there were fewer timely well child care checks (P=0.003) and less primary care provider continuity (P=0.05) in the 2 years prior to hospitalization. No associations between ambulatory care quality and ACSC hospitalizations were observed among CMC.

Conclusion: Ambulatory care quality, particularly timely preventive care and primary care provider continuity, may be associated with fewer ACSCs among children with non-complex chronic conditions. It is not clear whether existing ACSCs are associated with ambulatory care among CMC. Future work should identify hospitalizations which are potentially avoidable through high-quality ambulatory care for this vulnerable population.
EVALUATING A SCALABLE, ONLINE, MULTIDISCIPLINARY SBIRT TRAINING PROGRAM

Author: Matt Guerrieri

Department: Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health

Mentors: Richard L. Brown, MD; Mia Croyle, MS

Support: Summer Student Research and Clinical Assistantship, Department of Family Medicine and Community Health

Introduction: Although SBIRT is widely recommended, many healthcare professionals lack competence to deliver SBIRT, and many training programs lack expertise to teach it. At the University of Wisconsin, 2,025 trainees of multiple disciplines will complete an online SBIRT curriculum between 2016 and 2018. We are assessing whether the program enhances trainees’ intention, knowledge and competency to deliver SBIRT, beginning with the results of a 2016 pilot. Methods: With funding from SAMHSA’s SBIRT Medical Professional Training Program, we developed a two-part, online SBIRT training. Part 1 consists of ten learning modules that address the rationale and steps for performing SBIRT. Modules include narrated slideshows, video demonstrations, quizzes and discussion forums. Part 2 includes one-on-one practice sessions via videoconference between trainees and trained actors. To assess competence, a final videotaped session was graded according to a skills checklist. Analyses compared trainee perceptions, knowledge, competence, and intentions before and after training, by discipline, and by additional factors. Results: As of June 2016, 496 trainees completed the curriculum: 294 nursing (268 BSN, 26 DNP), 171 medical (MD), 17 rehabilitation psychology (MS), and 14 social work (BSW) students. Average completion time was 7 hours. Across modules, a mean of 85% of trainees rated each module “very” or “mostly clear,” and 82% rated the pace “about right.” Most trainees (68%) were satisfied or very satisfied with their training experience. After the training, mean SBIRT knowledge scores improved 8% (p<.001). Of trainees who attempted the final skills assessment, 430 (83%) passed in one attempt. Incorrect classification of risk category was the leading reason for failure. Between 80-90% of trainees expected to use the information gained in the training, expected it to benefit their patients, and reported that it enhanced their skills. Overall favorability toward implementing SBIRT did not change significantly after the training but remained high (5.15 out of 7). Only pre-training favorability and training usefulness measures correlated with post-training favorability (p<.001). Conclusions: The pilot curriculum was acceptable to trainees across disciplines and successful in teaching SBIRT delivery. Specific feedback informed curricular modification. With continued evaluation, online SBIRT training may help strengthen national capacity to deliver SBIRT.
RESIDENTS’ RESPONSE TO BLEEDING DURING A SIMULATED ROBOTIC SURGERY EXPERIENCE

Authors: Jessica L. Hammes, Jay N. Nathwani, Shlomi Laufer, Frank F. Jocewicz III, Carla M. Pugh

Department: Surgery, University of Wisconsin School of Medicine and Public Health

Mentors: Carla M. Pugh MD, PhD; Jay N. Nathwani, MD

Support: Shapiro Summer Research Program; Department of Defense Grant W81XWH-13-1-0080

Introduction: As minimally invasive surgery with the da Vinci robot continues to broaden in clinical application, there is a critical need to develop applicable training tools. The aim of this study is to assess performance measurement validity of our newly developed robotic surgery trainer. Our hypothesis is that residents will exhibit wide variations in their performance, unrelated to post-graduate year (PGY).

Methods: Improvements to our previous model enhanced the visual and tactile nature of tissue, provided an accurate surgical working volume, and increased the realism of the simulation. Surgical residents of varying specialties completed a pre-participation demographic survey, and were allowed 20 minutes to resect a pelvic tumor 5cm in diameter using the da Vinci robot*. At a standardized event in the simulation, venous bleeding began and participants attempted hemostasis with suture ligation. Potential blood loss was unlimited. Motion monitoring software recorded Path Length and Idle Time of the two instruments in use during the 10 seconds before and after bleeding began. A post-participation Likert Scale survey evaluated participants’ assessment of the model’s realism and their interest in using the model during their training. Scores ≥ 3 out of 4 in realism and scores ≥ 4 out of 5 in interest would qualify the model as having high fidelity and utility to surgical residents.

Results: Three of the seven (PGY 2-5, 71% Female) participants successfully resected the tumor in the allotted time. Participants demonstrated a wide range of performance in all metrics, and there was large variability in blood loss (Table 1). The average realism scores across all categories were rated as having high fidelity. 100% of participants “Agreed” or “Strongly Agreed” that the overall simulation was realistic (M=4.1 out of 5.0, SD=0.35). Additionally, 100% of participants either “Agreed” or “Strongly Agreed” that they would recommend the simulation to other residents (M=4.9 out of 5.0, SD=0.35). Conclusion: The results support that the new bleeding pelvic tumor simulator has the ability to discriminate resident performance in robotic surgery. The combination of clinical and motion metrics offers a two-fold performance assessment, analyzing both technical and decision-making abilities. Additionally, surveys indicate that residents are highly motivated to train on the model. The realistic tissue and operative conditions provide an unprecedented simulation experience that goes beyond virtual reality training and provides a unique experience for learners. Next steps include collecting additional performance data from expert surgeons. Future work will be development of a standardized curriculum for training on the model.

Table 1: Performance Metrics

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<td>Blood Loss (mL)</td>
<td>125</td>
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<td>0</td>
<td>0</td>
<td>0 (Total)</td>
<td>-</td>
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* Presentation of this study will include the following video clip of one participant’s attempt at hemostasis: (https://drive.google.com/file/d/0B9sj1QJBQ1wSQ2xlWFJvdEwxMIE/view?usp=sharing)
ASSESSING DOCUMENTATION PROVIDED FOR INTERHOSPITAL TRANSFERS OF EMERGENCY GENERAL SURGERY PATIENTS

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Mentor: Angela Ingraham, MD, MS

Support: Department of Surgery NIH grant T35DK062709

Background: Poor communication can lead to fragmentation of care and adverse patient outcomes. Studies of transitions of care within a single hospital and at discharge suggest significant communication deficits. Communication during transfers across hospitals, which are inherently complex and at high risk for communication failures, has not been well-studied in surgical populations. This study assessed the written communication provided during interhospital transfers of emergency general surgery (EGS) patients. We hypothesize that EGS patients are often transferred with incomplete documentation of the workup, diagnosis, and treatment provided at referring facilities leading to uncertainty at the accepting hospital and wasted resources. Methods: We performed a retrospective review of written communication during interhospital transfers of EGS patients. Patients transferred to our institution from outside emergency departments (ED) for emergency general surgical evaluation between 4/1/14 - 3/1/16 for 6 EGS diagnoses (appendicitis, cholecystitis, diverticulitis, bowel obstruction, perforated viscus, mesenteric ischemia) as assigned by accepting providers were included. Searching the existing comprehensive electronic medical record, which incorporates documents from referring hospitals, elements of written communication were abstracted in a standardized fashion and included the presence of outside records, documentation of the medical course and care, and information received after the patient’s arrival. Comprehensive descriptive statistics summarized the information communicated. Results: Over the two year period, 129 patients met inclusion criteria. 87.6% (n=113) of charts contained referring hospital documents. Substantial numbers of history and physicals (42.5% [n=48]), diagnoses (9.7% [n=11]), and reasons for transfer (18.6% [n=21]) were missing. 91 CT scans were performed; of which, final reads were absent for 76.9% (n=70). 45 ultrasounds and x-rays were performed; of which, final reads were missing for 80% (n=36). Services outside the ED were consulted at the referring hospital for 32.7% (n=37) of patients; consultants’ notes were absent in 89.1% (n=33). In 12.4% (n=14), referring facility paperwork arrived after the patient’s ED arrival time, and thus was not part of the original written communication provided. Conclusion: Effective communication is an essential component of patient care. This study documents that information critical to continuity of care is often missing in the written communication provided during interhospital transfers. Establishing the current state of this communication affords a foundation for the standardization of provider communication during interhospital transfers of EGS patients.
REVIEW OF ANTI-VEGF INJECTIONS AND SUSTAINED INTRAOCULAR PRESSURE INCREASE IN MULTIPLE CLINICAL TRIALS AT THE UNIVERSITY OF WISCONSIN

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Mentor: Barbara Blodi, MD

Support: Shapiro Sumer Research Program; Department of Ophthalmology and Visual Sciences; Mentor funds

Introduction: Anti-vascular endothelial growth factor (VEGF) agents are effective medications for the treatment of macular edema in retinal diseases such as diabetic retinopathy, age-related macular degeneration and retinal vein occlusion. There is no general consensus on whether repeated anti-VEGF injections cause long-term increases in intraocular pressure (IOP). The purpose of this study is to assess the risk of sustained, increased IOP in eyes with macular edema due to diabetes or central retinal vein occlusion following injections of anti-VEGF agents. **Methods:** A retrospective chart review of 51 patients with macular edema due to diabetes or central retinal vein occlusion was conducted. These patients previously participated in the randomized clinical trials at the University of Wisconsin, including 8 patients in DRCRnet Protocol T, 9 patients in SCORE2, 23 patients in CATT and 11 patients in DRCRnet Protocol I. In each study, IOP was measured at multiple visits using Goldmann applanation tonometry in both the study eye and non-study eye. Increased IOP was defined as either 1) IOP of at least 22 mm Hg and an increase of at least 6 mm Hg from baseline at 2 consecutive visits or 2) the initiation of ocular hypotensive therapy. **Results:** Of the 51 patients included in this study, 19 patients had diabetic macular edema, 23 patients had age-related macular degeneration, 2 patients had hemi-retinal vein occlusion, and 7 patients had central retinal vein occlusion. The patients were age 68.43 at diagnosis on average; 49% were men and 51% were women. The patients were treated with different anti-VEGF agents depending on the study protocol, including 14 patients with bevacizumab, 23 patients with ranibizumab, 9 patients with aflibercept, and 4 patients with steroids. Four patients had glaucoma or were on IOP-lowering medications prior to initiating anti-VEGF medications. The average number of anti-VEGF injections per patient received was 10.43 injections. 3 patients (5.8%) had increased IOP after treatment with anti-VEGF agents. The mean IOP of the study eye over the course of the study period was 14.7 mmHg and the mean IOP of the non-study eye was 15.1 mmHg. **Conclusions:** IOP increased in 5.8% of patients who underwent treatment with anti-VEGF agents, which is consistent with previous studies. Monitoring and treatment of increased IOP is critical in patients receiving anti-VEGF agents long-term.
THE SURVEY OF THE HEALTH OF THE WAUSAU AREA HMONG POPULATION PILOT STUDY

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Mentors: Kevin Thao, MD, MPH; Yang Sang Xiong, PhD

Support: Shapiro Summer Research Program; Department of Family Medicine and Community Health; Hmong American Center of Wausau; University of Wisconsin – Steven’s Point

Background: The purpose of the Survey of the Health of the Wausau Area Hmong Population (SHWAHP) study was to adapt, translate, and enact a pilot study in order to gather important health information about the Hmong American community in Wausau, WI and establish a baseline of health for the community. The Hmong are a large, underserved refugee population in Wisconsin that are facing many challenges due to their change in environment and acculturation process, and there is a lack of basic health information about them. Studies indicate that Hmong are at higher risk for cardiovascular disease and obesity than their white counterparts. Methods: The SHWAHP study utilized a two-part interview and sample collection. In the first part randomly sampled Hmong community members answered an oral questionnaire about health history, health habits/behaviors, and health knowledge and perceptions. They then were invited to a local clinic for the second part where they were also asked to volunteer for clinical measurements (height, weight, blood draw for routine lab screenings, etc.) Patients were provided financial compensation for their involvement. Statistical analysis of the health data are being performed using Statistical Analysis System software and will be compared to health data for the general Wisconsin population utilizing the Survey of the Health of Wisconsin (SHOW) database, particularly for the prevalence of chronic diseases such as diabetes and cardiovascular disease. Results: There are not yet definitive comparative results. Progress was made in recruiting participants, conducting interviews, and some statistical analysis. Conclusion: The SHWAHP study serves as a launching point in community-based participatory research in the Wisconsin Hmong community. The information gained by this study will provide epidemiological information about Hmong health that can be utilized to improve the health of Hmong Americans by identifying health disparities and establishing health priorities. Results and methodology from this study can inform future studies on the Hmong by providing a baseline of health status as well as establishing a model of community-based participatory research with the community.
DETECTION AND NEUROLOGICAL IMPACT OF CEREBROVASCULAR EVENTS IN NON-CARDIAC SURGERY PATIENTS

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Mentor: Robert Sanders, MD, PhD

Support: Shapiro Summer Research Program; Department of Anesthesiology mentor funds

Background: Delirium incurs a huge societal burden, due to in part due to its association with increased mortality; each additional day of delirium independently increases the risk of death by 10%. Increased morbidity leads to prolonged hospital length of stay with significant financial implications: delirium is estimated to cost $4-$16 billion annually. Delirium is associated with long-term neuropsychological and cognitive deficits, mandating a better understanding of the pathogenesis of delirium and the mechanisms underlying the prolonged disruption of cognitive processing. We hypothesized that (1) reduced functional correlation of activity between the dorsolateral PreFrontal Coretx (dlPFC) and Lateral Parietal regions of the brain predispose one to delirium, (2) that functional connectivity is further impaired in delirium and (3) this breakdown in connectivity is associated with inflammation (cytokine and substance P).

Methods: To assess the level of functional correlation between the dlPFC and LP regions of the brain, we used non-invasive preoperative and postoperative Magnetic Resonance Imaging (MRI) and preoperative and postoperative cognitive testing. Both before and after operation, consenting patients were assessed using the Montreal Cognitive Assessment questionnaire, the DigitSymbol Substitution Test (DSST), and the Trail Making Test (TMT-A&B). Patients were tested using the Repeatable Battery Assessment of Neuropsychological Status (RBANS), the Boston Naming test (BNT), and the Controlled Oral Word Association Test to test phonemic fluency.

Results: Thirty-three subjects were recruited and completed the study. 13 of the 33 (39.3%) were found to have postoperative delirium. Neurocognitive assessments were used as potential preoperative predictors of postoperative delirium. In comparing scores of three neurocognitive assessments, only one group of tests showed any significant differences between those patients that would become delirious and those that were not. The TMT-B showed those subjects who would not become delirious scored an average of 74.6, while those who would develop postoperative delirium scored an average of 129.3 (p=0.0340). In addition, the ratio of TMTB/TMTA showed those who would become delirious had an average ratio of 3.1, while those who would not become delirious had an average ratio of 2.3 (p=0.04444).

Conclusion: The data collected here shows that there is a cognitive assessment that is a predictor of postoperative delirium. Ratios of scores of the two trail making tests, TMT-B/TMT-A, are inversely correlated with executive function, and here are shown to be predictive of postoperative delirium. More work needs to be done to assess the level of functional connectivity in the dlPFC and the LP regions of the brain by MRI, as well as analysis of plasma levels of IL-6 and substance P, to determine their roles in possibly predisposing one to postoperative delirium.
UNPLANNED REINTUBATION AND DELAYED EXTUBATION FOLLOWING MULTILEVEL SUBCERVICAL SPINE SURGERY

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Mentor: Richard E. Galgon, MD, MS

Support: Shapiro Summer Research Program; Department of Anesthesiology

Background: Multilevel subcervical spine surgery has been associated with significant facial and upper airway edema. Combined with co-existing diseases and the need for post-operative opioid analgesia, patients may be at an increased risk of postoperative airway compromise which may require an unplanned reintubation or delayed extubation. However, there is limited data on the rate of unplanned reintubation or delayed extubation in patients who undergo this procedure. This study aims to examine the incidence and risk factors of unplanned reintubation or delayed extubation within 72 hours following multilevel subcervical spine surgery. Methods: After IRB approval, charts of patients who underwent a multilevel subcervical spine surgery between June 2014 and December 2015 were identified using departmental billing records and reviewed. Patients with planned reintubations and patients of single level or cervical procedures were excluded. Baseline characteristics and anesthetic, operative, and postoperative data were abstracted and analyzed. Intergroup comparisons for continuous and categorical variables were performed with independent t-tests and chi-squared tests, respectively. Association between each covariate and delayed extubation was tested using binomial logistic regression. A univariable model was fit for each of the covariates to produce an estimated odds ratio. Significance was assessed by applying a Bonferroni correction. Results: Five hundred encounters were reviewed. After excluding 33 encounters, 450 (96%; 95% confidence interval [CI] = [94%, 98%]) were successfully extubated, 15 (3.2% [1.9%, 5.2%]) had a delayed extubation and 2 (0.4% [0.01%, 1.55%]) had an unplanned reintubation. Age, sex, BMI, ASA classification, patient comorbidities, including obstructive sleep apnea and chronic obstructive pulmonary disease, and smoking status were not significantly different between groups. Compared to those with successful extubations, patients with delayed extubations were more likely to have operations with greater number of spine levels (4 ± 2 vs. 9 ± 4; p<0.001), operative time (434.6 ± 158.3 vs. 227 ± 108.2 min, p<0.001), amounts of intra-operative crystalloid (5183.3 ± 2499.5 vs. 2325.2 ± 1504.6 ml, p<0.001), transfused RBCs (1397.3 ± 1072.7 vs. 103.6 ± 317.1 ml, p<0.001) and blood loss (2315 ± 1339.2 vs. 551.8 ± 623.3 ml, p<0.001). In univariate analyses, the odds of delayed extubation increased by 32.6% for each additional spine level, by 14.9% with each 15 min increase in operative time, by 22.4% and 6.5% with each 15 ml increase of transfused RBCs or crystalloid, respectively, and by 16.2% for each additional 100 ml of blood loss (all p<0.001). Conclusion: This is the first study to investigate the rates of unplanned reintubation and delayed extubation in patients undergoing multilevel subcervical spine surgery. Fortunately, unplanned reintubation in this group remains uncommon and is comparable to the reintubation rate reported for cervical spine surgery [1]. Intraoperative factors, including greater number of spine levels, operative time, crystalloid infusion, blood transfusion, and blood loss, may be risk factors for delayed extubation after multilevel subcervical spine surgery.

Citation:
INVESTIGATION OF PATIENTS’ PERCEPTIONS REGARDING ANTIBIOTIC USE AND RESISTANCE IN GURGAON, HARYANA, INDIA

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Mentors: Ajay Sethi, PhD, MHS; Sharmila Sengupta, MD; Muneeb Ahsan

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Support: Shapiro Summer Research Program; Department of Population Health Sciences; S.N. BOSE Scholars Program

Background: Antibiotic resistance is a growing global threat. India, in particular, is a hotbed for cultivating antibiotic resistance, likely due to minimal regulations concerning production and distribution of antibiotics. It has the highest burden of neonatal deaths due to resistant infection-associated sepsis.1 India also has amongst the highest numbers for Methicillin-resistant Staphylococcus aureus (MRSA) and Carbapenem-resistant Enterobacteriaceae (CRE).1 As globalization leads to increased travel between the U.S. and India, amongst other countries, it results in greater opportunity for global spread of resistant infections. The purpose of this study is to survey patients’ perceptions regarding antibiotics and their contribution to antibiotic resistance. Patients are one of the biggest stakeholders in antibiotic resistance especially as self medication is extremely common in India.2,3 Their perceptions need to be understood in order to design effective solutions to antibiotic resistance. Methods: Patients and attendants were recruited from inpatient clinics and waiting rooms within a private tertiary care center, Medanta Medicity Hospital, located in Gurgaon, Haryana, India. Study participants were interview administered a survey that included demographic information and knowledge, attitudes, and practices regarding antibiotic use and resistance. Out of those approached, 150 (91%) subjects completed the survey, and 15 (9%) refused or were unable to complete the survey. Results: Preliminary data examination points to correlations between familiarity with antibiotics or resistance and education, occupation, income, and presence of healthcare workers in family/friend network. Conclusion: To date, our data support expected trends; with increased access to education, there is increased familiarity with antibiotics and resistance. This finding highlights the importance of access to education as a way to empower consumers of antibiotics to make well informed decisions and thus as a way to combat antibiotic resistance. Furthermore, studies must be conducted in government funded healthcare institutions to compare and contrast results found in this study, as patient populations of lower socioeconomic status primarily access public healthcare facilities. Perceptions of healthcare workers must also be assessed in order to determine their particular role in perpetuating the growing antibiotic resistance.

Citations:
PATIENT SATISFACTION WITH EMERGENCY PHYSICIANS: A COMPARISON STUDY

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**Department:** BerbeeWalsh Department of Emergency Medicine, University of Wisconsin School of Medicine and Public Health

**Mentors:** Brian Sharp, MD; Andrew Lee, MD

**Support:** Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

**Background:** Most emergency departments (EDs) in the US partner with Press Ganey to distribute their patient satisfaction surveys. Little research has been published regarding factors that influence the overall rating of the physician. Given the importance tied to these survey results, it is imperative to determine if physicians’ Press Ganey ratings can be used as a reliable indicator of the service they are providing. University of Wisconsin (UW) Health’s ED setup, with two different Madison sites staffed by the same physicians, provides an idea setting to conduct this study. **Objectives:** The goals of this study are to determine whether Press Ganey ED satisfaction scores for UW physicians working at two different sites, UW Hospital ED (UWED) and The American Center ED (TAC ED), vary between sites, and to identify factors contributing to any variation. **Methods:** We conducted a retrospective study of patients seen at UWED or TAC ED between September 2015 and March 2016 who returned a Press Ganey satisfaction survey. A database was compiled linking the patient visit with their responses on a 1-5 scale to questions such as overall rating of care and four other doctor-specific metrics. Visit-specific metrics such as wait time, labs received, prescriptions received, demographic data, and the attending physician were also linked. Scores for physicians staffing both EDs were averaged and compared between sites using t-tests. A regression analysis was used to determine the impact of visit-specific metrics on survey scores. **Results:** A total of 1,230 ED patients met the inclusion criteria (TAC ED=488, UWED=742). The overall rating of care metric was significantly lower at UWED compared to TAC ED (95% CI, 4.21-4.36 vs. 4.58-4.72). The same trend was observed when the five doctor-specific metrics were summed (95% CI, 21.70-22.36 vs. 23.00-23.64). Factors that correlated with higher scores included arrival-to-room time (p=0.000) and arrival-to-discharge time (p=0.002), both of which were longer at UWED. **Conclusion:** Press Ganey satisfaction scores for the same group of ED physicians varied significantly between sites. This suggests that these scores are more dependent on site-specific factors, such as wait times, than the quality of care provided by the physician.
TEXTURE ANALYSIS OF THE LIVER AT MDCT FOR ASSESSING HEPATIC FIBROSIS

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**Support:** Shapiro Summer Research Program, Department of Radiology

**Background:** Noninvasive imaging biomarkers for the assessment of liver disease and hepatic fibrosis are becoming increasingly important as causes and treatments of liver disease evolve. Imaging may help obviate the need for invasive tests such as biopsy and may be used both for diagnosis and potentially to assess response to therapy. **Purpose:** To evaluate CT texture analysis for staging of hepatic fibrosis (stages F0-F4). **Methods:** Quantitative texture analysis of the liver was performed on abdominal MDCT scans using commercially available software. Single slice ROI measurements of the total liver, Couinaud segments IV-VIII and segments I-III were obtained. A variety of CT texture parameters were associated with degree of hepatic fibrosis, including mean, entropy, skewness and kurtosis of the pixel histogram, particularly in segments IV-VIII on the portal venous phase. Texture parameters were correlated with biopsy performed within one year for all cases with intermediate fibrosis (F1-F3); biopsy was not indicated for all cases of end-stage liver disease (cirrhosis; F4) or for normal controls (F0). **Results:** The study cohort consisted of 455 adults (241 men, 214 women; mean age, 51 yrs), including a healthy control group (F0, n=204), and patients with increasing stages of fibrosis (F1, n=48; F2 n=40; F3 n=67; F4 n=96). Mean increased with increasing fibrosis and for detecting the presence of fibrosis (F0 vs F1-4), mean demonstrated an ROC AUC of 0.78 at medium filtration (and above 0.75 for coarse filtration), with a sensitivity and specificity of 74% and 74% using a threshold of 0.18. Entropy showed a similar trend. For significant fibrosis (≥F2), mean showed ROC AUCs ranging from 0.71-0.73 across medium and coarse filters with sensitivity and specificity of 71% and 68% using a threshold of 0.3, with similar ROC AUC and sensitivity/specificity for advanced fibrosis (≥F3). Kurtosis and skewness decreased with increasing fibrosis, particularly in cirrhotic patients. For cirrhosis (≥F4), kurtosis and skewness showed ROC AUCs of 0.86 and 0.87 respectively at coarse filters, with skewness showing a sensitivity and specificity of 84% and 75% using a threshold of 1.3. **Conclusion:** CT texture analysis may be helpful in detecting the presence of hepatic fibrosis and discriminating between stages of fibrosis, particularly at advanced levels. This tool is noninvasive and can be applied retrospectively.
DEVELOPMENT OF AN INSTRUMENTED CLUBFOOT MODEL

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Mentor: Kenneth Noonan, MD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

Background. Instrumented simulation models allow the capture and analysis of procedural performance in a quantitative manner, which may otherwise be limited to measures such as supervisory observation or patient outcomes. An instrumented clubfoot model allows for a standardized approach to the teaching and evaluation of the current clubfoot correction approach, the Ponseti method. This method involves manual manipulation of the foot in a precise manner and thus lends itself well to objective measurement. Identification and translation of the correct and incorrect actions of this procedure into a model with an integrated software real-time feedback interface was the objective of this project. Methods. In coordination with the Simulation Engineering for Surgical Education lab, prototype silicone infant lower limbs with clubfoot deformity were created. Orthopedic faculty input was used to refine the models with respect to realistic anatomy, appearance, feel, and flexibility. Two sensor classes were required: pressure sensors, for which analog force sensitive resistors were chosen, and position sensors. Several commercially available multi-axis microelectromechanical accelerometers and gyroscope devices were evaluated, and an integrated absolute position sensor (Adafruit BN055) was chosen. Sensor input was multiplexed using an Arduino Uno microcontroller. Data processing and evaluation logic was created in C++ under the Microsoft Visual Studio IDE, and Qt platform libraries were used for the user interface. Feedback was solicited from faculty in multiple sessions during the iterative development of the model. Results. Several prototype limbs were created and integrated into the software system. The software achieved data capture and labeling at sufficient rates and provided user feedback in a three-dimensional model of the foot with color-coded pressure gauges. However, the sensor data captured during testing indicates the need for further reproducibility testing in order to ensure a truly standardized model. Additionally, user interface changes will be required as further user experience testing is conducted. Conclusion. The model continues to be refined to become more realistic, to gain greater sensor data reproducibility, and to adapt the software user interface to ensure optimal real-time feedback. The model will be tested by field experts at the 2016 International Pediatric Orthopedic Symposium. This feedback will be used to further refine the model toward the goal of using it as a resident training device.
INVESTIGATING THE RELATIONSHIP BETWEEN USUAL DIET AND PREVALENCE OF INFECTION WITH MULTIDRUG-RESISTANT ORGANISMS IN HARYANA, INDIA

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Mentors: Nasia Safdar, MD, PhD; Daniel Shirley, MD, MS

Support: Shapiro Summer Research Program; Department of Medicine; Indo-U.S. Science and Technology Forum

Introduction: Antimicrobial resistance in bacteria causing serious infections is a global crisis. Many of these multidrug-resistant organisms (MDROs) can flourish in the human gastrointestinal tract if the normal gut microbiota, responsible for resisting invasion by pathogens, is altered due factors such as healthcare exposure, antibiotic use and diet. A high fiber diet may be associated with a lower risk of infection by MDROs. Many foods in the North Indian vegetarian diet are high in fiber. We hypothesized that the vegetarian north Indian diet, rich in fiber, is associated with a lower risk of infection with MDROs. We undertook a case control study to examine the relationship between usual diet and prevalence of infections with MDROs in the North Indian setting. Methods: We identified patients with MDRO infections (at least one or more of the following: Vancomycin-Resistant Enterococcus, Clostridium difficile, Methicillin-Resistant Staphylococcus aureus, Gram-negative bacteria resistant to 3 or more classes of antibiotics) and controls who did not have any infections. We administered a diet questionnaire to both groups of participants to collect data on usual diet and other risk factors. We performed descriptive statistics, univariate analysis, and multivariate logistic regression with infection with a MDRO as the dependent variable (binary outcome yes/no) and diet above as one independent variable. Results: 39 cases and 91 controls were included in the study. All cases had infections with gram-negative MDROs. Univariate analyses show length of hospital stay, connective tissue disease, hospitalization in the last 12 months, having a family member in the hospital, antibiotic use in the hospital, antibiotic use in the last 12 months, feeding tube use, central venous line use, and urinary catheter use all to be significantly different (P≤0.05) between cases and controls. Logistic regression showed a 2-fold increase in odds of infection with antibiotic use in the last 12 months (OR 2.86, 95% CI 1.11-7.34) and urinary catheter use (OR 5.16, 95%CI 1.76-15.10). Differences in meat, fruit and vegetable, and fiber consumption were not significantly associated with infection. Conclusions: We found that antibiotic use in the last 12 months and urinary devices were associated with a higher risk of infection. We did not find diet to be significantly associated with MDRO infection in this study population. Infection control within this population should focus on antibiotic stewardship and reducing urinary catheter use.
DEVELOPMENT OF AN ALGORITHMIC AID TO ASSIST COMMUNITY HEALTH WORKERS (CHWS) IN RURAL GUATEMALA WITH DIABETES TREATMENT

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Mentors: James Svenson, MD; Sean Duffy, MD

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine; Global Health Institute; Farrell Public Health Scholar Program

Background: An estimated 9.1 – 9.4 % of Guatemalans suffer from Type II Diabetes, with half of cases undiagnosed (1). In San Lucas Tolimán, Guatemala, access to diabetes care is limited by cost (average incomes are less than $1,000), physician shortage (there are two physicians for 40,000 inhabitants), and geography. This project seeks to expand and improve diabetes care offered in the rural community of San Lucas Tolimán, by providing CHWs with oral medication titration guidance. The first stage of this process, completed this summer, was the creation of an algorithmic design for a mobile health (mHealth) diabetes treatment application that will facilitate patient data storage and transmission, oral medication adjustment recommendations, and remote physician review. Methods: Product development was based upon a Community Health Assessment, which used chart review, CHW interviews, and patient interviews to understand current diabetes treatment in San Lucas Tolimán. We designed an idealized algorithm based on both the ideal care recommendations of the American Diabetes Association and International Diabetes Foundation, guidance from diabetologists at UWSMPH, and the limitations elucidated by the Community Health Assessment (2,3). Local physicians and health workers reviewed the algorithm for feasibility of implementation. Results: The end product is an iterative algorithm designed around monthly diabetes clinics, which are used to distribute medications and check Fasting Blood Glucose (FBG). Every three months, the previous three FBGs are averaged and compared to an idealized FBG target to determine each patient’s glycemic control. Based on the patient’s glycemic status, the algorithm recommends titration of medication dose derived from a pre-approved oral medication scheme. The application design permits patient data storage, remote physician chart review, and identification of dangerous patient states. Conclusion: The algorithm is currently being developed into an mHealth smart phone application with the goal of implementation in February 2017. Evaluation of the program’s effect on patient glycemic control and quality of life will continue throughout its implementation.

Citations:
INAPPROPRIATE ANTIBIOTIC PRESCRIBING FOR LONG TERM CARE FACILITY RESIDENTS IN OUTPATIENT SETTINGS

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Mentor: Michael Pulia, MD

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

Background: Inappropriate use of antibiotics in healthcare is a primary cause of the increase in multidrug resistant bacterial infections. Long Term Care Facilities (LTCFs) can act as reservoirs for resistance. The primary aim was to compare inappropriate antibiotic prescribing rates for LTCF patients across outpatient care-settings. Our secondary aim was to characterize antibiotic starts in LTCF patients by setting, infection type, and antibiotic class. Methods: Chart extraction from 5 Wisconsin LTCFs yielded 1,451 antibiotic prescribing events. Data included setting of prescription initiation, infection type, symptoms, vitals, laboratory values, and antibiotic prescribed. We excluded antibiotics prescribed following discharge from an inpatient unit or without a documented location of initiation. Cases were also limited to acute infections for which Infectious Disease Society of America (IDSA) consensus guidelines exist to assess appropriateness of empiric prescribing. 734 antibiotic events were included in the analysis. Comparisons were made via chi-square ($\chi^2$) and a multivariate logistic regression was performed. Results: Overall, 49% of antibiotic prescriptions were inappropriate. 50% of infections were urinary tract, 26% lower respiratory tract, and 24% skin and soft tissue. 87% of all infections were treated by the LTCF itself, 8% by outpatient clinics, and 5% by emergency departments. In unadjusted analysis appropriateness differed significantly by care-settings ($p=0.048$), with outpatient clinics having the highest percentage of inappropriate antibiotic starts (64%) compared to emergency departments (47%) and LTCF (48%). In our multivariate analysis, age and gender were not associated with an increased odds of inappropriate prescribing. However, patients who received treatment in an outpatient clinic had 2.92 increased the odds of inappropriate prescribing (95% CI 1.59-5.33) compared to LTCF. Additionally, treatment for lower respiratory and urinary tract infections increased the odds of inappropriate prescribing when compared to skin and soft tissue infections (OR 3.37, 95% CI 2.12-5.35 and OR 4.45, 95% CI 2.94-6.74 respectively). Conclusions: Overall, patients residing in LTCFs are at unacceptably high risk of receiving inappropriate empiric antibiotics. This risk increases when treated in outpatient clinics and for both lower respiratory and urinary tract infections. Future research should focus on identifying modifiable determinants of inappropriate prescribing in LTCF patients across settings, especially for those suspected of having urinary tract infections.
RESULTANT HISTONE DEGRADATION FROM RAPAMYCIN TREATMENT

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Mentor: Hasan Mukhtar, PhD

Support: Department of Dermatology; Shapiro Summer Research Program

Background: Throughout a cell’s life, nucleosomal histones are constantly undergo degradation and renewal. While the details of this process are not fully understood, there are factors that help accelerate and inhibit this process. **Methods:** Mouse embryonic fibroblasts (MEFs) were cultured and treated with different metabolic inhibitors: Rapamycin (inhibiting mTOR), U0126 (inhibiting MAPK), and LY294002 (inhibiting PI3K). Western blots were run for each one of these treatments, along with a control. Additionally, mice cells – both wild type and PTEN knockout – were treated with rapamycin and western blots were run for these groups. Finally, time trials of cells treated with rapamycin were also conducted, lysates made, and western blots were done. **Results:** For the MEFs, rapamycin was shown to bring about a clear reduction in histone H3 levels. U0126 and LY294002 did decrease H3 levels, but not to the extent that rapamycin did so. Similar results were seen the mice work as well: in both wild type and knockout conditions, rapamycin caused a marked decrease in histone H3 levels. As for the time trial, a gradual decrease in H3 levels was seen as the treatment continued for the 48 hours. **Conclusion:** In this study, we demonstrated the ability of rapamycin to cause a marked decrease in total histone levels in both mouse embryonic fibroblasts and wild type cells as well. While the mechanism for this decrease has not been fully understood, we suspected autophagy may play a role. The results shown here will be the foundation of future work concerning the ability of rapamycin to induce such epigenetic changes.
EFFECTIVENESS OF EMERGENCY DEPARTMENT CARE PLANS

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Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

Background: With healthcare expenditures growing rapidly, finding methods to reduce costs has become increasingly important. In the emergency department (ED), frequent users, patients with 5+ ED visits per year, comprise only 3.8-5% of the patient population yet account for 17-28% of total ED visits\(^1\). Thus, it is important to reduce unnecessary ED visits and shift chronic healthcare needs to the primary care setting. The objective was to determine the effectiveness of care plans in reducing the number of ED visits, lowering admission rates, and increasing primary and specialty care visits in frequent ED users. Secondary objectives were to evaluate length of stay and resource utilization post-intervention.

Methods: A retrospective case study design of frequent ED users, patients with 3+ visits in three months, identified 325 patients in the electronic medical record (EMR), 74 of whom had specific ED care plans that met inclusion criteria. A second reviewer analyzed all care plan violations to ensure consistency during the chart review. For the number of ED, primary and specialty care visits, and length of stay analyses, a linear mixed effect model with a square root, variance stabilizing transformation was used. A mixed effect Poisson model was used for admission rates. Finally, a mixed effect logistic regression was used to assess binary variables.

Results: In patients with ED care plans, ED visits decreased by 4.415 visits per patient in the six months post-intervention (95% confidence interval [CI], (3.123, 5.708); \(p < 0.001\)) and hospital admission rates decreased by 22.8% (95% CI, (5.1%, 45.2%); \(p<0.001\)). The change in primary and specialty care visits was not found to be statistically significant (\(p=0.153\)). Length of stay showed a cumulative decrease of 7.503 hours in female patients in the six months post-intervention (95% CI, (3.959, 11.411); \(p < 0.001\)). Males were not found to have a statistically significant difference in length of stay (95% CI, (-5.103, 2.935); \(p = 0.594\)). There was no significant effect on imaging post-intervention (Odds increased by 1.185 times; 95% CI, (0.856, 1.644); \(p = 0.303\)). Lastly, the odds of receiving narcotics decreased by 67% post-intervention (95% CI, (50.8%, 78.3%); \(p < 0.001\)). Conclusion: Patients with ED care plans showed a decrease in the number of ED visits, admission rates, and length of stay for females after implementation. However, care plans do not appear to have the desired effect of shifting frequent users to their primary or specialty care providers. A comprehensive case management program might provide more continuity of care, promote primary care visits, and increase the overall health of frequent emergency department users.

Citations:
SPINE MRI AND ACR APPROPRIATENESS GUIDELINES: UTILIZATION TRENDS FROM AN ACADEMIC EMERGENCY DEPARTMENT

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Departments: Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health; Department of Radiology, University of Wisconsin School of Medicine and Public Health

Mentors: Paul A. Anderson, MD, MS; Allison M. Grayev, MD

Support: Wisconsin Academy of Rural Medicine (WARM); Department of Orthopedics and Rehabilitation

Background: A contributor to medical resource overuse in the Emergency Department (ED) is inappropriate ordering of advanced imaging studies. Although magnetic resonance imaging (MRI) overutilization is documented in the outpatient setting, until recently there has been little data to quantify its overutilization in the ED. Spine imaging is of particular concern in regards to appropriateness, as previous studies have shown inconsequential or normal findings in 67.9-75% of lumbosacral spine MRI. Objective: We hypothesized that the University of Wisconsin-Madison Emergency Department (UW ED) overutilizes lumbar spine MRI. This study aimed to 1) apply accepted guidelines for spine imaging to determine potential overutilization, and 2) identify areas within current accepted guidelines that require further criteria to eliminate subjective interpretation. Methods: This study was IRB approved. Using the picture archiving and communication system (PACS), 262 adult subjects were identified who had a lumbar MRI ordered through the UW ED in 2015. Demographic data was collected from the medical record as well as ED diagnosis (Dx), differential diagnoses (DDx), presenting signs and symptoms, red flag presentation in regards to cauda equina syndrome (CES), and physical exam findings. The American College of Radiology Appropriateness Use Criteria (AUC) was chosen as the most comprehensive and validated published guideline, and each ED note and MRI order form was assessed using this criteria. A percentage of potentially inappropriate MRIs was calculated by dividing the number of MRIs that did not meet criteria by the total lumbar MRIs. Results: Low back pain (LBP) and radiculopathy were present in 85.5% and 87.4% of subjects respectively. Over one fifth of subjects (22.5%) presented with a prior history of lumbar surgery. CES was present in the DDx of 53.4% of subjects; 28.1% of these 140 subjects did not present with a red flag for CES. Of the total 262 subjects, 80.9% left the ED with a Dx of one or a combination of the following: LBP, disk herniation, radiculopathy, and/or muscle strain/sprain. The percentage of potentially inappropriate lumbar MRIs for the year of 2015 was found to be 23.3%. Conclusion: Our data suggests that at least one in every five lumbar spine MRIs ordered in the UW ED may be inappropriate. Our data also demonstrated a high incidence of suspected CES; however, many cases presented without red flags (28%) or a complete physical exam (68%). We believe actions to reduce potentially inappropriate imaging should include a review of the AUC guidelines, CES related education, and encouragement of complete physical exam taking and documentation.
UTILITY OF THE 10 HOUNSFIELD UNIT THRESHOLD FOR IDENTIFYING ADRENAL ADENOMAS: CAN WE IMPROVE?

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Mentor: Rebecca S. Sippel, MD

Support: Department of Surgery NIH grant T35DK062709

Background: Adrenal incidentalomas are identified on up to 5% of abdominal CT scans. Assessing such lesions for malignancy is essential for establishing appropriate patient follow up. A threshold of 10 Hounsfield units (HU) is currently recommended for differentiating benign adenomas from non-adenomas. Our study aims to evaluate the utility of the 10 HU threshold and to determine whether additional CT imaging features can be used to identify adenomas. Methods: We performed a retrospective review of a single institution’s prospective endocrine surgery database. Our cohort included 192 patients who underwent an adrenalectomy between 2001 and 2015 due to a unilateral adrenal mass (excluding pheochromocytoma). All masses that were non-adenomatous via surgical histology (adrenal cortical carcinomas, ganglioneuromas, metastases, etc.) were in the non-adenoma group. Imaging characteristics of adenomas and non-adenomas were compared. Sensitivity and specificity for detection of adenomas were calculated over a range of unenhanced HU values and using absolute washout >60%. Multivariate analysis was performed to identify predictors of adenomas. Results: Unenhanced HU values <10 were more common in adenomas compared to non-adenomas (47.6% vs. 6.7%, p<0.001), but less than half of the adenomas resected met this criterion. Two non-adenomas (1 lymphangioma and 1 metastasis) measured <3 HU. Non-adenomas were more likely to measure ≥4cm (p=0.001), have irregular borders (p<0.001), have a non-homogeneous appearance (p=0.006), and contain calcifications (p=0.028). These suspicious imaging features were also present in 12-39% of benign adenomas. Multivariate analysis revealed that HU ≤16 (OR 15.9, 95% CI 3.1-81.7, p=0.001) and smooth borders (OR 6.4, 95% CI 2.1-20.0, p=0.001) were both independent predictors of adenomas. The 10 HU cutoff had a sensitivity of 47.6% and a specificity of 93.3% (AUC=0.71, p<0.001). Raising the cutoff to 16 HU improved the sensitivity to 65.9% without detriment to specificity, which remained 93.3% (AUC=0.79, p<0.001). Absolute contrast washout of >60% had a sensitivity and specificity of 53.8% and 100%, respectively (AUC=0.61, p=0.011). In the cohort of patients with washout values available (n=33), if a lesion was <16 HU and/or had >60% absolute washout, the sensitivity and specificity increased to 96% and 100% (AUC=0.98, p<0.001). Conclusion: The traditional 10 HU threshold has a high specificity for identifying adrenal adenomas, but is limited by a poor sensitivity. Increasing the threshold to 16 HU has the potential to improve sensitivity without sacrificing specificity. A combination criteria of <16 HU and/or >60% absolute washout yielded both a high sensitivity and specificity and can thus be used to accurately identify adrenal adenomas and allow for appropriate selection of patients for non-operative management.

Citations:
DISTRIBUTION OF MICROPARTICLES IN IMMATURE BONE

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Department: Orthopedics and Rehabilitation, University of Wisconsin Madison School of Medicine and Public Health

Mentors: Matthew A. Halanski, MD; Ellen Leiferman, DVM

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

Background: Mineral coated microparticles (MPs) are small biologically engineered vehicles with several therapeutic applications: sustained delivery of biologically active proteins, visualization in vivo using MRI and tissue localization using an external magnetic field. Achondroplasia is a genetic disorder involving increased activity of fibroblast growth receptor 3 (FGR3), causing premature closure of the growth plate and severe stunted growth. A promising treatment for Achondroplasia is C-type Natriuretic peptide (CNP), which blocks the downstream action of FGR3. The major challenge with current CNP therapy is rapid clearance from plasma after injection. By using MPs in treatment for Achondroplasia, we could increase sustainability and localize drug delivery of CNP. Objective: We hypothesized that one: the MPs will distribute evenly throughout the diaphysis and epiphysis following injection and two: we can relocate the MPs to the physis using an external magnetic field after injection of superparamagnetic (SPIO) labeled MPs. Methods: An optimal injection, sectioning and imaging technique was developed through comparing several configurations of drilling/injection patterns into the epiphysis and diaphysis of cadaverous, immature mouse femurs. Injections were 1-2ul of Rhodamine labeled MPs in Phosphate buffered saline (PBS) at 2,10,25,50,100 mg/ml. Axial sections (1-2mm) of epiphysis were imaged using a Stereomicroscope, Nikon camera and Axiovision software. A sagittal section of the epiphysis was also imaged using the same technique at 25mg/ml. The fluorescence of both axial and sagittal sections were quantified using ImageJ software. Hematocrit tubes, injected with SPIO labeled MPs in PBS were placed into an MRI for 24 hours. These tubes were also transiently exposed to a rare earth magnet’s external magnetic field. Results: Diaphysis injections (n=3) showed uniform distribution throughout medullary cavity, without crossing the physis. Axial sections of the epiphysis (n=3) showed linear increase in fluorescence and even distribution throughout channels created by drilling. The sagittal section showed MP delivery within 0.4-1.3 mm of the physis. MRI was unable to localize the SPIO labeled MPs in the hematocrit tubes; however, exposure to rare earth magnets was able to localize MPs within the hematocrit tubes. Conclusions: In this study, I developed an optimal injection technique for MPs in immature bone, characterized MP distribution relative to the physis and demonstrated the ability to localize SPIO labeled MPs using an external magnetic field. Characterizing the distribution of MPs following diaphyseal and epiphyseal injections provides the opportunity to deliver combinations of therapeutic growth factors to different areas of the physis. These results support our hypothesis that MP can be evenly distributed throughout diaphysis and epiphysis upon injection. This work provides an injection and localization technique for future in vivo experiments using biologically active MPs.
RADIOFREQUENCY ABLATION OF PERICRANIAL NERVES FOR TREATING HEADACHE CONDITIONS: A PROMISING HOPE FOR HEADACHE PATIENTS

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Support: Shapiro Summer Research Program; Department of Anesthesiology

Background: Pericranial neuralgias are characterized by pain in the region corresponding to the pathway of a particular nerve or nerve root. Chronic daily migraines are consistently the most common symptom of patients suffering from pericranial neuralgia. As compared to episodic migraines, patients suffering from chronic migraines experience more total headache days, miss more days of school or work, and report their quality of life measured by “ability to function and feeling of well-being” as being severely impaired. Radiofrequency ablation (RFA) is an effective method for treating neuralgia of facial nerves presenting as chronic headaches and migraines, measured by reductions in headache medications, ER visits, and pain scores. Methods: This study was a retrospective chart review analyzing the success of RFA using a variety of pre- and post-procedure variables. The majority of patients were referred for RFA by the headache clinic at the University of Wisconsin-Madison after failure of medication management for treating the diagnosed headache condition(s). Each patient received two diagnostic blocks with more than 50% improvement in their pain. Prior to the RFA, one mL of 2% lidocaine was administered through a needle to provide local anesthesia. RFA was then performed with a 21 gauge needle in lesion mode at 80°C for 180 seconds, under IV sedation using small doses of Fentanyl and Midazolam. Results: Seven RFAs (9.7%) led to no improvement while the remaining patients (90.3%) experienced some degree of improvement. Patients who reported improvement (n=65, excluding the 7 RFAs with no improvement), reported an average percent improvement of 81.2% ± 18.7 (40-100%). Of the patients with successful RFAs, 70.7% are experiencing ongoing relief after their procedure or last follow-up. For all RFAs (n=72), the average percent improvement was 71.7% ± 28.8 (0-100%). Pain scores decreased from 6.6 ± 1.7 pre-RFA to 1.9 ± 1.9 post-RFA (p< 0.001) (n=72). Conclusions: The first-line treatment for pericranial neuralgias is pharmacotherapy, which has an efficacy of 50% and alleviates only 40% of symptoms. More invasive treatments like gamma knife surgery (GKS) or microvascular decompression (MVD) are approximately 80% successful at alleviating symptoms, but are associated with more complications than RFA. Our study reflects the success of RFA both in pain reduction and in patient improvement documented at approximately 80%, as supported by previous studies. RFA has become a promising new treatment for pericranial neuralgias, with similar success rates as GKS and MVD, but with minimal surgical risk and less complications. In order to determine length of pain relief, further patient follow-up is required.

Citations:
PROLOTHERAPY FOR SYMPTOMATIC KNEE OSTEOARTHRITIS: FUNCTIONAL OUTCOMES IN A QUALITY IMPROVEMENT PROJECT

Authors: Stephanie Lakritz, Margaret Smith, David Rabago, Bobby Nourani

Department: Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health

Mentors: Bobby Nourani, DO; David Rabago, MD; Supriya Hayer, MD; Michael Weber, MD

Support: Summer Student Research and Clinical Assistantship, Department of Family Medicine and Community Health

Background: Knee osteoarthritis (KOA) is a debilitating age-related disease resulting in joint stiffness, pain, and decreased function; current therapy is sub-optimal. Prolotherapy (PrT) is an injection-based treatment for musculoskeletal injury, including KOA. Clinical trials and meta-analyses identify PrT as a promising, cost-effective non-surgical treatment for KOA based on self-reported pain and function surveys, but its effects on objectively assessed physical function is unknown. **Objective** To determine whether PrT improves both subjective self-reported outcomes and objective functional measures in adults with symptomatic KOA compared to baseline status during routine clinical care. **Methods:** This prospective quality improvement project will follow 10 clinic-based family medicine patients undergoing treatment with PrT for knee OA for the first time. Inclusion criteria includes adults with at least 3 months of symptomatic knee OA recruited from clinical and community settings. Participants will receive extra-articular injections of 15% dextrose solution and intra-articular PrT injections of 25% dextrose solution at one, five, and nine weeks, with as-needed treatments at weeks 13 and 17. We will assess whether these patients will report knee-specific and general quality-of-life improvement. Additionally, we will see if these self-reported changes correlate with improved performance on objective knee-related measures. Self-reported assessments include the Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain score and the EuroQual 5D-5L health outcome score collected at baseline, 3, 6, 9, and 12-months post-procedure. Functional assessments include 3 Osteoarthritis Research Society International (OARSI) performance-based tests, computerized gait analysis, and accelerometer activity at baseline and 6-months post-procedure. **Results:** Baseline data collection is complete for 8/10 patients. WOMAC (55.47±22.06 points) and EuroQual 5D-5L index score (0.698±0.124 points) data suggest mild-to-severe KOA at baseline. Current collection data suggests that this QI project is clinically feasible. **Conclusions:** Although data collection and recruitment for this prospective pilot project is ongoing, we hypothesize that the results will reveal that the self-reported changes in pain and quality-of-life are associated with improvements in objectively measured physical function in patients treated with PrT for KOA.
FACTORS PREDICTING RADIATION THERAPY IN EARLY STAGE BREAST CANCER IN PATIENTS AGE 70 AND OVER

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Mentor: Jennifer G. Steiman, MD

Support: Shapiro Summer Research Program; Department of Surgery

Background: Radiation therapy (RT) is recommended as standard of care for women undergoing breast conserving surgery (BCS) for an invasive breast cancer (BC) as a way to decrease the risk of loco-regional recurrence (LRR). In 2004, Cancer and Leukemia Group B (CALGB) reported the results of a randomized trial (9343), which sought to determine if women ≥70 years of age with clinical stage I, estrogen receptor (ER) positive breast cancer could omit radiation in the setting of adjuvant hormonal therapy (HT). Omission of RT resulted in a low rate of LRR at 5 years (4%). Population studies assessing practice patterns years after the publication (2009-2011) demonstrated that 65-88% of women ≥70 continued to receive RT after BCS. Receipt was often associated with age, tumor size, and grade. These studies, however, are limited, as they cannot assess the relationship with other factors that may influence decision making such as Ki67 and margin status. Our objective was to examine receipt of RT for women ≥70 at our institution and identify patient and tumor factors associated with its recommendation.

Methods: Retrospective data was obtained with IRB approval through the institutional cancer registry for women aged ≥70 diagnosed with an invasive BC from January 2014 - December 2015 (n=44). Inclusion criteria were patients with a pathologic stage I, ER+ breast cancer who underwent BCS and received HT. Patient (age), tumor (grade, molecular tumor subtype, Ki67), and treatment characteristics (margin status) were abstracted from the patient chart. Statistical analyses were done using Chi square tests. Results: Overall, 59% (n=26) were recommended RT. Factors associated with a recommendation for RT included Her2neu+ status (p=0.05) and grade 3 tumors (0=0.03), with all patients meeting these criteria being recommended RT. Similarly, all patients with a Ki67 >45% (n=5) were recommended RT. No association amongst age was observed. Few patients had positive margins, limiting this analysis. Conclusion: Consistent with prior population studies, the majority of patients ≥70 years of age were recommended RT, despite strictly meeting criteria for CALGB 9343. Recommendations appear to be influenced by Her2neu status and grade. Her2neu was not collected as part of CALGB 9343; thus, further research should focus on the relationship between Her2neu status and outcomes without RT. Additionally, given the high ongoing use of RT, future studies should identify factors influencing provider decision-making regarding RT and application of CALGB 9343 to patients in their clinical practice. This will allow for opportunities to improve the quality of care provided to older breast cancer patients.
INTERMEDIATE TERM OUTCOMES AFTER PRIMARY TOTAL HIP ARTHROPLASTY: A COMPARISON OF METAL ON METAL VS HIGHLY CROSS-LINKED POLYETHYLENE BEARING SURFACES

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Mentor: Richard Illgen, MD

Support: Wisconsin Academy of Rural Medicine (WARM); Department of Orthopedics and Rehabilitation

Background: Large head metal-on-metal (MOM) total hip prostheses are relatively new technology. At our institution all such implants were utilized from 2006-2010, therefore intermediate to long-term follow-up data is lacking. The goal of this study is to compare Zimmer Durom MOM implant failure and dislocation rates to Zimmer Trilogy metal-on-polyethylene (MOP) rates greater than four years postoperatively. Methods: We retrospectively compared failure and dislocation rates in patients with Durom MOM implants (n=155) to those receiving Trilogy MOP implants (n=154). Minimum follow-up was set at four years, and failure was defined as revision, or persistent groin pain with pending revision. Results: Failure after a mean of 7.6 years was significantly higher in the Durom group (26.5%) than the Trilogy group after a mean of 7.7 years (5.2%) (p<0.001). Reasons for failure included pseudotumor formation, persistent pain, aseptic cup loosening, trauma, infection, and dislocation. Dislocation was far more prevalent in the Trilogy group (5.8%) than the Durom group (0%) (p=0.002). Conclusions: The Durom component statistically decreased the risk of dislocation compared with MOP total hip arthroplasties. The implant also eliminates the risk of polyethylene wear over time. However, other complications led to approximately 5 times higher failure rates at intermediate follow-up than MOP. The major contribution of this project is the prolonged follow-up period, as well as an investigation into the mechanism of failure, and why certain implants failed earlier than others. Our study supports the necessity for continued close monitoring of all patients that have received MOM prostheses, and continued data collection as more long-term outcomes become available.
Predicting Second-Look Transurethral Resection Utilization and Its Impact on Recurrence of Non-Muscle Invasive Bladder Cancer

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Department: Urology, University of Wisconsin School of Medicine and Public Health

Mentors: Tracy Downs, MD

Support: Shapiro Summer Research Program; Department of Urology

Introduction: A second-look Transurethral Resection (TUR) functions to confirm no residual cancer after a complete initial resection of a bladder tumor or when further pathological information is needed. The American Urological Association (AUA) moderately recommends performing a second-look TUR for high-risk, high-grade Ta tumors and strongly recommends a second-look TUR for T1 tumors within six weeks. The aim of this study is to determine major predictors of a second-look TUR utilization at UW hospital and to evaluate its impact on recurrence of bladder cancer. Methods: A retrospective study of patients who underwent a total of 88 second-look TURs after an initial complete resection were evaluated from a total of 505 patients who had at least one Transurethral Resection of Bladder Tumor (TURBT) from 2000-2016. Chi square analysis and multivariate logistic regression were performed to find predictive indicators of a second-look TUR and second-look TUR’s impact of recurrence. Results: Significant predictors of second-look utilization include: physician (P=.0006), stage and grade (P<.0001), era (P=.0017), tumor size (P<.0001), and BCG therapy (P<.0001). Multifocal tumors were associated with a lower second-look TUR utilization. Second-look TURs showed a significant reduction in recurrence for Ta-low grade (P=.011), but not for T1-high grade tumors (P=.6224). Conclusions: Important predictors of a second-look TUR at our institution largely depended on the physician and tumor characteristics. Despite AUA guidelines, second-look TUR only reduced recurrence for Ta-low grade tumors.
ASSESSING THE RISK OF HYPERCALCEMIC CRISIS IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

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Mentors: David Schneider, MD, MS; Reese Randle, MD

Support: Department of Surgery NIH Ruth L. Kirschstein National Research Service Award (NRSA) Short-Term Institutional Research Training Grant (Parent T35)

Background: Hypercalcemic crisis (HC) is a rare, potentially life-threatening complication of hypercalcemia. Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia and can manifest as hypercalcemic crisis. This study aims to identify patients with PHPT at greatest risk for developing HC.

Methods: This retrospective cohort study included patients with a pre-operative calcium of at least 12 mg/dL undergoing initial parathyroidectomy for PHPT from 11/2000–03/2016. This cohort was then separated into two groups: 1) those with HC, defined as those patients hospitalized and treated for hypercalcemia, and 2) those without HC. We compared the two groups using Mann-Whitney U tests and chi-squared tests where appropriate. Multivariable logistic regression identified predictors of HC. Additionally, we performed a classification tree (CART) analysis to produce a decision tool that can classify patients by risk of HC. Results: Of the patients meeting inclusion criteria, 29 (15.8%) had HC and 154 (84.2%) did not. The two cohorts were similar in age, gender, alcohol use, smoking status, BMI, and Charlson comorbidity index (CCI). Patients with HC were more likely to have a history of kidney stones than patients without HC (31.0% vs. 14.3%; P=0.039). Compared to those without HC, patients with HC also had higher pre-operative calcium (median 13.8 vs. 12.4 mg/dL; P<0.001), higher pre-operative parathyroid hormone (PTH) (median 318 vs. 160 pg/mL; P=0.001), and lower pre-operative total vitamin D (median 16 vs. 26 ng/mL; P<0.001). Cure rates with parathyroidectomy were similar in both groups, but nearly double the proportion of patients with HC required resection of more than one gland compared to patients without HC (24.1 vs. 12.3%, P=0.12). In multivariable analysis, higher pre-operative calcium (Odds Ratio [OR] 1.7, 95% Confidence Interval [CI] 1.1-2.5, P=0.01), elevated PTH (OR 1.0, 95% CI 1.0-1.0, P=0.01), and history of kidney stones (OR 3.0, 95% CI 1.1-8.2, P=0.04) were independently associated with HC. The CART decision tree revealed that over 90% of patients with a calcium ≥ 13.25 mg/dL and a CCI ≥ 4 developed HC. Additionally, 60% of patients with calcium ≥ 13.25, CCI < 4, and PTH ≥ 394 also had crisis. The CART model carried an overall predictive accuracy of 90%, and a positive predictive value of 76%. Conclusions: These data indicate that patients with calcium ≥ 13.25, PTH ≥ 394, and a CCI ≥ 4 are at increased risk for developing HC. The decision tool reported here can help identify patients at greatest risk for developing HC, and allow surgeons to expedite parathyroidectomy accordingly.
EFFECTS OF INTRALIPID ON SERUM PARTITIONING OF CANCER-TARGETING ALKYLPHOSPHOCHOLINE ANALOGS

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Mentor: John S. Kuo, MD, PhD

Support: Shapiro Summer Research Program; Department of Neurological Surgery

Introduction: Alkylphosphocholine (APC) analogs are lipophilic small molecules that selectively target a broad spectrum of human cancers. Radioactive iodine-labeled (CLR1404) or fluorescent APC analogs (CLR1501, CLR1502) are progressing to clinical trials for cancer imaging and therapeutic applications. Pharmacologic strategies to shift the serum partitioning of APC agents from the protein-bound layer (predominantly albumin) to the lipoprotein layer may optimize pharmacokinetics, thus improving timing of APC administration with imaging or surgery. Intralipid, an FDA approved essential fat formulation composed primarily of triglycerides that yields free fatty acids following lipolysis, may decrease the amount of albumin-bound APC analogs through competitive binding of fatty acids. This study assesses whether Intralipid increases the lipoprotein-bound fraction of APC analogs while decreasing the albumin-bound fraction in human plasma.

Methods: Fresh unfrozen human plasma samples were incubated with APC analogs (\(^{125}\)I-CLR1404, CLR1501, CLR1502) and Intralipid and compared to control samples that contained plasma and APC analogs without Intralipid. To measure the drug partitioning in each layer following ultracentrifugation, assays for the percent activity or fluorescence corresponding to labeled APC were performed.

Results: Addition of Intralipid increased APC partitioning to the plasma lipoprotein layer from 0.64% to 3.78%, 7.33% to 14.40%, and 6.15% to 11.26% for \(^{125}\)I-CLR1404, CLR1501, and CLR1502 respectively. Concomitantly, the albumin-binding percentage decreased from 98.07% to 94.48%, 85.93% to 79.32%, and 90.34% to 84.64% with the use of Intralipid (p<0.05).

Conclusion: These data suggest that the APC partitioning to the lipoprotein fraction increases at the expense of partitioning to the albumin-bound fraction due to Intralipid administration. Since lipoprotein-bound drugs have increased bioavailability and faster half-lives following high fat diets, the use of Intralipid to elevate plasma fatty acid levels may allow faster tumor cell APC uptake. Reducing the time needed between drug administration and cancer imaging or surgery would facilitate clinical adoption of these cancer-targeting agents. Pharmacokinetics optimization of APC analogs with Intralipid should be explored further.
IMPROVED COOKSTOVE EFFECTS ON PERSONAL CARBON MONOXIDE EXPOSURE IN SAN LUCAS TOLIMÁN, GUATEMALA

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Mentor: James Svenson, MD, MS

Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine, Friends of San Lucas Mission

Introduction: Installation of planchas mejoradas (improved ventilated cookstoves) has been shown to improve 24-hour carbon monoxide (CO) exposure and particulate matter (PM) profiles in the Guatemalan highlands. However, a 2015 UWSMPH survey in San Lucas Tolimán, Sololá, found high average levels of CO at 5.5% that did not correlate with village or stove type, contrary to results of previous studies. This is important in that continuing chronic exposure may lead to neurologic, rather than just respiratory effects.¹

Objective: The purpose of this study is to evaluate the effects of cookstoves on carbon monoxide levels in the villages surrounding San Lucas Tolimán.

Methods: This was a cross sectional observational study conducted in six rural communities on Lake Atitlan in southern Guatemala. To assess diurnal variation, blood carboxyhemoglobin concentrations (SpCO) were measured at three different times during the day: morning, midday, and early evening. Type and location of the stove used by the patient were recorded as well as any respiratory, eye, and low level CO poisoning symptoms. Results: 122 patients were included. Patients completed an average of six CO spot checks over a three day period. CO averages by stove type varied only slightly (SpCO 5.465% for open fire stoves, SpCO 4.664% for improved stoves, SD2.3155) and were not statistically significant. CO averages by time of day were also minor and not statistically significant. Exposure differences by community were also not significant. Conclusion: The results of this study found high average SpCO levels in all participants, similar to those expected in tobacco smokers and largely independent of stove type and time of day. This lack of correlation suggests that improved cookstoves used in these communities may be able to reduce an individual’s exposure to particulate matter, but might not be able to improve exposure to CO. Some contributor other than cookstoves may be a greater driver in determining individual CO exposure in this area. Chronic excessive CO exposure for children and adults may present concerning long term health implications. Both further study of other potential carbon monoxide sources in the San Lucas area and of long term health impacts of continued exposure are necessary.

Reference:
EFFECTS OF STROKE AND HEAD AND NECK CANCER ON PROXIMAL ESOPHAGEAL CONTRACTION USING HIGH RESOLUTION MANOMETRY

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Support: Department of Surgery NIH T32DC009401; R21 DC011130

Introduction: Patients with stroke or head and neck cancer (HNCa) often experience long-term effects of dysphagia. Along the swallowing pathway, the proximal esophagus exhibits a unique contractile property compared to the rest of the esophagus. There is currently no clear understanding of how the proximal esophageal contraction is altered in a pathological state. The purpose of this study is to evaluate the effects of stroke and HNCa on swallowing-related proximal esophageal pressure. Methods: We analyzed retrospective swallowing pressure data from 62 healthy adults, 9 patients with stroke, and 17 patients with HNCa. Each participant performed three swallows of 1-3 mL of normal saline. High resolution manometry was used to measure four variables: proximal esophageal contraction amplitude; contraction duration; pharyngo-esophageal transition time from the velopharynx; and pharyngo-esophageal transition time from 1 cm above the upper esophageal sphincter (UES). A one-way analysis of variance (ANOVA) was done to compare variables between the three groups. We hypothesize that patients with stroke and HNCa have longer pharyngo-esophageal transition time, shorter contraction duration, and lower proximal esophageal contraction amplitude than in healthy people. Results: Patients with stroke experienced significantly longer pharyngo-esophageal transition time from the velopharynx than healthy participants and HNCa patients (p < 0.01). Patients with stroke exhibited longer pharyngo-esophageal transition time from 1 cm above the UES than both controls and HNCa patients (p < 0.01). HNCa patients had significantly longer pharyngo-esophageal transition time from 1 cm above the UES than healthy participants (p < 0.05). The control group experienced significantly longer contraction duration than both stroke and HNCa groups (p < 0.05 and p < 0.01, respectively). No significant differences in contraction amplitude were observed (p > 0.05). Conclusion: Patients with stroke and HNCa experience delayed onset of proximal esophageal contraction and shorter contraction duration. These findings may be helpful to clinicians for understanding the effects of stroke and HNCa on swallowing. Future directions to address our limitations include evaluation of the proximal esophageal contraction with different bolus volumes, consistency, and swallowing techniques.
THE RELATIONSHIP BETWEEN CAREGIVER BURDEN, PATIENT BEHAVIORAL SYMPTOMS, AND MEMORY CLINIC SERVICES

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Support: Shapiro Summer Research Program; Department of Medicine; Wisconsin Alzheimer’s Institute; Department of Veterans Affairs Geriatric Research, Education, and Clinical Center; Wisconsin Alzheimer’s Disease Research Center

Introduction: The Wisconsin Alzheimer’s Institute (WAI) Dementia Diagnostic Clinic Network was developed to increase access to dementia diagnostic services and dementia-capable care throughout Wisconsin. These clinics will become increasingly important, as it is projected that 130,000 Wisconsin residents will be diagnosed with Alzheimer’s disease by 2025\(^1\). Wisconsin caregivers annually provide millions of hours of unpaid care\(^1\). People with dementia may exhibit behavioral symptoms such as aggression, depression and anxiety, yet limited research directly links these symptoms to measures of caregiver burden and how this impacts care provided to patients and loved ones. Identifying the relationship between patient behavioral symptoms and caregiver burden can help target patient care and direct provision of caregiver resources to best support those impacted by dementia. Our objectives were to characterize the relationship between patient behavioral symptoms, as rated by the Revised Memory and Behavior Checklist (RMBPC) Frequency scale and caregiver burden as rated by the RMBPC Reaction scale for patients seen in the WAI clinic network between 2008 and 2015 and to utilize these results to evaluate services provided to patient/caregiver dyads during initial memory evaluations. Methods: From 2008-2015 WAI received initial memory evaluation datasheets (n=9,448) from the clinic network containing patient demographics, domain-specific cognitive scores, depression scores, diagnoses, family history, and information regarding care and referrals provided. 1,314 datasheets with both RMBPC Frequency and Reaction scores were collected. Pearson Correlations, Chi Square Tests, and Mann-Whitney Rank-Sum T-Tests were conducted to analyze patient characteristics, caregiver burden, and clinic services provided between the two groups. Results: Caregivers reported increased distress when patients showed more frequent behavioral symptomology as rated by the RMBPC Frequency and Reaction scales (r= 0.745, p<0.0001) suggesting that patient behaviors contribute to caregiver burnout. Caregiver Reaction scores had a slight negative association with patient global cognitive function (r=-0.0844, p=0.00376, n=1,176), but were not significantly related to domain-specific measures of immediate memory, delayed memory, or visuospatial construction (all p>0.14). Patient behavioral symptoms correlated with increased depression scores (r=0.255, p<0.0001). Patients and caregivers who reported frequent behavioral symptoms and caregiver distress were more likely to be counseled on caregiver support and referred to outside resources (p< 0.03). Patients with lower Mini-Mental Status Exam scores were also more likely to be referred out to community resources (p< 0.001). Conclusion: Patient behavioral symptoms contributed to caregiver burden in our cohort of 1,314 patient/caregiver dyads. Only 14% of respondents filled out both RMBPC questionnaires suggesting limitations with broad usage of these tools. Of those who filled out the RMBPC, dyads reporting higher levels of behavior symptoms or increased caregiver distress were more likely to be educated regarding caregiver support and referred to community resources. More research needs to be done to evaluate these relationships in the WAI clinic network, including possible implementation of a more widely-usable caregiver burden tool and patient behavioral symptom questionnaire.

Citation:
PROSTATIC FIBROSIS CONTRIBUTES TO BLADDER OUTLET OBSTRUCTION IN MEN WITH SMALL PROSTATES

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Support: Department of Surgery NIH grant T35DK062709

Introduction: Hounsfield units (HU) is a quantitative measure of radiodensity on CT and has previously been used as a surrogate marker for liver and lung fibrosis. We used HU as a surrogate marker for prostate fibrosis to test the recently formulated hypothesis that prostate fibrosis contributes to bladder outlet obstruction and lower urinary tract symptoms (LUTS) in aging men. Methods: From a database of more than 300 men who have undergone surgery for BPH/LUTS with complete pre-operative urodynamic evaluation, we identified 38 patients for whom non-contrast axial pelvic CT scan images were available. The mean prostate HU was determined by averaging the HU of ellipsoid selections of the proximal, middle, and distal prostate. The bladder outlet obstructive index (BOOI) was calculated using the formula $P_{\text{det}}Q_{\text{max}} - 2Q_{\text{max}}$ and the resulting value is used to classify patients as obstructed (BOOI ≥ 40), equivocal (BOOI 20 – 40), or unobstructed (BOOI < 20). Results: Correlations of prostate volume (18.34-184.7, mean 62.84), prostate radiodensity (13.5-53.3, mean 36.6 HU) and BOOI (6-140, mean 53.12) were performed using linear regression analysis. This revealed a significant positive relationship between prostate volume and BOOI (p-value = 0.015) but only a weak positive relationship between prostate radiodensity and BOOI (p = 0.2186). Linear regression with interaction suggests that the effect of fibrosis on obstruction decreases as the volume increases. For example, for a prostate volume of 20 cc, an increase of HU by 1.0 is associated with an increase of BOOI of 1.45. For a prostate volume of 100 cc, an increase of HU by 1.0 is associated with an increase of BOOI of 0.10. (p-value=0.61). Further analysis shows that at prostate volumes less than 47 cc the contribution of density to BOOI is always greater than prostate volume (p-value=0.387), while at prostate volumes greater than 90 cc, the contribution of volume to BOOI is always greater than the effect of density (p-value=0.406). Conclusion: These preliminary studies suggest that both prostate volume and fibrosis contribute to bladder outlet obstruction but that the contribution of fibrosis to obstruction is relatively much greater in smaller prostates. This is consistent with clinical impression and with the relatively better outcomes achieved with transurethral incision of the prostate in men with small prostates.
THE IMPACT OF DIRECTION OF DISPLACEMENT, PIN CONFIGURATION, AND SURGEON TRAINING ON CLINICAL AND RADIOGRAPHIC OUTCOMES IN TYPE III PEDIATRIC SUPRACONDYLAR HUMERUS FRACTURES

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Support: Wisconsin Academy of Rural Medicine (WARM); Department of Orthopedics and Rehabilitation

Background: Displaced supracondylar humerus fractures are associated with higher rates of neurovascular injury, malunion and are treated surgically. Lateral displacement likely disrupts the medial periosteum and may be prone to higher rates of fixation failure when treated with all-lateral pinning providing only lateral stability. This study aims to evaluate the impact of fracture displacement, pin configuration and surgeon training on clinical and radiographic outcomes.

Methods: Patients aged two to twelve years with Gartland type III fractures were identified over a ten-year period at an academic center and a local community hospital. Fracture characteristics and surgeon training were recorded. Pin configuration, coronal, and sagittal alignment were recorded from postoperative radiographs and at final follow up. Initial, postoperative, and final neurovascular status was recorded. Complications recorded included permanent neurovascular deficit, malunion, rotational instability, and reoperation rate. Statistical analysis included chi-squared, Fisher’s exact, and T-tests. Results: 1715 patients were identified, yielding 151 type III fractures. 99 were included in the analysis. Posteromedially displaced fractures had a higher rate of coronal malunion (p=0.002), while posterolaterally displaced fractures had increased extension malunions (p=0.035). Straight posterior displacement had a lower total malunion rate (p=0.048). All-lateral constructs had increased rotational instability as compared to cross-pinning (p=0.009), and trended towards increased combined malunions (p=0.054), with no difference in neurovascular complications. Laterally displaced fractures trended toward being less rotationally stable with all-lateral fixation (p=0.073). Laterally-based constructs that had no rotational instability had a mean pin spread of 15.2 mm at the fracture site, as compared to 9.2 mm for rotationally unstable constructs (p=0.026). There was no difference in complications for fellowship vs non-fellowship trained surgeons for neither fixation type.

Conclusion: For type III supracondylar humerus fractures, all-lateral fixation has higher rates of rotational instability. Increasing the spread of pins at the fracture site limits this. Posteromedially and posterolaterally displaced fractures have higher rates of coronal and sagittal malunion, respectively, while straight posteriorly displaced fractures appear more stable. Lateral fixation is less rotationally stable, but this may be mitigated by wider pin spread at the fracture. Displacement direction appears related to malunion rates. It is safe to treat displaced supracondylar humerus fractures without fellowship training.
EFFICACY OF TRANSVERSUS ABDOMINIS PLANE STEROID INJECTION FOR TREATING CHRONIC ABDOMINAL PAIN

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Support: Shapiro Summer Research Program; Department of Anesthesiology

Background: Transversus abdominis plane (TAP) block is a procedure in which local anesthetics are injected in between the internal oblique muscle and transversus abdominis muscle. Historically, this procedure has been done in order to treat acute abdominal pain that accompanies a variety of surgical procedures. This study was conducted to evaluate the efficacy of the TAP block procedure in patients experiencing chronic abdominal pain and that have failed other forms of pain management. Methods: This was a retrospective analysis that included collecting data about 30 patients who received 45 TAP blocks for treating chronic abdominal pain between 1/1/2014 and 5/20/2016. Data collected included demographic data, surgical history, medication use, improvement following each block, and the side on which the procedure was performed. Data was compared before and after each block. In completing the procedure, Ultrasound (US) was used in all blocks to identify the TAP between the internal oblique and transversus abdominis muscle. The site was anesthetized using lidocaine 1%, then a solution formed of Bupivacaine 0.25% and Triamcinolone was injected into the TAP. In unilateral blocks, 8 mls of bupivacaine 0.25% mixed with 40 mg of Triamcinolone were injected. In bilateral blocks, 9 mls of Bupivacaine 0.25% and 40 mg of Triamcinolone were injected on each side. Injections were done under direct US visualization ensuring spread of the medication into the appropriate plane and using 22 gauge spinal needle on the syringe to deliver the medication. The analgesic efficacy was assessed via improvement of pain levels before and after the procedure was performed. Results: The TAP block improved pain in 79.5% of the performed blocks. The percent improvement was 54.7 ± 36.4% for an average duration of 84 ±108 (0-490 days) for the 44 patients with complete data. There was significant reduction in the use of Gabapentin before and after procedure (p< 0.05). Conclusion: Our study showed success of TAP steroid injections, which alleviated chronic abdominal pain 79.5% of the time. TAP steroid injection can be a helpful modality for treating chronic abdominal pain resistant to medication management.
HEALTHCARE WORKER PERSPECTIVES OF MOTIVATION TO REDUCE HOSPITAL-ACQUIRED INFECTIONS

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Support: Shapiro Summer Research Program; Department of Medicine

Background: Preventing the transmission of hospital-acquired infections (HAI) is essential for patient safety. HAI are adverse events that are considered preventable if evidence-based practices are followed. It has been estimated that between 44,000 to 98,000 individuals per year die as a result of preventable medical errors. In efforts to reduce HAI, hospitals have created protocols for healthcare workers to follow to streamline the implementation of best-practice guidelines into their workflow. However, adherence to such complex behavioral interventions to reduce HAI can be challenging and requires motivation and drive to consistently sustain. We undertook a qualitative study to examine differences among healthcare worker motivation for reducing HAI. We applied the Consolidated Framework for Implementation Research (CFIR) model to analyze motivation behind healthcare workers’ approaches to infection prevention in order to determine facilitators and barriers to successful intervention implementation. Methods: A phenomenological qualitative study of healthcare workers was conducted to explore factors influencing motivation to consistently apply evidence-based preventive measures. Ten semi-structured interviews were performed of individuals involved in the implementation of HAI prevention efforts at various levels. Interviews were recorded and transcribed, and data were analyzed using a thematic approach based on the CFIR model. Results: The eight most influential topics within the CFIR model discussed by interviewees were: 1) Patient Needs & Resources, 2) External Policy & Incentives: Financial Motivation, 3) Available Resources, 4) Goals, Monitoring, & Feedback, 5) Culture, 6) Implementation Climate, 7) Leadership Engagement, and 8) Evidence Strength & Quality. The majority of participants recognized patient safety as their primary motivation for HAI prevention efforts. Many acknowledged the benefit that national policy implementation has provided by bringing attention to a need for greater resources for prevention, and by motivating leadership to support workers in their prevention efforts. Many interviewees discussed the impact that the culture of the hospital has had on their motivation to improve HAI prevention. Conclusion: Several factors influence healthcare worker motivation to reduce HAI. Future studies in other hospital settings should examine if perspectives in academic learning centers differ from those found in non-academic learning centers and by healthcare worker role.

Citations:
LONG-TERM OUTCOMES FOLLOWING MESH-AUGMENTED VAGINAL PROLAPSE REPAIR

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Support: Shapiro Summer Research Program; Department of Obstetrics and Gynecology

Background: In 2002, the US Food and Drug Administration (FDA) cleared the first surgical mesh product specifically for use in prolapse, leading to a large increase in the use of mesh for prolapse repair1. Six years later, they released a warning that transvaginal placement of surgical mesh for prolapse was associated with severe complications2. Synthetic mesh has been used at our institution for transvaginal prolapse repair since the mid-1980s, uniquely positioning us to characterize long-term outcomes decades after surgery.

Methods: We conducted a retrospective chart review of all patients who underwent vaginal surgery for pelvic organ prolapse with synthetic mesh augmentation between 1985 and 2010 at a single academic institution in the Midwest. A list of potential eligible patients was generated through Current Procedural Terminology (CPT) codes used by our hospital billing systems since 1985, and only patients who received synthetic mesh were included. Descriptive analyses were performed from data abstracted from electronic medical records of eligible patients to characterize the sample and to determine factors associated with complications both during and after hospitalization such as infection, mesh extrusion, hospital readmission, as well as rate of subsequent pelvic surgery.

Results: Among 197 potential patients identified, 92 (47%) were eligible for inclusion and underwent surgery between July 2002 and October 2010. Overall, 21% (19/92) experienced complications during hospitalization and 38% (35/92) experienced complications after hospitalization. Concomitant hysterectomy was statistically significantly associated with complications during hospitalization (OR=8.3, p=.002). Twenty patients (20%) had documented mesh extrusion: 9 (10%) in the anterior compartment, 13 (12%) in the posterior compartment, and 1 (1%) in the apical compartment. Posterior mesh extrusion was more common with a T-incision as compared to vertical or horizontal incision (p=.021). Obese patients (n=42, 47.7%) were more likely than overweight (n=27, 30.6%) and normal weight patients (n=19, 21.5%) to develop infections after surgery (p=.051), and particularly more likely to develop UTIs (p=.031). 24 patients required subsequent pelvic surgeries; women younger than 65 (n=56, 60.9%) were more likely than older women (n=36, 39.1%) to have a subsequent mesh-related procedure (p=.003).

Conclusions: The overall rate of complications following surgery for prolapse with vaginal mesh placement was high (almost 40%), and was higher in obese women and those who underwent concomitant hysterectomy at the time of prolapse repair. The most common site of mesh extrusion was the posterior compartment and T-incision significantly increased this risk. Younger women were more likely to undergo additional surgical intervention. The next step in this research is to invite these women to complete a quality of life questionnaire and physical examination to augment these preliminary data. Our hope is that our findings can be used to inform pre-operative counseling of patients considering these procedures about long-term outcomes and risks of complications.

Citations:
HOW MOTION TRACKING RELATES TO END PRODUCT QUALITY IN LAPAROSCOPIC PROCEDURES

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Support: Shapiro Summer Research Program; US Army Medical Research Acquisition Activity grant (W81XWH-13-1-008)

Background: Objective measures of surgical skill are needed to improve the feedback trainees receive during their surgical education. Research using motion tracking technology has helped to quantify surgeons’ dexterity into performance metrics such as path length, working volume and motion smoothness. This work has successfully shown a difference in these metrics when comparing experts and novices. However, comparing motion metrics with end product quality could provide specific feedback on psychomotor skills and how trainees may improve task completion quality. The purpose of this study is to identify and model the relationship between motion metrics and a quantitative measure of end product quality (“hernia repair score”) in a simulated laparoscopic ventral hernia (LVH) repair. We hypothesize that lower values of path length, working volume, and motion smoothness relate to higher hernia repair score.

Methods: Surgical residents (PGY 2-3, N = 39) from Midwestern programs performed a simulated LVH repair. During the procedure, three electromagnetic sensors were placed on each hand (thumb, index finger, and wrist). Position data was used to calculate path length, working volume, and motion smoothness during the placement of the first transfacial suture. After the simulation, the hernia repair was rated using a previously validated checklist to score the quality of mesh attachment on a 24-point scale. To prepare the data, a log transform was applied to the motion smoothness data and factor analysis was used to combine metrics from the six sensors into one or two standardized variables. The relationship between these standardized variables and hernia product score was modeled using linear regression.

Results: Multiple regression analysis tested if path length significantly predicted hernia repair score. The results indicated that the path length of the dominant (β = -2.084, p = .021) and non-dominant hand (β = -1.830, p = .040) explained 26.1% of the variance in hernia repair score (R² = .261, F(2, 30) = 5.284, p = .011). However, multiple regression analysis showed that working volume did not significantly predict hernia product score (R² = .083, F(2, 31) = 1.412, p = .259). A simple regression analysis demonstrated that the log transform of motion smoothness (β = -2.878, p = .001) significantly predicted hernia product score, explaining 28.9% of the variance (R² = .289, F(2, 31) = 12.616, p = .001).

Conclusions: Regression analyses show that shorter path lengths and smoother movements significantly predict higher hernia repair quality. While the independent variables account for less than 30% of the variance, it is noteworthy that the motion metrics of a single stitch have significant, predictive validity for final product outcomes. While additional work is needed, these findings have significant implications for the potential use of motion tracking in measuring surgical performance.
EVALUATION OF A ‘FLIPPED CLASSROOM’ PILOT OF THE ADVANCED LIFE SUPPORT IN OBSTETRICS (ALSO) CURRICULUM

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Support: Summer Student Research and Clinical Assistantship Program, Department of Family Medicine and Community Health

Background: Advanced Life Support in Obstetrics (ALSO) is an emergency obstetrics skills training program that is taught to thousands of resident and attending physicians and other clinicians annually in the US and actively in 50 other countries. The ALSO curriculum is being redesigned as a “flipped classroom” with pre-course, on-line learning and testing plus on-site workshops and discussions. The objective of this project is to evaluate a June 2016 pilot of the course as compared to standard ALSO courses. Methods: Surveys and group feedback sessions were completed with 31 participants and 22 instructors to address content, web interface, course design, testing, and satisfaction with each course component. This data was qualitatively assessed and compared with responses from a standard ALSO course. Practical skills test results were compared with a comparison group from a standard ALSO course. Results: Participants in the pilot course preferred the combination teaching style of online and in-person learning for 14/16 ALSO chapters. Based on the survey information gathered, the majority of participants used the online slides (81.9%) and video capture (52.5%) as means of study. The testing in the pilot course was also successful as 100% of participants passed all written and skills testing. Participants in the pilot course also scored the same or better in 20 out of 24 individual skills as compared to a standard ALSO course. The qualitative assessment instructors’ comments found that there was a fear of participants’ potential lack of preparedness with the “flipped classroom” format; this fear was determined to be unproven. Conclusions: Overall, the “flipped classroom” format of the ALSO course was very well received and the lessons learned will be used to inform further flipped classroom development by the American Academy of Family Physicians and the local course directors and faculty who provide ALSO instruction.
IMPACT OF COMPLICATIONS AFTER PANCREATECTOMY IN THE ACS-NSQIP PROCEDURE-TARGETED DATABASE

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Support: Shapiro Summer Research Program; Department of Surgery

Background: Existing federal quality initiatives primarily target a number of nonspecific postoperative complications that are easy to measure without regard for their relative value, such as surgical site infection, venous thromboembolism, adverse cardiac events, and respiratory complications. The impact of these and other procedure-specific complications on the clinical and resource utilization of pancreatectomy patients is not currently known. We employ an empirical approach to examine the potential impact of a series of complications following pancreatectomy on mortality and resource utilization in order to identify the highest value targets for quality improvement interventions. Methods: Patients from the 2014 ACS-NSQIP Pancreatectomy-Targeted Participant Use File were included for analysis. The frequency of 2 procedure-specific and 7 non-specific postoperative complications were determined. Multivariable poisson regression with log link and robust error variance was used to determine the independent associations between individual complications and 30-day patient morbidity and mortality. Adjusted relative risk estimates from these models were used to calculate adjusted population attributable fractions (PAFs) as a measure of complication impact. Results: There were 5,047 patients who underwent pancreatectomy in the study period. The most frequent complications included bleeding (18.3%), pancreatic fistula (18.1%), organ/space surgical site infection (11.4%), and delayed gastric emptying (11.3%). Bleeding and pneumonia were the complications with the largest overall impact on 30-day end organ dysfunction and mortality in our study population. Prolonged hospital stay was most associated with delayed gastric emptying and pancreatic fistula. Hospital readmission was most attributable to organ/space surgical site infection and pancreatic fistula. Conclusion: Bleeding, pneumonia, pancreatic fistula, delayed gastric emptying, and organ/space surgical site infection have relatively large impacts on the clinical and resource utilization outcomes of patients who undergo pancreatectomy. Most of the complications that are targeted by existing federal quality initiatives (urinary tract infection, venous thromboembolism, and surgical site infection) have comparatively small impacts on this patient population. Redirecting initiatives towards the postoperative complications which matter the most would likely improve their effectiveness.
HAS THE AFFORDABLE CARE ACT ALTERED SOCIOECONOMIC DISPARITIES IN PATIENT OUTCOMES AFTER TRAUMATIC BRAIN INJURY?

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Background: The Patient Protection and Affordable Care Act (ACA) amounts to the most influential U.S. healthcare legislation in half a century, extending insurance coverage to 20 million Americans since its inception in 2010. Several ACA provisions mean to improve socioeconomic (SES) disparities in health, such as expanded access to care and quality improvement initiatives. Given that SES impacts patient outcomes after traumatic brain injury (TBI), we aimed to gauge the ACA’s effect on SES disparities in patient outcomes after TBI. Methods: The National Trauma Data Bank was utilized to identify TBI patients in two time periods: before (2008-2009) and after (2011-2012) ACA implementation. Our primary outcomes included hospital length of stay (LOS) and in hospital mortality. Using univariate and multivariate regressions models, while controlling for gender, age, geographical region, plus injury mechanism, type, and severity, we evaluated the impact that race and insurance status had on our endpoints. Data analysis was conducted with STATA, where p-values of <0.05 were considered significant. Results: The study examined 54,958 TBI patient outcomes from 2008-2009 and 84,033 from 2011-2012. The Medicaid population underwent a 21% decrease in the LOS coefficient, from 2.76 days (95% CI = 2.49 – 3.02; p = 0.000) to 2.17 days (95% CI = 1.98 – 2.37; p = 0.000), as compared to the Privately Insured. Despite this reduction in hospital days, hospital mortality remained unchanged for Medicaid patients, with odds ratios of 1.19 in 2008-2009 (95% CI = 1.02 – 1.39; p=0.03) and 2011-2012 (95% CI = 1.04 – 1.36; p = 0.009), when compared to the Privately Insured. Conclusion: Our study observed that within the Medicaid population, after implementation of the ACA, TBI-related in hospital mortality did not change while hospital LOS decreased. These findings correlate with decreased clinical risks. Further before and after studies over longer time periods are warranted to assess causal impact of the ACA on SES disparities in healthcare.
PREDICTION OF STRESS FRACTURE BASED ON DXA DERIVED INDICES OF STRENGTH

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Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

Introduction: Stress fractures are prevalent, debilitating injuries in athletes caused by the repetitive mechanical loading associated with running. While bone structural and anthropometric factors have been studied regarding their correlation with stress fractures, these parameters, specifically tibia specific dual-energy X-ray absorptiometry (DXA), have not been effectively used as predictive models of stress fracture in elite collegiate running athletes. The purpose of this study is to develop a model integrating focal tibia DXA-derived parameters and anthropometric data to predict stress fractures in collegiate athletes.

Methods: Retrospective chart review. The anthropometric data (age, height, weight, tibia length), general medical information (injury, diet, nutrition history), and dual-energy X-ray absorptiometry (DXA) data of 48 collegiate runners (24 men, 24 women) were analyzed for the index period, 8 clinician diagnosed stress fractures were recorded. We used multiple logarithmic regression analysis on fracture cases and controls to create a predictive model of stress fracture.

Results: Preliminary data indicate total bone mass, total lean mass, and age to be predictors of stress fracture, data from DXA derived strength parameters are currently being analyzed. For each 100g increase in total bone mass, the odds of experiencing a stress fracture decrease by 53% (OR=0.47; 95% CI: 0.25-0.90; p=0.02) after controlling for total lean body mass. No other associations were detected between the tibia predictors adjusted by total lean body mass (g) and occurrence of stress fractures. Conclusion: Our preliminary data show that anthropometric variables are better predictors than tibial DXA derived bone parameters in predicting stress fracture in collegiate running athletes. Further studies with greater sample size would be useful in showing correlation between DXA parameters and stress fracture.
EFFECTS OF INHALED FLUTICASONE ON UPPER AIRWAY COLLAPSIBILITY IN PATIENTS WITH ASTHMA

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Funding Support: Shapiro Summer Research Program; Department of Medicine; 1I01CX000579-01 United States Department of Veterans Affairs Merit Award

Rationale: OSA is prevalent among individuals with asthma. Either inhaled corticosteroid therapy or asthma itself may affect upper airway collapsibility (Teodorescu M. et al, JCSM, 2014; 10 (2): 183-193). We aimed to assess the effects of inhaled fluticasone (FP) on upper airway collapsibility during sleep, as measured by critical closing pressure (Pcrit), in relationship to standard wakefulness lung physiologic parameters. We hypothesized that FP will increase upper airway collapsibility (more positive Pcrit) by changing the dynamic with the lower airways obstruction and improving the degree of air-trapping.

Methodology: A 4-month, randomized-controlled experiment of high dose (HiFP; 1,760mcg/day) treatment or low dose (LoFP; 88mcg/day) inhaled FP (control group) was conducted. Pcrit was derived from the pressure-inspiratory flow relationship in the flow limited range during stable stage 2-3 NREM sleep. Severity of airflow obstruction (Forced expiratory volume during first second of forced vital capacity [FEV1]) on spirometry, lung volumes (Residual Volume/ Total Lung Capacity [RV/TLC]) and the Asthma Control Questionnaire (ACQ—full version) were assessed before and after treatment.

Results: To date, 8 steroid-naïve subjects (4 males, mean [±s.d.] age 35±14yrs, BMI 25±5 kg/m²) with well-controlled asthma (ACQ 0.89±0.43, FEV1 [%predicted] 87±7) and without significant sleep-disordered breathing (AHI 3±6 events/hour) were randomized (n=4/group), and had complete data sets throughout the protocol. Abovementioned baseline variable were not different among the two groups (all p-values >0.10); likewise, their baseline Pcrit was similar (0.12±0.91 vs. -2.93±3.67 cmH2O, p=0.19, in HiFP vs. LoFP). There were no significant group differences in Pcrit change (-2.01±2.82 vs. -0.79±2.53 cmH2O, p=0.54, in HiFP vs. LoFP). Within groups, the change in Pcrit did not relate to change in ACQ (β-estimate=3.15, p=0.35), FEV1 [%predicted] (β-estimate= -0.12, p=0.52) or RV/TLC [%predicted] (β-estimate=0.04, p=0.64).

Conclusions: In this small sample of otherwise healthy subjects with well-controlled asthma, treatment with high dose inhaled FP did not affect the Pcrit, as compared to low dose FP. No relationships emerged between changes in Pcrit during sleep with degree of airways obstruction or lung hyperinflation during wakefulness. Further testing in larger samples and, although technically challenging, employing lung physiologic measures during sleep may be necessary.
TEXTURE ANALYSIS OF RENAL CELL CARCINOMAS AT MDCT FOR PREDICTING PATHOLOGY

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Support: Shapiro Summer Research Program; Department of Radiology

Background: Tumors possess pathological heterogeneity which can be diagnostic for patient outcome as well as treatment efficacy. Patients with tumors that develop a greater degree of heterogeneity experience poorer outcomes which can be attributed to aggressiveness or decrease response to treatment. Biopsy and imaging are typically used for the histological analysis and staging of tumors, respectively. However, biopsy is invasive and not representative of overall tumor composition, and imaging is restrictive to the reader’s visual acuity and interpretation. Therefore, biopsy and traditional imaging are unable to comprehensively analyze the composition of tumors. This project aims to assess texture features of small renal cell carcinomas (T1a, <4cm) for predicting key pathologic features.

Methods: Quantitative CT texture analysis of small renal cancers (T1a, <4cm) was performed on noncontrast and portal venous phase abdominal MDCT scans with a ROI at the largest cross-sectional diameter of the tumor. Texture parameters were correlated with pathologic data from surgical resection, including histology and nuclear grade, as well as microarray analysis in a subset (n=40) including Ki67 index, CRP, and microvessel density (CD135/CD31).

Results: Portal venous phase images were available in 249 patients (105 women, 144 men; mean age, 56.6 years). CT texture features of standard deviation, mean of the positive pixels, and entropy of the pixel histogram were significantly associated with histologic cell type (clear vs non clear; p<0.001). Entropy and mean of the positive pixels also showed some relationship with nuclear grade, although not statistically significant. In the microarray analysis subset, kurtosis of the pixel histogram was associated with CD105/CD31 (p=0.002). Noncontrast CT images were available in 174 patients (72 women, 102 men; mean age, 57.5 years). Although the association with histology was not as strong as on the portal venous phase, in the subset of patients with microarray data, SD was found to correlate with CRP (p=0.08), kurtosis with CRP (p=0.004), CD135/CD31 (p=0.002), and with Ki 67 index (p<0.001).

Conclusion: CT texture features were significantly associated with important histopathologic features of small renal cancers. These non-invasive measures can be performed retrospectively and may provide useful information when determining follow up and treatment of small renal cancers.
TAGGING CAR T CELLS TARGETING GD2+ PEDIATRIC NEUROBLASTOMA USING CRISPR CAS9

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Background: Human T cells have been engineered to express chimeric antigen receptors (CARs) that target cancer associated antigens. Although CAR T cells have been successfully used to treat hematological malignancies such as leukemia, they are only just beginning to be used to combat solid tumors. As of now, solid tumor trials have highly variable outcomes. One possible cause of the differences in response may be due to incomplete understanding of expression levels of the CAR on the T cell surface. Typically, CAR T cells are engineered using viral methodologies. This results in CARs being inserted at random sites in the genome which can cause different surface level expression. Alternatively, there is a prokaryotic immune system involving clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR associated proteins (Cas) that cuts DNA at a specific sequence. This system can be modified to target a desired sequence of DNA. This project involves utilizing the CRISPR/Cas9 system to more precisely genetically engineer CAR T cells that recognize GD2+ neuroblastomas in the context of pediatric oncology. Methods: The aim is to deliver anti-GD2+ CARs to T cells via CRISPR/Cas9 in the AAVS1 safe harbor locus. This decreases the disparity in gene copy number by placing the CARs under the same promoter. The tags will be created by introducing small in-frame insertion and deletions (indels) in nonfunctional regions of the anti-GD2+ CAR using non-homologous end joining repair. The tags are read using reverse transcription of the mRNA from the cells followed by next generation sequencing. This will provide information of the indels created in the nonfunctional regions of the CARs, and will allow cells to be tracked and analyzed. Results: Anti-GD2+ CAR T cells were generated and placed into single-well plates in order to facilitate expansion. Conclusion: The engineering of tagged CAR T cells has many promising implications. Studies can be performed that monitor the levels of cytotoxicity of CAR T cells and how it correlates with cell surface expression of the CAR. Once the cytotoxicity is determined, the tags can be used to differentiate the cells and analyze them on a molecular basis. The cells can then be selected for in vivo experiments to try to maximize anti-tumor effects. In the future, we hope to inject the successful in vitro tagged CAR T cells into xenograft mouse models with GD2+ tumors. If the tumors respond to the treatment, the CAR T cells will be isolated and sequenced to determine which mutations lead to a positive outcome.
TEST-RETEST RELIABILITY, PREDICTIVE VALIDITY, AND GROUP LEVEL SENSITIVITY OF IMMEDIATE POST-CONCUSSION ASSESSMENT AND COGNITIVE TESTING

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Support: Shapiro Summer Research Program; Department of Radiology; Department of Orthopedics and Rehabilitation, US Army Medical Research and Materiel Command under Contract No. W81XWH-12-C-0204

Background: For athletes in contact sports, preseason computerized neurocognitive testing (CNT) is commonly administered to estimate premorbid functioning for comparison to post-concussion performance. CNTs, like the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), offer many logistical advantages over previous testing methods. Recently, ImPACT became the first and only concussion-specific solution to be granted medical device clearance by the Food and Drug Administration (FDA). Previous analysis of ImPACT has shown mixed results. This study looked at the test-retest reliability, predictive validity, and group level sensitivity of ImPACT in Division I collegiate athletes.

Methods: Athletes completed baseline concussion testing prior to the 2014 fall and winter sport seasons. Baseline sessions included ImPACT along with a variety of other measures. Those who went on to sustain concussions, as well as matched controls, were retested within 24 hours of injury as well as at 8, 15, and 45 days post-injury. The four ImPACT composite scores were analyzed.

Results: Baseline testing was completed by 237 athletes. 27 athletes were concussed during the study period. Athletes who sustained concussions were not different on any demographic variable or baseline ImPACT scores than athletes who did not sustain a concussion. Test-retest reliability for the control subjects between the 24 hour and 8 day time points showed intraclass correlation coefficients for ImPACT ranged from 0.71 to 0.86. No ImPACT composite scores at the baseline or 24-hour post-injury time points predicted total number of days lost from sport, with 24 hour r values ranging from -0.25 to 0.08. Concussed subjects scored significantly worse than control subjects on two of four composites at 24 hours and one of four composites at the 8 day time point. There were no significant differences between groups at any other time point.

Conclusion: Over a seven day test-retest interval, ImPACT showed strong test-retest reliability. ImPACT was not able to predict recovery time from concussion, and after 24 hours, ImPACT did not show sufficient sensitivity to the effects of concussion. Within 24 hours of injury, when concussed athletes should show major cognitive deficits, only two of four composite scores were able to show differences between the concussed athletes and matched controls. At day eight after injury, only one of four composite scores showed differences between groups. The outcomes of this study, as well as previous analysis, suggest there is not sufficient evidence for FDA approval of ImPACT as a concussion-specific medical clearance device.
EFFECT OF GALECTIN-3 ON NEURONAL CELL SURVIVAL IN RESPONSE TO OXYGEN GLUCOSE DEPRIVATION

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Background: Ischemic stroke causes oxygen and glucose deprivation (OGD) in the brain, leading to neuronal death mediated in part by dysregulated cytokine expression. Galectin-3 (Gal-3) is a carbohydrate-binding lectin with an established role in cell proliferation, migration, and angiogenesis, but its role in protection and repair from ischemic stroke is poorly understood. Gal-3 has been shown to stimulate growth of endothelial cells and neural progenitors in vitro, whereas antibody-mediated blockade of Gal-3 signaling suppresses angiogenesis and neural progenitor proliferation in the brains of rats subjected to cerebral ischemia. Gal-3 is thus emerging as an attractive molecular target for neuroprotection and post-stroke neurorepair. Objective: To establish neuronal cell lines overexpressing Gal-3 and to evaluate the ability of these cells to survive and recover from OGD and re-oxygenation in vitro. Methods: The LSGAL3 gene, which encodes human Gal-3, was transfected into two neuroblastoma cell lines: Neuro-2a (mouse) and B35 (rat). Transfections were done using Lipofectamine 2000 reagent with either the pEGFP-hGal3 plasmid, which contains the LGALS3 gene tagged with GFP, or the pEGFP-N2 control plasmid, which contains GFP only. Cells were subjected to 4 hours of OGD followed by 20 hours of re-oxygenation. Survival was then assessed quantitatively using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium) cell viability assay. Results: Successful transfection of all cell lines was confirmed by visualization of GFP under fluorescence microscopy. Expression of Gal-3 in Neuro-2a cells was further verified by immunofluorescent staining. Gal-3 expression significantly improved cell viability under OGD conditions for both Neuro-2a and B35 cells compared to control (p<0.01). Conclusion: Gal-3 can be efficiently overexpressed in both mouse and rat neuronal cell lines. Increased expression of Gal-3 confers a significant survival advantage to neuronal cells following in vitro ischemia and re-oxygenation. Future studies should be aimed at elucidating the molecular mechanism involved in Gal-3-induced neuroprotection, which may reveal new molecular targets in the prevention and treatment of stroke. Additionally, an immediate next step will be to conduct in vivo experiments to test whether transplantation of these Gal-3-overexpressing cells can improve outcomes in preclinical animal models of stroke.
SURGICAL START TIME AS A FACTOR INFLUENCING HOSPITAL LOS AFTER SHOULDER ARTHROPLASTY

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Introduction: Increased hospital length of stay (LOS) in patients undergoing shoulder arthroplasty contributes to increased cost and potential morbidity. Prior studies have identified many patient factors that are associated with increased LOS; the most common of which include age, female gender, and medical comorbidities(1,2,4,6,11,13,14,15). The purpose of this study was to find if surgical time of day affected hospital LOS for patients who underwent a shoulder arthroplasty procedure. Methods: We conducted a retrospective chart review of 256 patients who underwent shoulder arthroplasty at UW hospitals between January 2011 and May 2016. Our cohort was split into three groups based on surgical start time (defined as time of incision: <10 am, 10am-1pm, >1pm). Hospital LOS was defined as the length of time between the time of incision and patient discharge. We then used multivariate analysis to control for confounding variables and determine if surgical start time had a significant effect on hospital LOS. To find the optimal surgical start time that minimized hospital LOS, we used ROC analysis to identify the time that maximized the balance between sensitivity (probability of having LOS<1 day) and specificity (probability of having LOS>1 day). Results: We found that the surgical start time was a significant factor affecting hospital LOS after shoulder arthroplasty(p<0.001). The optimal surgical start time to minimize LOS was 12:47pm. Conclusion: Our study identified an optimal surgical start time(12:47pm) to reduce hospital LOS after shoulder arthroplasty which can be utilized by healthcare teams to schedule procedures for high risk patients to reduce hospital LOS. This will ultimately lead to better outcomes and reduce hospital costs.
PAPILLARY THYROID MICROCARCINOMA: DECISION-MAKING, EXTENT OF SURGERY, AND OUTCOMES

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Support: Department of Surgery NIH T35DK062709 grant

Background: Thyroid cancer is the fastest growing malignancy in the United States largely due to a 4-fold increase in papillary thyroid microcarcinoma (PTMC), tumors ≤1 cm. Nationally, 73% of PTMC patients undergo total thyroidectomy (TT) despite equivalent long-term outcomes with less extensive surgery. The objective of this study was to investigate patient and surgeon decision-making about the extent of surgery for PTMC. Methods: We conducted a retrospective review of papillary thyroid cancer patients operated on at a single institution from 2008 to 2016. Patients were included if their largest tumor was ≤1 cm and no other type of thyroid cancer was present. For patients diagnosed prior to surgery, decision-making about the extent of surgery was reviewed in all available documentation and categorized into patient or surgeon reasons. Data analysis was performed using Fisher’s exact, Chi-square, or Student’s t-tests as appropriate. Results: We identified 125 patients who had PTMC. The mean (± SD) age of the patients was 50.1 (± 14.6) years, and 85.6% (n=107) were female. The mean tumor size was 0.51 ( ± 0.3) cm. Overall, 27.2% of the patients underwent a thyroid lobectomy (TL; n=34), while 72.8% had a TT (n=91). Of the 125 patients, 19 (15.2%) were diagnosed preoperatively. These patients were similar to the rest of the cohort with respect to all variables, except a significantly higher proportion of patients had a TT (94.7% vs. 68.9%, p=0.01). In all cases, the documented reason for patients choosing the extent of surgery was the surgeon’s recommendation. Analysis of surgeon decision-making demonstrated that the most common reasons a TT was recommended were the potential for multifocal disease (8.7%), ease of follow up (8.7%), and patient history (8.7%). In 47.8% of cases, no specific reason for the surgeon’s recommendation was documented. Analysis of outcomes revealed that 5.3% (n=1) of the preoperatively diagnosed PTMC patients had a permanent complication, which was nearly double that of the rest of the cohort (2.8%, n=3; p=0.5). Conclusion: These data suggest that surgeon’s recommendations drive decision-making about the extent of surgery in preoperatively diagnosed PTMC patients and the vast majority undergoes TT. With recent guidelines supporting TL or active surveillance as the primary treatment for clinically node negative PTMC, further examination of the disparities in PTMC treatment decisions is needed to ensure that patients receive the most appropriate, preference-based care.
FEASIBILITY OF AN IMAGE-BASED MOBILE HEALTH PROTOCOL FOR POSTOPERATIVE WOUND MONITORING

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Introduction: Surgical site infection (SSI) is the most common nosocomial infection and a leading cause of unplanned hospital readmission among surgical patients. Many of these infections develop in the critical interval between hospital discharge and routine follow-up. If diagnosed at an early stage, SSI can often be treated in the outpatient setting. However, patients rarely recognize early stage wound infections causing them to present with an advanced infection requiring rehospitalization or operative reintervention. An intervention to prevent these catastrophic consequences would represent a substantial improvement in patient care. To address this, we developed and pilot tested a mobile health application (app) and protocol of remote wound monitoring using smartphones for vascular surgery patients at a large tertiary care academic institution.

Methods: We are currently recruiting 40 patients following vascular surgery. Eligible patients are 18 years of age or older with an incision at least 3 cm in length. Patients participate in a training session to learn to use the iPhone and the wound monitoring app. Following hospital discharge, patients send digital images of their wound and responses to a short survey daily for two weeks. Experienced healthcare providers on the vascular surgery service review these submissions daily and contact patients for any concerning findings.

Results: Since June 2016, 69 patients have been screened, 30 of whom were eligible for participation. Twenty-three have consented to participate and been enrolled (77% consent rate). Forty-seven percent of participants were novice smartphone users. Participants completed training in an average of 18 minutes, with an average system usability score of 85.2 (scale 0-100). Forty-six percent of participants submitted data every day, with an average of 1 day missed per participant. A provider reviewed submissions an average of 9.3 (range 0.1-43.7) hours after submission. Review took an average 2.5 (range 1-33) minutes per patient, with an average total 7.9 (range 1-39) minutes per day. Two participants were readmitted, one of whom fell on their amputation stump. One early wound infection was detected using submitted images and treated on an outpatient basis; no wound infections developed undetected in monitored sites. Patient satisfaction has been universally high upon completion.

Conclusion: Vascular surgery patients and their caregivers are willing to participate in a mobile health program aimed at remote monitoring of postoperative recovery, and they are able to complete the program with a high level of fidelity and satisfaction. Such a program is easily integrated into existing service lines and does not add a significant clinical burden. Preliminary results indicate the ability to detect and intervene on wound complications at earlier stages and prevent hospital readmission and potentially catastrophic wound complications.
Introduction: Healthcare disparities based on race and socioeconomic status have been documented in the literature; however, data on how these factors affect outcomes in patients experiencing severe thoracic trauma is lacking. This study aims to identify potential disparities in treatment and outcomes in this patient population. Methods: the National Trauma Data Bank was queried for all rib fracture patients with ISS scores>15 between 2007-2012. A univariate and multivariate logistic regression model was run which controlled for patient co-morbidities, age, ISS, and associated injuries. Patient outcomes in length of stay, mortality, discharge disposition, and in hospital procedures were compared between patients of varying race and insurance status to white and privately insured patients, respectively. Results: A cohort of 69,424 patients were selected for analysis. 87.1% of patients were white, 10.2% African American and 1.98% Asian. 14.2% of patients were covered by private insurance vs. 30.1% by Medicare and 21.5% by Medicaid. 34.1% were uninsured. Uninsured ((OR = 1.753; CI = 1.468- 2.094), Medicaid (OR = 1.568; CI = 1.295-1.898), and Medicare (OR = 2.768; CI = 2.313-3.313) patients had higher in hospital mortality than privately insured patients. Uninsured patients (OR = 0.804; CI = 0.745, 0.867) were less likely to exceed the median hospital stay, while Medicaid (OR = 1.445 CI= 1.331-1.568) and African American patients (OR = 1.144, CI + 1.083-1.208) were more likely to exceed the median hospital stay than those privately insured. Medicare (OR = 1.103; CI = 1.004-1.212) and Medicaid (OR = 1.328; CI =1.210-1.458) patients were more likely to received an epidural during the course of care than privately insured patients, but there were no other statistically significant differences with regards to race or insurance status. Medicaid (OR=1.330; CI = 1.216-1.453) and African American patients (OR = 1.081; CI = 1.018-1.148) were more likely to require mechanical ventilation than privately insured or White patients. Finally, uninsured patients (OR = 0.572; CI = 0.505-0648) were less likely to receive continuing medical care after hospitalization in a nursing facility or acute care rehab center. In contrast, Medicaid (OR=1.412; CI = 1.249-1.595) and Medicare (OR = 3.661; CI = 3.252- 4.121) patients were more likely to be discharged to one of these facilities. Conclusion: when examining healthcare disparities among thoracic trauma patients, we documented less significate differences among racial groups than among insurance statuses. Overall, we found the uninsured were more likely to be discharged early to their homes while Medicare and Medicaid patients were more likely to be discharged to a care facilities such as nursing homes or acute care hospitals. We also found the privately insured had lower mortality than Medicare, uninsured and Medicare patients. Further research is needed on whether changes implemented by affordable Care Act have helped to eliminate this disparities.
PREDICTORS AND COMORBIDITIES OF FOOD INSECURITY

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Background: Food Insecurity is a household-level economic and social condition of limited or uncertain access to adequate and nutritional food. Food insecurity has been linked with diabetes and obesity, as well as anxiety, depression, and behavioral disorders. The UW Department of Pediatrics piloted a screen for food insecurity. We describe demographic characteristics of screened patients, comparing risk factors and health outcomes between food insecure (FI) patients and non-FI patients. Methods: Four physicians at a UW pediatrics clinic participated in the pilot and gave a two-question screen to patients at well-child visits. We extracted the following variables on all screened patients: sex, age, race, ethnicity, insurance type, height, weight, BMI, BMI percentile, and any diagnosis of diabetes, hypertension, sleeping problems, restless leg syndrome, anemia, elevated blood lead levels, depression, anxiety, or attention deficit disorders. We then determined if any of the variables were significantly correlated with a positive food insecurity screen.

Results: Over the eight-month screening period, a total of 1330 patients were screened for FI, and 30 screened positive. Insurance type was a significant predictor for FI; patients on public/no insurance had 6.386 times greater odds of being FI than those on private insurance (CI 3.806, 13.293). Also, diagnoses of anemia and ADD/ADHD were both significantly higher in the FI group. The odds of having anemia was 8.467 times greater for FI patients than non-FI (CI 3.034, 23.625), and the odds for having ADD/ADHD was 9.269 times greater for FI patients than non-FI (CI 2.382, 36.074). All other comorbidities were comparable between the two groups. Conclusion: These results provide useful information to clinicians as the screening process moves towards widespread adoption. It is important to know what patient populations are at risk for FI and to understand the accompanying health implications to appropriately assist patients who screen positive. These results also inform an expanded investigation that will be conducted once screening is implemented throughout all UW Pediatric clinics. This larger study will have greater power to detect differences that could not be discerned in this small pilot investigation. A longitudinal study component will determine if FI patients either change to food secure or have some comorbidities alleviated, which may be indicative of successful social interventions.
PRE-SURGICAL RENAL MASS BIOPSY REDUCES UPFRONT TREATMENT COSTS FOR SMALL RENAL MASSES

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Introduction: Approximately 15-20% of incidental renal masses ≤4cm are benign tumors such as oncocytomas or lipid poor angiomyolipomas (AML), which can be managed non-surgically. Increasing utilization of small renal mass biopsy (SRMB) may reduce treatment of benign tumors, decreasing upfront costs and preserving renal function in untreated patients. The objective of this study is to evaluate if increasing SRMB utilization reduces surgical treatment and upfront (30 day) costs of care management for patients with benign small renal masses. Methods: Clinical and pathologic data were reviewed from patients with incidental renal masses ≤4cm who were treated surgically and/or received SRMB from 2003-2015. Patients not considering surgery were excluded. Patients were divided into 2 cohorts (2003-2009 and 2010-2015) for analysis to reflect increased SRMB utilization at our institution since 2010. Institution specific Medicare costs for 2015 were used to calculate costs of surgery and biopsy in all patient cohorts. Results: Of 437 patients with renal masses ≤4cm, SRMB was performed in 6% of 199 patients treated from 2003-2009 and 54% of 238 patients from 2010-2015. The rate of surgery for benign tumors from 2003-2009 was higher than 2010-2015, 19.7% vs. 12.3%, p=0.04. Patients treated without biopsy from 2010-2015, benign surgery rate was 21.8%. From 2010-2015, 42 patients with benign tumors were identified using SRMB and avoided surgery (10 AML, 32 oncocytoma). Given the upfront cost of $2,020.44 USD for ultrasound guided biopsy and $12,153.01 USD for partial nephrectomy, cost of care per patient were calculated each two cohorts. The cost per patient in the 2003-2009 vs. 2010-2015 cohort was $12,274.85 USD vs. $11,094.98 USD. Increased biopsy utilization was associated with $1,179.86 (9.6%) cost savings per patient. For 2010-2015, increased use of biopsy saved $280,840 USD in estimated upfront treatment costs. Conclusion: Pretreatment biopsy reduces surgery for benign tumors and decreases the upfront cost of care per patient by $1,179.86 USD. Increasing utilization of biopsy for small renal masses decreases overall treatment cost and preserves renal function in patients with benign tumors who avoid treatment.
DYSMENORRHEA IN WOMEN WITH ULCERATIVE COLITIS

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Introduction: Dysmenorrhea and Ulcerative Colitis (UC) are a disorder and disease, respectively that commonly affect women of menstrual age and have overlapping symptoms. Despite this, the relationship between the two is poorly understood. The aims of this study were to explore the impact of dysmenorrhea on pain severity and pain medication use in UC as well as the relationships between dysmenorrhea, UC disease activity, and health-related quality of life (HRQOL).

Methods: This was a case–control study that involved comparing menstruating women diagnosed with UC to their healthy counterparts. All subjects were administered a questionnaire in a clinic setting that addressed dysmenorrhea, pain severity, medication use, menstrual distress, and HRQOL. UC disease activity was also assessed. HRQOL was compared among cases and controls that reported dysmenorrhea. Results: 50 cases diagnosed with UC and 65 healthy controls were studied. Women with UC reported dysmenorrhea more frequently than women without with borderline significance (p=0.091). Dysmenorrhea was associated with higher pain scores among cases and controls (p<0.0001). When assessing quality of life, there were no significant differences between cases and controls with dysmenorrhea during either the premenstrual or menstrual phases. However, those with UC and dysmenorrhea were found to experience greater menstrual distress during the intermenstrual phase than healthy counterparts with dysmenorrhea (p=0.041). UC subjects with dysmenorrhea were also found to have lower overall health and vitality, as well as lower physical well-being (p<0.0001, p=0.0315, p=0.02 respectively). Reported disease activity and HRQOL among UC subjects with and without dysmenorrhea did not vary significantly. Conclusion: Dysmenorrhea is common in women both with and without UC, but has not clearly shown to contribute or add to the pain experienced by those with UC. Although those with UC and dysmenorrhea were found to have lower HRQOL than their healthy counterparts with dysmenorrhea, this may be due to disease activity and not directly related to menstrual health. This is supported by the lack of significant difference in HRQOL between UC subjects with and without dysmenorrhea. These findings may be due to well-controlled chronic disease in the UC subjects. Additionally, UC subjects may also have higher pain tolerance due to a higher baseline level of pain than their healthy counterparts.
OPIATE PRESCRIPTIONS AT EMERGENCY DEPARTMENT DISCHARGE FOR BACK PAIN ARE ASSOCIATED WITH LOWER REVISIT RATES AT 3, 9, AND 30 DAYS

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Introduction: The goal of this investigation was to examine the difference in emergency department (ED) revisit rates between adult patients with a diagnosis of back pain discharged with or without an opiate prescription. We hypothesized that patients prescribed opiate drugs would be more likely to return to the ED at 3, 9 and 30 days. The ultimate goal is to identify and divert patients that are more likely to return to the ED. Methods: We retrospectively analyzed a dataset of 134,109 patient visits to a single, academic ED. All patient visits between January 1, 2011 and December 31, 2013 were examined. This analysis studied all adult patients discharged with a diagnosis of back pain (ICD9 codes: 724.0-724.9, 846.0-846.9). Using discharge prescription information, the experimental group was those patients discharged with a prescription for opiate drugs, while the control group was those patients discharged without opiate painkillers. The primary outcome was all-cause ED revisit at 3, 9, and 30 days. A multiple logistic regression model was used to analyze the effect of opiate prescriptions on revisit, using the following control variables: age, sex, race, Emergency Severity Index acuity, length of stay in the ED, arrival mode, season of visit, hour of visit, and diagnosis. Results: 69,048 adult patients were discharged from the ED during the study, and of those, 3,082 received a diagnosis of back pain. After controlling for the above factors, we found that for back pain patients, an opiate prescription was correlated with decreased odds of revisit at 3, 9, and 30 days. Conclusions: Among patients discharged from the ED with back pain, prescribed opioids are correlated with decreased odds of an ED revisit at 3, 9 and 30 days, as compared to those back pain patients discharged without opiate pain medication. Further investigation is needed to examine patient attitudes towards effectiveness of opiate pain medication as opposed to other forms of treatment.
ACTIVE CASE FINDING OF TUBERCULOSIS AMONG TIBETAN REFUGEES IN INDIA

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Background: Tuberculosis (TB) remains one of the largest causes of morbidity and mortality worldwide, infecting approximately 9.6 million people and killing 1.5 million people per year. Passive case finding (PCF) has previously been the cornerstone of diagnosis: the testing of symptomatic individuals who present to healthcare facilities. A complementary strategy to PCF is active case finding (ACF). ACF relies on healthcare practitioners to visit and screen communities at high risk for TB. Tibetan refugees within India are one such group with over twice the TB prevalence of Indians (431 cases per 100,000 people vs. 181 cases/100,000 people). This study aims to assess the efficacy of ACF among Tibetan refugees in India using GeneXpert, a PCR-based diagnostic tool, and to determine the cost such a program incurs. Methods: ACF was conducted in a total of 16 locations between November 2015 and July 2016. All locations selected served as communal living settings for Tibetans. Participants were screened using a three step process consisting of a risk questionnaire, physical exam, and laboratory diagnostic panel. Results: A total of 2,914 persons were screened for TB. Seven of 16 locations reported at least one TB case, with a total of 17 cases identified. Overall TB prevalence was 583 cases per 100,000 persons. Cough > 1 week, abnormal apical chest radiograph findings, and pallor were all found to be statistically significant predictors of TB (p<0.05). Cases detected through ACF were more likely to be sputum smear negative compared to cases detected through PCF (76.5% vs. 44.4%). All cases identified were GeneXpert positive. The cost per case of TB detected was $254.69 per case. The incremental cost effectiveness of GeneXpert as compared to sputum smear/chest radiograph was $177.17 per case. Conclusions: ACF-detected TB prevalence was higher than the general prevalence of TB among Tibetans indicating a high TB burden in communal living settings. Cough > 1 week, abnormal apical chest radiograph findings, and pallor should be highly considered for future TB screening. Cases identified during screening were at an earlier stage of disease than those identified through PCF, highlighting the shortcomings of sputum smear diagnosis for ACF. The cost per case identified was very low compared to other ACF studies, despite the added costs of GeneXpert testing. GeneXpert has been shown to be a highly useful and cost-effective tool in diagnosing sub-clinical cases of TB. Future studies should examine the long-term impact of GeneXpert-based ACF on TB incidence.
EFFECTS OF PROLOTHERAPY FOR TREATMENT OF SYMPTOMATIC OSTEOARTHRITIS:
A RETROSPECTIVE CHART REVIEW

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Support: Summer Research and Clinical Assistantship, Department of Family Medicine and Community Health

Background: Osteoarthritis (OA) is a high-impact chronic condition affecting 33.6% of the U.S. population by age 65; current therapy is sub-optimal. Prolotherapy (PrT) is an injection-based treatment for OA. Controlled studies and meta-analyses document improvements following PrT in self-reported pain and function, but its effects in routine practice are unknown. Objective: To assess changes in pain and function and patient satisfaction following PrT for OA in clinic-based patients. Methods: A retrospective medical chart review was performed on 30 consecutive adult outpatients seen by two family medicine physicians in five clinics in the Madison, Wisconsin area over a 2-year period. Subjects who had completed at least one round of treatment with PrT for joint OA were identified. Extracted chart data included demographics, treatments histories, and outcomes. Patients were contacted via telephone for interviews. During these interviews patients were asked to rate knee pain before and after PrT on a 0-10 numeric pain scale at rest and with mild and moderate activity. Satisfaction ratings were collected and assessed along with data on how many patients went on to receive further treatment, such as surgery, after PrT. Results: 23 of 30 patients (54.74±12.63 years, 7 female) were reached for follow-up telephone interviews. Matched paired t-tests compared self-reported pain levels before and after PrT at rest and with mild and moderate activity as (Pre-PrT: M=2.41±2.64, Pre-PrT: M=4.66±2.64, Pre-PrT: M=6.17±2.79, p<0.001). Patients reported high satisfaction ratings (M=7.68/10) and 22 of 23 (95.6%) patients would recommend the procedure to a friend. Side effects were also minimal with 2 of 23 patients reporting negative side effects of syncope and nausea with injection and no adverse events. However, 5 of 26 patients (19.23%) went on to receive additional treatment for their joint injuries following PrT. These procedures included total knee arthroplasty, osteopathic manipulations, and perineural injections. Conclusions: These data suggest clinical effectiveness of PrT for treatment of OA in a routine family medicine setting with high patient satisfaction and minimal side-effects. Furthermore, these results warrant future dissemination and implementation research.
THE IMPACT OF A CLINICAL PATHWAY ON THE EMERGENCY DEPARTMENT LENGTH OF STAY IN CHILDREN WITH APPENDICITIS

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Support: Shapiro Summer Research Program; BerbeeWalsh Department of Emergency Medicine

Background: Despite the availability of advanced imaging technology and diverse diagnostic tests in the Emergency Department (ED), the evaluation of appendicitis remains complicated. To address this issue, appendicitis clinical pathways have been recommended to standardize and streamline the evaluation process. It has not yet been fully described whether the implementation of an ED appendicitis clinical pathway results in decreased length of stay. Objective: To evaluate the impact of a clinical pathway on ED length of stay in patients diagnosed with appendicitis before and after the implementation of a clinical pathway. Methods: A chart review was performed on all pediatric ED patients diagnosed with appendicitis (age < 18 years) at tertiary academic pediatric emergency department before and after the implementation of an appendicitis clinical pathway. Time stamps were extracted for the following times: when first MD assigned, first labs ordered, imaging ordered, antibiotics ordered, disposition determined, and ED departure. First MD assigned was used as the start of the clinical evaluation process and time intervals were calculated going forward. An adjustment period of three months was allowed after the clinical pathway was implemented. Differences in time intervals were analyzed using chi-squared test, t-test, or Wilcoxon-Rank sum test, and p-values were adjusted using the Holm-Bonferroni method. Results: A total of 139 patients were analyzed during the study period. There were 66 patients with a diagnosis of appendicitis before implementation of the clinical pathway (5/1/2014 – 1/31/2015) and 73 patients after the implementation (5/1/2015 – 1/31/2016). Gender proportions (62.1% versus 58.9% male) and mean ages (11.3 versus 11.5 years) were similar between the pre- and post-implementation groups. Time interval from first MD assigned to first imaging started (p=0.039) and time to departure (p=0.009) decreased from pre-implementation to post-implementation. Additionally, use of ultrasound increased while the use of CT decreased after implementation of the clinical pathway (p<0.001). Conclusion: The implementation of a pediatric appendicitis clinical pathway, which includes performing an ultrasound before a CT scan, resulted in significant reduction of length of stay for children diagnosed with appendicitis in the ED.
CLINICAL CHARACTERISTICS CAN DIFFERENTIATE PERITONSILLAR FROM INTRATONSILLAR ABSCESES: A RETROSPECTIVE IMAGING STUDY

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Support: Shapiro Summer Research Program; Department of Radiology

Background: Peritonsillar abscess is a common infection that is located between the palatine tonsil capsule and pharyngeal constrictor muscles. In contrast, intratonsillar abscess is an abscess that occurs within the tonsillar parenchyma. Intratonsillar abscesses are typically treated conservatively whereas peritonsillar abscesses often require incision and drainage. The purpose of this study is to determine the clinical signs and symptoms that can differentiate a peritonsillar from an intratonsillar abscess as validated by contrast-enhanced computed tomography. 

Methods: A 10-year retrospective chart review was performed from 2006 through 2016 to identify patients who (1) presented to our hospital with either a peritonsillar (PTA) or intratonsillar (ITA) abscess and (2) who received imaging at the time of initial presentation; 91 abscesses were identified. Individual patient medical records were then reviewed for the following clinical signs and symptoms: muffled voice, drooling, trismus, tonsillar abnormality, uvular deviation, uvular edema, peritonsillar or soft palate fullness, tonsillar erythema or exudate, and soft palate erythema. The patient’s imaging by computed tomography (CT) at their initial encounter was then reviewed by three experienced board-certified neuroradiologists to establish an imaging diagnosis of either a PTA or ITA; abscesses with imaging findings suggestive of a combined PTA and ITA were excluded from our study. Chi-square analysis and a two-tailed student t-test were then calculated to determine statistically significant associations between clinical characteristics and an imaging diagnosis of a PTA or ITA. 

Results: Contrast-enhanced imaging of the neck identified 51 PTAs and 26 ITAs; 14 abscesses possessed imaging characteristics of both PTA and ITA and were excluded from our study. Muffled voice (p=0.02), uvular deviation (p=0.01), and soft palate or peritonsillar fullness (p<0.001) are each independently associated with an imaging diagnosis of PTA.

Conclusion: Peritonsillar abscess is associated with muffled voice, soft palate or peritonsillar fullness, and deviation of the uvula. These clinical signs can be used to guide clinicians in differentiating between peritonsillar and intratonsillar abscess and to prospectively identify those patients that may substantially benefit from additional imaging.
TUMOR TREATING FIELDS ARE EFFECTIVE IN TEMOZOLOMIDE RESISTANT GliOBLASTOMA CANCER-LIKE STEM CELLS

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Support: Shapiro Summer Research Program; Department of Neurological Surgery

Introduction: Tumor Treating Fields (TTFs) are a novel antimitotic, non-invasive, externally applied cancer treatment being developed for use against many human solid cancers. Glioblastoma (GBM) is the most frequently diagnosed adult brain malignancy, with a median survival of less than 2 years after the standard therapeutic regimen of maximal surgery followed by radiation and temozolomide (TMZ) chemotherapy. In a Phase 3 clinical trial (NCT#00916409), addition of TTFs to current therapies significantly increased overall and progression free survival for newly diagnosed GBM. TTFs are FDA-approved for newly diagnosed and recurrent GBM. We report the first study of TTFs alone, or combined with TMZ, against GBM stem-like cells (GSC) expressing different levels of the therapy resistance DNA repair enzyme, O-6-methylguanine DNA methyl-transferase (MGMT), to test the hypothesis that TTF is effective against TMZ-resistant GSC.

Methods: Effects of TTFs and TMZ were studied in the patient-derived 22 GSC (MGMT-expressing, TMZ resistant) and 33 GSC (non-MGMT-expressing, TMZ sensitive) cell lines with continuous application of in vitro TTFs at varying frequencies to GSC cultures using the Inovitro system (Novocure Ltd). The effects of varying doses or frequencies of TMZ, TTFs, and combined TMZ+TTFs on GSC proliferation and sphere-forming ability were analyzed. Results: We have previously determined in vitro that 200 kHz is the optimal TTF frequency to inhibit GSC proliferation, identical to the clinical trial frequency. At 200 kHz, TTFs significantly inhibited proliferation (22 GSC: 61±10.8%; 33 GSC 56±9.5%; p<0.05) and clonogenic tumor sphere formation (22 GSC: 38±2.6%; 33 GSC: 60±7.1%; p<0.05) in both TMZ-resistant and TMZ-sensitive GSC subtypes. In combination, TTFs and TMZ (at IC25, IC50, IC75 concentrations) showed an additive interaction. Conclusion: This is the first study to directly demonstrate that TTFs can overcome TMZ-resistance in GBM cancer stem cells (GSC), and reports the effects of TTFs on GSC proliferation and clonogenic tumor sphere formation with equivalent effectiveness against both therapy resistant and sensitive GSC subtypes (+/- MGMT expression). The combination of TTFs and TMZ was additive, and supports the hypothesis that TTF acts via a mechanism independent of TMZ-mediated DNA alkylation. Further study of TTFs in additional human cancers and in potential combination with other therapeutics will be needed to optimize TTFs as a new therapy option for human cancer.
IMPLEMENTATION OF BEST PRACTICES IN CONTRACEPTIVE CARE

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Support: Summer Student Research and Clinical Assistantship, Department of Family Medicine and Community Health

Background: Half of pregnancies in the United States are unintended, which is higher than most other developed nations. Despite recent reductions in unintended and teenage pregnancy rates, there remain ample opportunities for family physicians to increase their role in ensuring comprehensive contraceptive care. Methods: We reviewed recommendations made by the Centers for Disease Control and Prevention (CDC), American Academy of Family Physicians, American College of Obstetricians and Gynecologists, and other professional groups before conducting a literature review to determine best practices for implementation of these recommendations. Our goal was to consolidate practices and lessons from other projects and studies into a practical guide for family physicians and clinic managers. Results: Our five simple recommendations are:

1) Routinely Screen Reproductive Intentions
   a. Ask about pregnancy intentions in the upcoming year then provide counseling as appropriate.
   b. Models include the One Key Question® approach and the CDC Reproductive Life Plan framework.

2) Decouple Provision of Contraception from Unnecessary Exams
   a. Pelvic exams, pap smears, and sexually-transmitted infection tests are generally not recommended and often represent unnecessary barriers.

3) Expand Long-Acting Reversible Contraception (LARC) Counseling and Access
   a. Reduce barriers to LARC-methods, such as IUDs and implants, through tiered contraceptive education and same-day insertion.
   b. There are very few contraindications for LARC methods, which should be considered for most women.

4) Follow CDC Guidelines for Initiation and Continuation of Contraception
   a. Quick-start methods, 1-year provision of oral contraceptive pills, and increasing the window for Depo-Provera shots may improve coverage.

5) Routinely Counsel About and Advance-Prescribe Emergency Contraception Pills (ECPs)
   a. Advance prescriptions of ECPs reduce logistical and financial burdens for women.
   b. Counseling should note that ulipristal acetate ECPs (e.g. ella®) may be more effective than levonorgestrel ECPs (e.g. Plan B®) for women with a BMI> 25 kg/m².

Conclusion: We hope that family medicine practices can incorporate these simple recommendations, such as asking about pregnancy intentions and providing contraceptive counseling, into their clinical workflow by utilizing the entire care team. Electronic health record (EHR) functionalities and online resources can encourage providers to ask about reproductive plans and better provide contraceptive care.
SCREENING IN TRAUMA FOR OPIOID MISUSE PREVENTION

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Support: Shapiro Summer Research Program; Department of Family Medicine and Community Health, Wisconsin Partnership Program

Introduction: Opioid and heroin misuse and overdose are on the rise in the United States and have reached epidemic levels.\(^1,2\) Use of prescription opioids from an ED visit was the most common preceding drug use in heroin users in the United States, and studies have shown that victims of traumatic injury are at an increased risk for opioid misuse and addiction.\(^3,4,5\) However, there is currently little known about what screening tools are effective for identifying risk of potential opioid misuse. Considering that experiencing trauma is a considerable risk, it is crucial that a standardized and effective screening tool is developed to identify these patients in the trauma center and act appropriately to help prevent development of an opioid misuse disorder. **Methods:** This study is separated into four phases of data collection. Phase 1 was a 24-question survey of trauma center staff regarding current screening practices and barriers to implementing screening tools. This anonymous, online survey was sent to all trauma medical directors and coordinators in levels I-IV trauma centers in Wisconsin. Phase 2 was comprised of a summit and focus group including study contributors and trauma center nurses, physicians, and social workers. The goal of the focus group was to identify barriers to implementing a screening tool for opioid misuse risk in trauma centers, consider measurable characteristics that could indicate the potential for development of an opioid use disorder, and to discuss effective pain management. Phase 3 is a survey of trauma patients at UW Health that fit a predetermined set of criteria, who will then be followed for 6 months and monitored for the development of an opioid misuse disorder. Phase 4 will take the information gathered from Phase 3 to create an opioid misuse screening tool, which will then be piloted at Gundersen Health System, Theda Clark Medical Center, Medical College of Wisconsin, and Ministry St. Joseph’s Hospital. Data regarding the reach, effectiveness, adoption and implementation of this tool will be collected. **Results:** In Phase 1 of the study, responses were obtained from 21 trauma center staff. Respondents included nurses, physician assistants, psychologists, physicians, health educators, and trauma coordinators at levels I-IV trauma centers. Only 1 respondent answered that their trauma center did not use screening for identifying risky or problem alcohol use. However, 56.25% of respondents answered that their institution screened for other drug use, and only 14.92% of respondents claimed that their institution used screening particular for opioid misuse. For opioid use screening, 50% of respondents used a clinical interview for screening, 25% used standardized questionnaires, described as “RN asks patient upon admission,” and 25% used lab tests (urine/blood). When asked what factors might help facilitate screening for opioid misuse risk, respondents claimed that “more routine use of PDMP,” “development of a simple screening tool,” “more resources,” “increased education for the nurses/providers,” “time, staffing, reimbursement for doing so,” and “having a specific path for positive screen” would all be useful. **Conclusion:** Risky or problem alcohol use is routinely screened for in Wisconsin trauma centers, and methods used tend to be standardized, established methods and pathways. However, when it comes to drug use screening, and in particular, opioid use screening, fewer hospitals employ screening methods in the trauma center. This is concerning, because there is a major issue of opioid misuse but a lack of corresponding screening and intervention. It is important to develop a standardized method for identifying opioid misuse risk in trauma centers, so that these patients can be identified sooner and intervention or treatment can be used, if necessary.

Citations:
A RETROSPECTIVE DTI STUDY ON THE EFFECT OF DISTANCE BETWEEN BRAIN TUMOR AND SUPERIOR LONGITUDINAL FASCICULUS AND CINGULUM ON PERIOPERATIVE LANGUAGE OUTCOMES

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Support: Shapiro Summer Research Program; Department of Radiology

Background: Diffusion Tensor Imaging (DTI) captures images of the major white matter tracts in the brain by assessing the magnitude and directionality of water molecule diffusion. DTI has been shown to be a valuable tool in pre-surgical planning, but its use is not yet fully standardized indicating the need for further research. Objective: The purpose of this study was to investigate the validity of DTI use as a preoperative planning tool by analyzing the effect of lesion to tract distance (LTD) for two language associated tracts: the superior longitudinal fasciculus (SLF) and cingulum, on preoperative verbal fluency (VF) scores and perioperative clinical language deficits. Methods: The study included patients with primary brain tumors who had surgical resection of their tumors (n=43). Preoperative phonemic VF scores were collected preoperatively and morbidity data was collected from medical records. In order to collect LTD data, color coded fractional anisotropy DTI images were overlaid onto contrast enhanced T1 or T2 weighted images. SLF and cingulum were defined with Kenichi Oishi’s MRI Atlas of Human White Matter, 2nd Ed. Results: Dominant language hemisphere SLF LTD’s were significantly correlated to preoperative VF by Pearson’s correlation coefficient analysis (R=0.31 and p=0.045). Language dominant SLF LTD values were categorized into <1 cm, 1-2 cm, and >2 cm groups. These groups showed significant differences in regards to stable, new, and persistent postoperative deficits by chi-square analysis (p=<0.0001, p=0.0089, p=0.00037). For the new deficits, the <1 cm, 1-2 cm, and >2 cm categories had the following proportion of patients with deficits: 0.36, 0.56, 0.050 respectively. Stable and persistent postoperative measures followed a similar trend. Dominant cingulum LTD values organized by SLF LTD categories of <1 cm, 1-2 cm, and >2 cm were as follows: 10.11, 10.23, and 22.39 mm. Additionally, if patients were grouped by whether or not they had either dominant SLF or cingulum LTD of <1 cm or >1cm, there was a significant difference in outcomes with all new postoperative deficits in the <1 cm group (p=0.00062). Conclusion: VF correlated to SLF LTD, supporting the validity of DTI use as a pre-surgical planning tool. While the SLF LTD comparison to clinical deficits was significant, we unexpectedly found the greatest average number of deficits in the 1-2 cm category for all three significant measures. Small study size and the similar average cingulum LTD values for both the <1 and 1-2 cm SLF LTD categories may have affected this analysis. Still, no significant effect of cingulum LTD alone was shown, so the effect of cingulum LTD on outcomes should be further investigated.
ASSESSING CHILDHOOD FITNESS IN WISCONSIN SCHOOLS: A QUALITATIVE STUDY

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Support: Shapiro Summer Research Program; Prevention Innovations in Medical Education (PRIME-Madison)

Background: Considering the gravity of the obesity epidemic, there is limited data about children’s fitness levels in the United States. Cardiorespiratory fitness specifically, is predictive of long-term health outcomes and can be measured with the Progressive Aerobic Cardiovascular Endurance Run (PACER). Many schools conduct regular fitness assessments including the PACER, but no centralized data source exists. The purpose of this project was to identify the main barriers to the creation of a statewide database of childhood fitness and the strategies to overcome them.

Methods: Semi-structured interviews were conducted with 13 key-informants with an average of 17 years of experience working with child fitness. Participants included school administrators at district and state levels, physical education teachers, public health researchers, and other physical education organizations. Questions addressed two domains: 1) barriers to implementation and 2) strategies to address barriers. Qualitative analysis of interview transcripts was conducted using Dedoose software and two coders identified main themes independently. Inter-rater reliability was high during training (kappa=0.95). Main themes within each domain (barriers & strategies) were analyzed using descriptive statistics to compare proportions of participants mentioning each concept. Co-occurrence of mentioned concepts within the same discreet segment across interviews was also analyzed.

Results: Main barriers to conducting fitness assessments or uploading de-identified results were cost, limited staff time, and dislike of assessments. All participants expressed interest in the creation of a statewide database of school fitness. Nearly all participants mentioned the following strategies for implementation: training & education, build trust & buy-in from schools, and local control & empowerment.

Conclusion: This study highlights the need for increased collaboration between school systems, public health organizations, and healthcare providers in tracking childhood fitness as means to address the obesity epidemic. The PACER is a simple, cost-effective and evidence-based assessment that could provide much needed data. Such data could prove valuable to public health resource allocation.
ASSESSMENT OF THE DIURNAL VARIABILITY OF LIVER FAT CONCENTRATION IN HUMAN SUBJECTS

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Support: Shapiro Summer Research Program; Department of Radiology

Introduction: Hepatic steatosis is characterized by excess buildup of lipids within hepatocytes of the liver and affects approximately 30% of American adults. Recently, the proton density fat fraction (PDFF) has emerged as an accurate, precise, robust, and reproducible quantitative imaging biomarker of hepatic steatosis that is able to non-invasively quantify fat throughout the whole liver. PDFF is obtained using magnetic resonance imaging (MRI) and measures the ratio of the density of hydrogen protons from fat to the density of all mobile hydrogen protons. PDFF is a fundamental property of tissue, enabling inherent reproducibility across different imaging sites and MRI platforms. Because of its potential for diagnosis, monitoring, and assessment of interventions, previous studies have attempted to standardize PDFF as a biomarker and assess its sensitivity and variability. However, the diurnal variability of liver fat concentration is not well understood. This is important to understand, in order to determine if the response to diet, exercise, or drug therapy is significantly affecting the liver fat concentration. Therefore, the purpose of this work is to use MRI-based PDFF mapping to assess the diurnal variability of liver fat concentration in human subjects.

Methods: Six were recruited to participate in the study. Using a research-dedicated 1.5T MRI scanner, subjects were scanned during six “visits” over a 24-hour period: before and after a standardized breakfast, before and after a non-standardized lunch, late afternoon on day one, and before breakfast on day two. Each visit included three scans to assess the test-retest repeatability of the fat measurements, with the subject exiting and re-entering the MR scanner for each scan. PDFF maps were reconstructed via reconstruction algorithms on the scanner and analyzed using OsirX, a widely used image processing program. Liver fat fractions were measured in each of nine Couinaud liver segments (determined by functional anatomy) using the largest possible circle-shaped region of interest (ROI) in each segment. ROI measurements were made for each scan and the mean fat fraction for each visit was determined.

Results: Four subjects had a baseline pre-breakfast fat fraction between 0.79% and 1.2%. The highest baseline fat fraction was 3.6%; the lowest was 0.79%. Across all subjects, no clear trends emerged for whether liver fat fraction changed after meals or throughout the 24-hour period of the study. For individual subjects, fat fraction was observed to both rise and fall after meals without a consistent pattern. The largest change in fat fraction observed for any subject when comparing scans before and after the standardized breakfast was 0.21%. The smallest change observed before and after the standardized breakfast was 0.06%. When comparing the maximum and minimum fat fraction values obtained for each subject over the 24-hour study, the largest variation observed was 0.62% and the smallest variation observed was 0.21%. The two subjects with the highest variation (i.e., largest difference between their maximum and minimum fat fractions) were the two subjects with the highest baseline fat fraction.

Conclusion: While we are unable to draw any conclusions at this point in the study, we plan to recruit six additional subjects with a wider range of baseline fat fractions, especially those with higher baseline fat fraction. Our preliminary data suggest there may be a correlation between higher baseline fat fraction and a greater diurnal variability of liver fat concentration, which we plan to investigate further. Recruiting additional subjects also will provide us with increased statistical power to conclude whether liver fat concentration varies significantly throughout the day.

Citations:
COMPARATIVE OUTCOMES FOR PATIENTS WITH EARLY ONSET RENAL CELL CARCINOMA FOLLOWING SURGERY

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Mentor: E. Jason Abel, MD

Support: Shapiro Summer Research; Department of Urology

Introduction: The overall incidence of RCC has leveled off after a steady increase over last 2 decades, while the annual percentage change in some groups has actually increased. The largest increase in incidence has been in the age groups from 20-45 years old. While the median age of diagnosis for renal cell carcinoma (RCC) is 64 years old, the lowest decile of RCC patients includes patients less than 46 years (designated early onset RCC) in population based studies. The purpose of this study is evaluate oncologic and perioperative outcomes following surgery for early onset RCC compared to older patients. Methods: Comprehensive clinical information for all RCC patients treated surgically from 2000-2016 at University of Wisconsin Hospital. Univariate and multivariate Cox proportional hazards analyses were used to identify risk factors associated with survival or disease recurrence. Results: A total of 151 (15.1%) and 845 (84.6%) were patients were <46 and ≥ 46 years old respectively. For early onset RCC, the median age was 39.5 years old (IQR 35.8-43.9) vs. 60.6 years old (IQR 53.80-67) for the older comparison group. The median follow-up time was 54.1 (29.3-87.9) months for both groups. In early onset RCC, 40 (26.5%) patients were offered genetic counseling. Patients were found to have an associated familial syndrome in 2 (1.3%) under 46 and 2 (0.2%) in over the age of 46. Percentage overall survival at 5 years for early onset vs. older RCC was 82% vs. 65%, (p= 0.02). Recurrence in non-metastatic patients was identified in 5 (1.08%) and 33 (8.78%) patients for early onset vs. older RCC (p= 0.34). Charlson Comorbidity Index > 1 was found in 21 (23.86%) and 175 (46.54%) early onset vs. older RCC respectively(p=.0001). There was no difference in asymptomatic presentation between age groups, 72.41% vs. 64.97% (p=0.1858). After multivariate analysis, the only independent predictor of recurrence found was tumor diameter (HR 1.227, 95% CI 1.11-1.356). Conclusion: Patients with early onset RCC do not appear to have worse OS or tumor recurrence rates. Tumor diameter is the only independent factor predictive for recurrence in non-metastatic RCC treated surgically.
HOSPITALIST CO-MANAGEMENT OF PEDIATRIC PATIENTS: A SYSTEMATIC REVIEW AND META ANALYSIS

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Mentors: Kenneth Noonan, MD; Dan Sklansky, MD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

Background: Research shows the benefit of multi-disciplinary care for adult patients after orthopedic procedures [1]. However, the benefits of incorporating a hospitalist or multi-disciplinary team into the recovery of pediatric patients is limited. The purpose of this study is to complete a systematic review and meta-analysis of existing evidence that incorporation of a pediatric hospitalist will reduce the length of stay and cost of recovery for orthopedic pediatric patients. Methods: The systematic review was registered with Prospero (CRD42016042858) and a meta-analysis was performed to assess changes in length of stay. Six medical databases were queried to obtain articles for initial screening. Study quality was assessed using the criteria created by Downs and Black and independently reviewed by two investigators [2]. The length of stay (LOS) for patients and other relevant data were extracted. A sensitivity analysis was completed on the impact of each individual study. Results [3,4,5]: Search terms returned 718 unique articles, with three studies that met the inclusion criteria after investigator review. All three articles that met inclusion criteria reported on the impact of hospitalists on patients receiving spinal fusion. Each study reported a reduction in the LOS with hospitalist involvement, although only two of the three studies reached statistical significance. The pooled data showed a reduction in LOS of 0.61 days (Standard Error 0.13) for the hospitalist group, however the change was not statistically significant (p=0.09). These studies also reported similar complication rates and similar pain management between the groups. Heterogeneity analysis showed that ~93% of the variation in the data was due to study differences. Conclusions: There is limited data available to demonstrate the advantage of hospitalist involvement in the care of pediatric orthopedic patients. Although the studies are in agreement that involvement could be a benefit via reduced LOS, this analysis did not reach statistical significance. To further understand the potential for improvement, additional studies need to be conducted that more carefully control new variables, include a broader patient population, and add larger numbers of patients.

Citations:
PATIENT-REPORTED QUALITY OF LIFE AFTER BARIATRIC SURGERY: A SINGLE INSTITUTION ANALYSIS

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Support: Department of Surgery NIH T35DK062709 grant

Introduction: Bariatric surgery is the most effective method for weight loss and comorbidity resolution among patients with severe obesity. However, there are limited data describing its impact on patient-reported quality of life (QoL). We sought to determine the impact of bariatric surgery on patient-reported QoL and identify variables associated with higher postoperative QoL. Methods: QoL data were collected from patients (n=209) who underwent bariatric surgery at a single institution from Jan 2010 through Dec 2012. QoL scores were obtained by administering the Moorehead-Ardelt Quality of Life Questionnaire II (MAQoLII) during clinical visits. The MAQoLII is a validated survey addressing self-esteem, physical activity, social life, work ability, sexual functioning and approach to food. Cumulative scores can range from 3.0 (“Very Good”) to -3.0 (“Very Poor”). Patient and surgical variables were collected from a retrospective bariatric surgery database. A repeated measures ANOVA test was used to analyze the trend in QoL scores over a one year time period. Multivariable logistic regression was used to generate odds ratios for variables hypothesized a priori to be associated with higher QoL postoperatively. A non-responder analysis was performed to identify potential sources of selection bias. Results: Patients lost an average of 59.1% (±19.0) of their excess body weight and their mean body mass index (BMI) decreased by 13.3 kg/m² (±12.4) one year after surgery. 41.6% of patients (n=87) responded to the MAQoLII at one year. Mean QoL scores increased from 0.82 preoperatively to 1.66 one year postoperatively (p<0.001). Patients scored higher in each facet of MAQoLII one year after surgery: self-esteem (0.36 vs. 0.22), physical activity (0.31 vs. 0.11), social life (0.36 vs. 0.28), work ability (0.22 vs. 0.07), sexual functioning (0.16 vs. 0.04) and approach to food (0.26 vs. 0.11). On multivariable analysis, higher QoL was associated with private insurance/self-pay vs. Medicare (OR 3.87 [95%CI 1.36–11.0]). There was no association between QoL and gender, race, preoperative BMI and comorbidities, or excess weight loss. The non-responder analysis indicated that responders were older (49.4 vs. 45.3) and more likely to be Caucasian (93.2% vs. 83.5%). Conclusion: Bariatric surgery patients experienced significant improvements in quality of life one year after surgery. Modifiable predictors of a high quality of life after bariatric surgery remain unclear and will require additional investigation.
USE OF ULTRASOUND FOR DISTINGUISHING NON-PERFORATED FROM PERFORATED APPENDICITIS IN CHILDREN

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Support: Shapiro Summer Research Program; Department of Surgery

Background: Acute appendicitis is one of the leading causes of surgery in children\(^1\). Recent clinical trials suggest that simple acute appendicitis in pediatric patients can often be successfully treated non-operatively with antibiotics\(^2\). Conversely, perforated appendicitis requires urgent appendectomy or percutaneous drainage and a prolonged course of antibiotics\(^3\). As treatment strategies for perforated and simple acute appendicitis diverge, effective imaging to identify the presence or absence of perforation preoperatively is increasingly important. Ultrasound has a demonstrated effectiveness in diagnosing acute appendicitis, but its ability to detect perforation has not been well elucidated. **Methods:** We retrospectively analyzed health records of all pediatric patients who presented to a single pediatric Emergency Department with suspected appendicitis from 11/1/2014 to 12/31/2015. We abstracted data from radiology reports, operative notes, and pathology reports to determine the effectiveness of ultrasound at predicting perforated appendicitis based on concordance of ultrasound and surgical findings. We used the only evidence-based definition for perforation that is associated with an increased risk of abscess formation, a hole in the appendix or fecalith in the abdomen at the time of operation\(^4\). **Results:** A total of 480 ultrasounds for suspected appendicitis were performed during the study period. 85.6% of patients with appendicitis were successfully diagnosed using ultrasound. Of these 95 patients, 28 (29.5%) were perforated at operation and 67 (70.5%) were not perforated. The interpreting pediatric radiologist’s impression of perforation was correct 81.1% of the time with a specificity of 86.6% and sensitivity of 67.9%. **Conclusion:** These data suggest that ultrasound is a reliable measure for identifying appendicitis and perforation in children with a sensitivity and specificity comparable to reports for computed tomography (CT) scans\(^5\). The negative predictive value of ultrasound for perforation should allow safe attempts at non-operative management of appendicitis if perforation is not seen.

Citations:
IMPROVING METABOLIC HEALTH THROUGH DECREASED CONSUMPTION OF BRANCHED CHAIN AMINO ACIDS

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Mentor: Dudley Lamming, PhD

Support: Shapiro Summer Research Program; Department of Medicine; Wisconsin Partnership Program, NIH

Background: Type II diabetes is on the rise in the United States and in Wisconsin. In 2009, approximately 8% of the people of Wisconsin had Type II diabetes, while another 25% of people over the age of 20 were estimated to be pre-diabetic. Without significant intervention such as exercise and dietary intervention, most people with pre-diabetes will eventually develop Type II diabetes. Thus far, dietary interventions in diabetes have largely focused on reducing caloric intake. However, this diet is notoriously difficult to sustain. Recent findings show that reducing protein intake may positively impact one’s health. While the pathway still remains unclear, past research indicates the three branched chain amino acids (BCAA) - leucine, isoleucine, and valine - may have a significant impact on the development of diabetes and weight gain. Researchers hypothesize that BCAA may stimulate the mechanistic target of rapamycin complex 1 (mTORC1) protein kinase, which may affect glucose tolerance and insulin sensitivity. Our goal was to test the hypothesis that decreasing the dietary consumption of BCAA or all amino acids (AA) will increase glucose tolerance and insulin sensitivity and stimulate weight and fat loss of mice fed a high fat, high sucrose diabetogenic diet (HFD).

Methods: Prior to the intervention, 64 mice were fed HFD for 10 weeks and 16 mice were fed a normal diet of rodent chow. After performing a glucose and insulin tolerance test as well as determining their body composition, the mice from the high fat diet were placed on high-fat amino acid defined diets with control levels of amino acids or with reduced levels of either BCAAs or all amino acids. Over the following 12 weeks, we completed glucose and insulin tolerance tests, determined body composition to assess fat loss during the intervention, and collected fasting blood in order to analyze insulin content by ELISA.

Results: Mice on HFD with low BCAA and low AA show significant benefits to their metabolic health. By week 3, mice on these diets lost ~28% of their body weight and ~13% fat mass. By week 3, mice on these diets also significantly increased their glucose tolerance and insulin sensitivity (p-value<0.001).

Conclusion: This study shows that reducing either total AA or specifically reducing BCAAs in the diet significantly increases metabolic health in mice. In future studies, our lab will study the effects of a diet with reduced BCAA to gain insight for how this may affect humans. If these studies produce significant results, patients with pre-diabetes will have another option for treatment with a more sustainable diet, and mechanistic studies may enable the identification of a new pathway that can be targeted pharmacologically.

Citations:
PLATELET-RICH PLASMA IMPROVES LONG TERM OUTCOMES IN TREATMENT OF CHRONIC TENDINOPATHY

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Mentor: John Wilson, MD, MS

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

Introduction: Tendinosis is a common source of pain and disability that is often refractory to conservative therapy. There currently is no consensus on the appropriate treatment of chronic tendinopathy. The purpose of this study was to assess the long term effectiveness of Platelet-Rich Plasma (PRP) injections for patients suffering from chronic tendinopathy. Methods: A prospective case series of 122 patients was conducted to report subjective patient pain and disability following intratendinous PRP injection. Patients previously treated for chronic tendinopathy were administered validated, site specific pain and disability surveys for knee, elbow, or foot/ankle depending on treatment location. Injection sites were patellar tendon, Achilles tendon, or lateral epicondyle of the humerus. Statistical analysis compared baseline and long-term (>1 year) post-injection times using the linear mixed effects model. Results: Initial surveys were sent out in early August after IRB approval was obtained. Data collection is currently in progress. In addition to comparing baseline and long-term outcomes, demographic data will also be analyzed to look for variability in treatment outcomes. Conclusion: Once data collection is finished, survey results will be compared to baseline survey scores using a linear mixed effects model. When complete, this study will add insight on the effectiveness of PRP as a treatment modality for patients suffering from chronic tendon pain and disability. Future studies will compare PRP treatment to a randomized control group.
DISCONCORDANCE BETWEEN HISTOLOGIC AND VISUAL ASSESSMENT OF TISSUE VIABILITY IN EXCISED BURN WOUND TISSUE

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Background: Depth of injury determines the regenerative capacity of a burn wound, and thus the need for surgery. Tangential excision is the preferred method in the surgical debridement of burn wounds and involves the sequential removal of layers of injured tissue until there is visual evidence of viable tissue. Intraoperative assessment of burn depth relies primarily on visual inspection by the surgeon. While prior studies have utilized hematoxylin and eosin (H&E) staining to demonstrate inconsistency in clinical burn depth analysis, details regarding the cellular viability of burn wounds is unknown. The goal of this project is to further elucidate the distinction between nonviable and viable wound tissue through histological analysis. The information gained from this study can be used to guide development of new technologies to enhance the precision of surgical debridement.

Methods: Patients identified as having deep partial thickness (DPT) or full thickness (FT) burn wounds were taken to the operating room for excision and grafting. A 4mm biopsy of the wound area was first obtained, followed by sequential tangential excision of the surrounding injured tissue. Representative sections from each burn site were processed with H&E to visualize tissue morphology. A lactate dehydrogenase (LDH) assay was used to qualitatively ascertain tissue viability. K15, a marker of the mitotically active basal layer of the epidermis, was detected using standard immunohistochemical (IHC) methods.

Results: Cells expressing K15 were found sporadically throughout excised tissue, primarily in eccrine sweat glands and hair follicles. Interestingly, K15-positive cells were detected in tissue from both DPT and FT wounds. Similarly, LDH showed viable cells in both DPT and FT burn tissue with staining concentrated around adnexal structures. However, H&E demonstrated evidence of re-epithelialization in DPT wounds only. There was disconcordance between viability determined histologically and clinical identification of FT burn injury, with some tissue excised from FT burns containing an abundance of LDH-stained cells.

Conclusion: The current method of utilizing visual assessment to determine depth of injury is imprecise. Our histologic data supports the hypothesis that viable tissue is removed during excision, suggesting that a better clinical approach is necessary. Furthermore, excising viable tissue removes any possibility of the tissue participating in wound healing. While our data demonstrates the presence of healthy basal keratinocytes in both DPT and FT wounds, additional IHC studies using proliferation and stem cell markers will further illuminate the regenerative potential of burn tissue. Moreover, previous studies using H&E analysis alone falsely portray the degree of thermal injury and should not be used in research or clinical determination of depth. Future studies focused on the assessment of collagen health in burn wounds will provide additional information necessary to determine overall thermal damage in burn tissue.
CORRELATION BETWEEN LIPOPROTEIN(A) LEVELS AND AGE OF ONSET OF CARDIOVASCULAR DISEASE IN FAMILY MEMBERS OF A PEDIATRIC FAMILIAL HYPERCHOLESTEROLEMIA POPULATION

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Support: University of Wisconsin Cardiovascular Research Center; Department of Pediatrics, Division of Cardiology

Background: Familial hypercholesterolemia (FH) is a common inherited dyslipidemia characterized by markedly elevated low-density lipoprotein cholesterol (LDL-C) that is present from birth. Affected individuals carry up to 100-fold increased risk of premature onset of cardiovascular disease (CVD). Elevated Lipoprotein(a) [Lp(a)] ≥ 50mg/dL is considered a non-modifiable independent risk factor for premature onset of CVD in adults, but its impact in children is not well understood. Although studies indicate there may be an increased risk of CVD in adult FH populations with elevated Lp(a), little is known about its impact on pediatric populations with FH. Objective: To assess the correlation between elevated Lp(a) levels in a pediatric population diagnosed with FH and the age of onset of CVD in family members. Methods: Retrospective chart review identified 79 children from 50 families diagnosed with FH at the University of Wisconsin Pediatric Preventative Cardiology Clinic from 2/2011-6/2016. Patients were categorized based on their Lp(a) level; normal (<30mg/dL), borderline (30-49mg/dL) and high (≥50mg/dL). Premature onset of CVD in family members was defined as onset of CVD in a family member (parent, grandparent, aunt, or uncle) at age <50 years for males and <60 years for females. Ordinal logistic regression modeling was used to evaluate the association between Lp(a) category and earliest age of onset of CVD events in family members. Results: Children with a family member with early onset CVD were more likely to have an Lp(a) ≥50 mg/dL than those children with no family history of CVD (OR 3.41, 95%CI 0.9,12.85), although this trend did not reach statistical significance. A child with FH who has a relative with an early CVD event had a 63% chance of having an Lp(a) ≥50 mg/dL. Conclusion: Children with FH who have a family history of early onset cardiovascular disease were more likely to have Lp(a) >50 mg/dL than children with FH who had no family history of either premature CVD or any CVD. Further studies are needed to determine if earlier or more aggressive treatment of children with FH and concomitant elevated Lp(a) is needed to adequately treat their potentially increased risk for premature CVD.