2017 Student Research Forum
Podium Abstracts

(By Session and Room Number)
ASSOCIATIONS BETWEEN PAIN COPING AND OPIOID USE: 1-MONTH FOLLOW-UP RESULTS OF A PROSPECTIVE STUDY IN A COHORT OF TRAUMATIC INJURY PATIENTS

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Support: Summer Student Research & Clinical Assistantship Program through the Department of Family Medicine and Community Health

Background: Opioid use disorders, opioid overdose, and related complications are at crisis levels and rising throughout Wisconsin and the United States. Individuals sustaining traumatic injury represent a population at particular risk, due to historical and injury-related factors. Thus, there is a crucial and urgent need to develop effective screening, assessment, prevention and treatment interventions, for opioid use disorders and related complications in the setting of injury. Methods: This prospective cohort study followed inpatients admitted to a Regional Level I Trauma Center for traumatic injuries who continued using prescribed opioid pain medications following discharge. Forty-nine patients completed baseline pain catastrophizing scale (PCS) and provided information about their opioid medication use and dosage at one-month post-discharge follow-up. Twenty-three patients continued to take prescribed opioid medication at one-month post-discharge and were included in the current analyses. Results: Controlling for morphine equivalent daily dose (MEDD) at baseline, multiple regression showed that baseline PCS score was positively associated with MEDD at one-month post-discharge in this sample. ($\beta=0.996 [0.431, 1.561]; p=0.001$; $R^2$ of PCS = 0.402). The patient health questionnaire 9-item (PHQ-9) measure for depression and generalized anxiety disorder 7-item (GAD-7) were also completed at baseline, but were not significantly associated with our outcome variable, and therefore excluded from the final model. Conclusions: In the current sample of traumatic injury inpatients, findings indicated that a baseline measure of pain catastrophizing predicts ongoing opioid medication use and dosage at one-month post-discharge from an inpatient trauma unit. As the study sample accumulates (goal n = 295), the assessment of pain catastrophizing in addition to other important clinical variables will support the development of a sensitive and parsimonious model for opioid risk screening aimed at identifying trauma patients at risk for prolonged opioid medication use and misuse.
CONTRACEPTIVE CHOICES AMONG HIGH LEVEL FEMALE ATHLETES

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Background: While the limited research on contraceptive use in female athletes is replete with studies on oral contraceptive pills (OCPs), there is no large, descriptive study to date that has characterized female athletes’ use of other contraceptive methods, such as long-acting reversible contraceptives (LARCs). Additionally, there are no studies on female athletes’ subjective assessment of how their menstrual cycle affects their sport performance. The purpose of this study is to investigate the primary contraceptive choices among collegiate female athletes and the influencers of their choice. Methods: This was a descriptive online-based cross-sectional survey study. A survey was distributed to 455 NCAA Division I female student-athletes at the University of Wisconsin over three weeks. Bivariate chi-square and descriptive statistical analyses were performed using STATA. Results: Response rate was 49% with a total of 213 respondents from 11 different sports. The majority (67%) of women were sexually active with male partners. Most participants, regardless of sport, used oral contraceptives (58.7%), while 15.5% used barrier methods and 12.7% used LARCs. Participants’ choice of contraception was influenced primarily by healthcare providers (42%), followed by family (32%), teammates (15%), and coaches (11%). Almost half (47%) of respondents reported that their athletic performance was worse during their natural (without influence of contraceptives) menstrual cycle; participants using contraception were significantly more likely to report performing worse on their natural menstrual cycle than on their contraceptive-influenced menstrual cycle ($P < .001$). There was no significant difference between primary method of contraception used and plans for future pregnancy. Conclusion: This study shows that the majority of female student-athletes use OCPs for contraception and menstrual regulation. Although 60% of participants do not desire pregnancy for at least seven years, the minority of participants uses a long-acting method. Additionally, almost half of the participants reported worse performance while menstruating without the influence of contraception, but many have not considered other methods for menstrual regulation, such as LARCs that could have a potential outcome of amenorrhea. These data provide an opportunity to educate both student-athletes and athletic departments about different forms of contraception and menstrual regulation in female athletes.
IDENTIFYING CANDIDATE NOVEL GENES FOR PRIMARY CONGENITAL GLAUCOMA

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Background: Primary congenital glaucoma (PCG) affects infants when their eye pressure increases, causing damage to the retina and optic nerve and leading to vision loss and eventual blindness. The pathophysiology of the disease lies in the aqueous humor (AH) outflow pathway. Abnormally high production of AH by the ciliary body or poor drainage through the trabecular meshwork/Schlemm’s canal can lead to increased intraocular pressure (IOP) - the basis for glaucoma.\(^1\)\(^2\) While PCG is the major cause of blindness in children worldwide,\(^3\) there is still much to be uncovered regarding its molecular etiology. The proportion of PCG patients attributed to mutations in the CYP\(1B1\) gene can range from 20% in Western populations to 100% in highly consanguineous populations.\(^4\) This leaves a large proportion of PCG unexplained. The objective of this project was to identify novel candidate gene mutations that may underlie PCG. Methods: Saliva from 3 families was collected using an Oragene kit. DNA was extracted following the prepIT.L2P protocol, and was sent to Novogene for exome sequencing. Exome variants were filtered using SVS software (Golden Helix) to remove those that were common in the population, not evolutionarily conserved, not predicted to have a functional effect, or were poorly covered in the sequencing data. Candidate gene variants were excluded/prioritized based on a review of the existing literature, and then verified (not an exome sequencing artifact) by Sanger sequencing. Results: From an initial 103,043 gene variants, 9 were prioritized as good candidates, and those in the **SH3PXD2B** and **LRP2** genes were investigated further. Both genes were mutated in a singleton family. **SH3PXD2B** contained an in-frame insertion of 6 bases, and **LRP2** had a missense variant. Mutations in **SH3PXD2B**, which encodes an adaptor protein required for podosome formation, can cause autosomal recessive Frank-Ter Haar syndrome - a skeletal dysplasia with glaucomatous eye symptoms.\(^5\)\(^6\) **LRP2** encodes a multi-ligand endocytic receptor involved in the uptake of various bioactive molecules by the epithelia.\(^7\) Zebrafish lacking this gene show buphthalmos and elevated IOP – the hallmarks of PCG.\(^8\) Conclusion: In a patient with PCG, we identified heterozygous rare variants in **SH3PXD2B** and **LRP2**, two genes with reported autosomal recessive glaucoma phenotype associations. These data suggest that dinogenic heterozygous mutations in **SH3PXD2B** and **LRP2** may be a novel molecular basis for PCG disease. Further research will investigate how these variants effect gene function, culminating in the generation of animal models to prove these variants are sufficient to cause PCG phenotypes.

Citations:

EXAMINING THE IMPACT OF USING THE SIMPL APPLICATION ON FEEDBACK IN SURGICAL EDUCATION

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Support: Shapiro Summer Research Program; Department of Surgery

Introduction: The System for Improving and Measuring Procedural Learning (SIMPL) smartphone application allows attending physicians to provide dictated feedback to surgical residents. The impact of this novel feedback medium on the quality of feedback given is unknown. The purpose of this study was to compare the quality of operative performance feedback given via SIMPL to feedback given in-person.

Methods: We collected operative performance feedback given both in-person and via SIMPL on a variety of surgical procedures from four surgical attending physicians to nine general surgery residents over the course of six weeks. We coded each feedback encounter using a speech acts taxonomy, Verbal Response Modes (VRM), in order to compare how feedback is delivered in-person versus via dictation. We also evaluated the quality of each feedback encounter using a validated resident survey and a third-party scoring system adapted from validated rubrics.

Results: Nineteen SIMPL and 18 in-person feedback encounters were evaluated. Chi-square tests for equality of proportions showed feedback provided via SIMPL was more directive—containing thoughts, perceptions, evaluations of resident behavior, or advice—than in-person feedback (p=0.01). SIMPL feedback also contained more presumptuous utterances—in which the physician reflected on and assessed resident performance or offered suggestions for improvement—than in-person feedback (p=0.01). Resident survey of feedback quality had a possible range of scores from 10 to 50, with a higher score representing better quality feedback. A t-test showed no significant difference between the quality of the feedback given via SIMPL and in-person (p=0.073). The average score was 47.74 (SD=2.997) for SIMPL feedback and 45.33 (SD=4.765) for in-person feedback. Third party assessment was performed by two evaluators with an intraclass correlation of 0.957. A t-test showed no significant difference between the quality of the feedback given via SIMPL and in-person (p=0.486). The average score was 23.40 (SD=3.75) for SIMPL feedback and 22.25 (SD=5.94) for in-person feedback, with a possible score range of six to 30 and a higher score representing better quality feedback.

Conclusion: Although feedback given via SIMPL was significantly more direct and based on the attendings’ perspective, the quality of the feedback did not differ significantly. Use of the SIMPL application to deliver resident operative performance feedback is a reasonable alternative to in-person delivery of feedback.
EFFICACY OF REAL-TIME US COMPRESSION IN DECREASING DISTANCE AND ENABLING PERCUTANEOUS BIOPSY OF DEEP TARGETS IN THE ABDOMEN AND PELVIS

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Support: Shapiro Summer Research Program, Radiology R/D Committee

Introduction/Background: There are a variety of imaging modalities available for guidance of percutaneous biopsy including CT, US, and fluoroscopy. US is operator dependent and requires some expertise for optimized imaging guidance, but is portable, cost effective, and does not utilize ionizing radiation. US is also a real-time modality that is ideal for image-guided biopsy in solid organs and non-air containing structures. Another potential advantage of US is the compression applied to the probe when imaging a target. This compression may shorten the distance from skin to target, improve visualization, and displace intervening structures such as bowel. However, there is increasing utilization of CT guidance for percutaneous biopsy at many centers, and some operators may shy away from US guidance for biopsy particularly in large patients or for deep targets. The purpose of this study was to evaluate the utility of active US compression in decreasing distance to biopsy target and enabling a safe percutaneous biopsy route to deep structures in the abdomen and pelvis.

Methods: This study is HIPAA compliant and IRB approved. A retrospective review of US-guided biopsies from 2006 present was performed. Patients with abdominal targets (mesentery, pelvis, retroperitoneum) were included and skin-to-target distances were measured on pre-procedure CT and US images obtained during biopsy. Patients were grouped by skin-to-target distance, including 0-3 cm, 3-6 cm, 6-10 cm, and greater than 10 cm. “Deep” abdominopelvic targets were defined as > 6cm in distance. The difference in distance to target between US and CT was collected, and the % decrease from compression calculated. Patient BMI, biopsy procedural details, diagnostic yield, and complication rate were also recorded.

Results: A total of 428 biopsies were assessed (183 M, 245 F; mean age, 62.2 years; mean BMI, 28.21). Distance to target was 0-3 cm in 111 patients, 3-6 cm in 178 patients, 6-10 cm in 118 patients, and greater than 10 cm in 21 patients. A total of 139 of these targets were categorized as deep (>6 cm skin to target distance on CT). The average skin-to-target distance in the entire cohort was 5.1 cm on CT and 3.7 cm on US, with an average decrease in distance of 11%. However, as skin-to-target distance increases, increased compression aids in decreasing distance and thus greater % decrease in distance to target. For targets 3-6 cm, a mean 17% decrease in distance was identified with compression. For targets 6-10 cm, distance was decreased by 40% at US, and for targets >10 cm, distance was reduced by 49%. In addition, on the planning CT, about 10% of patients (n=42) had no safe identifiable path for CT-guided biopsy, most commonly due to intervening bowel, which was displaced at US and enabled safe biopsy trajectory. US-guided biopsy in this cohort was a robust technique with diagnostic yield of approximately 90% and favorable safety profile with complications noted in approximately 1% of procedures.

Conclusions: US guidance for percutaneous abdominal biopsy has many potential advantages including real-time needle visualization, low cost, and lack of ionizing radiation. Advantages specifically related to compression are demonstrated here, with decreased skin-to-target distance of greater than 40% for deep targets in addition to displacement of intervening structures such as bowel, creating a safe path for biopsy in the 10% of cases not feasible with CT. In addition, US-guided biopsy demonstrates high diagnostic yield and favorable safety profile. US should be considered as a first line modality for biopsy guidance, even for deep targets in the abdomen pelvis.
ANALYSIS OF PULMONARY VASCULAR IMPEDANCE AND REMODELING IN ISCHEMIC HEART FAILURE

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Mentors: Naomi Chesler, PhD; Jennifer Philip, MD

Support: Shapiro Summer Research Program, Cardiovascular Research Center, Madison Community Foundation, Department of Biomedical Engineering

Background: Pulmonary hypertension secondary to left heart disease (PH-LHD) is the most common form of pulmonary hypertension and a leading cause of morbidity and mortality in patients with heart failure (HF). The mechanisms underlying the pathologic pulmonary vascular remodeling in PH-LHD remain poorly understood. This study aims to characterize the development of PH-LHD in a mouse model of ischemic HF. Methods: Male C57/BL6 mice ages 6-8 weeks underwent left anterior descending artery ligation to induce myocardial infarction (MI). Sham animal underwent thoracotomy alone. Mice were studied at 12-weeks post-surgery. Cardiac function was assessed noninvasively via echocardiography and invasively via catheterization. Isolated lung perfusion was also performed. Pulmonary vascular fibrosis was assessed with picrosirus red histology staining. Results: MI mice demonstrated evidence of HF at 12-weeks post-surgery evidenced by reduced left ventricle (LV) ejection fraction (35.2±3.5% vs 52.5±1.7%, p<0.01) and increased LV volumes (167±20 vs 87±3 µL p<0.01) compared to Sham mice. Diastolic dysfunction was present, evidenced by increased isovolumic relaxation time (22.1±1.0 vs 17.8±0.6 ms, MI vs Sham, p<0.01). MI mice also developed significant biventricular hypertrophy (increased LV and RV weights) compared to Sham mice. Development of PH-LHD was demonstrated by increased RV systolic pressure (29.0±1.2 vs. 19.6±1.0 mmHg p<0.01) in MI mice compared to Sham mice. In addition to increased LV end diastolic pressure (8.6±1.5 vs 2.0±0.1 mmHg p<0.05), MI mice had significant elevation in pulmonary vascular resistance (PVR), measured ex vivo (5.8±0.4 vs 4.1±0.6 mmHg-min/mL, MI vs Sham, p<0.05). Consistent with increased PVR, which suggests small pulmonary arteriolar narrowing, there was a 70.6% increase in perivascular collagen in the pulmonary arterioles post-MI compared to sham (p<0.001). Conclusions: This study used a model of ischemic HF to study and characterize the development of PH-LHD. We demonstrate the development of pulmonary perivascular fibrosis and increased PVR, key pathologic features of human PH-LHD. Future studies with this novel animal model will improve understanding of the pathophysiology of this deadly disease as well as help to identify novel therapeutic targets.
COMPETENCE-BASED MASTERY LEARNING FOR CHEST TUBE PLACEMENT: A STUDY OF ANXIETY, CONFIDENCE, AND PERFORMANCE

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Support: Shapiro Summer Research Program, Department of Surgery

Introduction: Simulation-Based Mastery Learning (SBML) has been demonstrated to be an effective educational tool for procedural skills. The relationship between anxiety, confidence, and performance in graduating senior medical students utilizing a SBML module has not previously been described. This study proposes a SBML model for chest tube insertion and evaluates anxiety, confidence, and performance in graduating medical students during an intern preparatory course just prior to graduation.

Methods: Fourteen graduating medical students completed a two-week surgery intern preparatory course, which included a SBML Module for chest tube insertion. Prior to the course, baseline Trait anxiety was assessed using the short form State-Trait Anxiety Inventory (STAI). Learners used a moderate fidelity model to demonstrate placement of a chest tube on course day 1 (Pretest) and course day 4 (Posttest). Prior to the Posttest, learners watched a standardized chest tube placement video and participated in a one-hour didactic session followed by supervised deliberate practice. Any learner who did not achieve mastery received remediation. On course day 10, learners completed a Retention Test on a live animal model. Prior to each skill test, learners reported State anxiety with the STAI; immediately following each skills test, learners again completed the STAI and the Cato Confidence Scale. The Mastery Learning checklist was validated by faculty trauma surgeons to reflect a level expected of an incoming surgical intern. Student scores were analyzed via a repeated measures ANOVA. Results: Mastery was not attained by any learner during the pretest. During the Posttest and retention test, 92.2% of learners achieved mastery. With remediation, all achieved mastery. Applying a 95% confidence interval, assessment scores increased (Mean + SD; Day 1: 34.7 + 5.3 vs Day 4: 50.4 + 1.9 vs Day 10: 50.5 + 0.7; p < .001), post-skill anxiety decreased (10.4 + 3.1 vs 6.6 + 2.1 vs 7.1 +2.2; p < .001), learner confidence increased (2.6+ 0.6 vs 3.4 + 0.7 vs 3.6 + 0.6; p < .001) and State anxiety decreased significantly compared to Trait anxiety (Trait: 10.9 + 2.1 vs Day 1 State: 10.1 + 3.3 vs Day 4 State: 8.5 + 3.6 vs Day 10 State: 8.4 +3.5; p=.012). There was no significant difference between the average reduction in State anxiety between all tests (1.3 + 1.6 vs 1.9 +2.9 vs 1.4 + 2.0; p=.474) or in pre-skill anxiety (10.1 + 3.3 vs 8.5 + 3.6 vs 8.4 + 3.5; p=.060). Conclusion: Implementation of a SBML chest tube insertion module resulted in improved learner confidence and performance while significantly decreasing post-skill anxiety. After one week, high rates of technical skill retention were identified. Applying SBML to a chest tube insertion module to ensure competence and skill retention in senior medical students should be further implemented and explored.
DUAL PI3K/BCL INHIBITION IN COLORECTAL CANCERS WITH APC AND PIK3CA MUTATIONS

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Support: Shapiro Summer Research Program; Department of Medicine

Background: Colorectal cancer is a leading cause of cancer-related death in the United States\(^1\). In 20% of human colorectal cancers mutations in the PIK3CA gene are present resulting in a constitutively active form of PI3K and most commonly occur concomitantly with the loss of adenomatous polyposis coli (APC)\(^2\). Copanlisib is a pan-class I PI3K inhibitor that has demonstrated potent anti-tumor and pro-apoptotic activity in tumor cell lines. While Copanlisib has shown promise for the treatment of non-Hodgkin lymphoma in Phase I/II clinical trials, it has not yet been used for the treatment of colorectal cancer\(^3\).

Objective: To examine the response of colorectal cancers with Apc and Pik3ca mutations to an agent targeting PI3K and whether combination treatment with a pro-apoptotic agent inhibiting BCL-2, BCL-X\(_L\), and BCL-W affects that response. Methods: Colorectal cancer spheroids with Apc and Pik3ca mutations generated from transgenic mice were cultured in Matrigel and treated by exchanging feeding media containing desired concentration of each agent over the spheroids. Spheroids were treated with regular feeding media (control), 200nM ABT263 (inhibiting BCL), 200nM Copanlisib (inhibiting PI3K), or combination treatment of ABT263 and Copanlisib. The spheroid culture response was quantified as the median relative change in the sphere diameter, comparing pre- and posttreatment 4x optical microscopic images to those obtained 48 hours post-treatment. Results: Untreated colorectal cancer spheroids had a median growth in sphere diameter of 137%. ABT263 did not significantly affect growth; however, Copanlisib significantly reduced median sphere size by 24.6% (p=8.4*10^{-26}) and the combination treatment reduced median sphere size by 33% which was significant to both control and copanlisib only treated spheres (p=1.1*10^{-26} and p=0.014 respectively). Induction of apoptosis in these spheres treated with the combination regimen was confirmed with immunofluorescence for cleaved caspase 3. Conclusion: In this study, we demonstrated the ability of Copanlisib alone and combined with ABT263 to cause a marked decrease in sphere size of colorectal cancer spheroids with Apc and Pik3ca mutations. Future tests will look to better understand how the change in sphere size mechanism involves apoptosis through immunofluorescence staining and western blots for proteins involved in apoptosis and cell growth. The results shown here will be the foundation of future work concerning the ability of Copanlisib to treat PIK3CA mutant cancers other than non-Hodgkin lymphoma such as colorectal cancer.

Citations:
DIAGNOSTIC ACCURACY OF MRI AND US FOR EVALUATION OF FEMALE PELVIC PATHOLOGY

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Support: Shapiro Summer Research Program; Department of Emergency Medicine

Background: When evaluating non-pregnant women presenting to an emergency department (ED) with right lower quadrant abdominal pain that is not specifically concerning for gynecological pathology, the American College of Radiology recommends using contrast-enhanced computed tomography (CE-CT). Conversely, pelvic ultrasound (US) is recommended when obstetric or gynecologic etiology is suspected. Due to the overlap in symptomatology of patients with gastrointestinal, gynecological, and other disease processes, it is common for women with lower abdominal pain to undergo both CE-CT and US. However, CE-CT exposes patients to ionizing radiation, a known carcinogen, and US quality is operator-dependent. We hypothesized that CE-MR could provide the same diagnostic information as US as well as data usually requiring CE-CT when evaluating non-pregnant patients with acute lower abdominal pain.

Methods: This is a HIPAA-compliant and IRB-approved prospective single-center study of patients undergoing evaluation for possible appendicitis at the ED of an academic tertiary care hospital. Patients were eligible for that study if they were at least 12 years old and had a CE-CT scan of the abdomen/pelvis ordered. For this analysis, only those patients who were female and underwent pelvic US (in addition to CE-CT) were included. Following routine CE-CT, participants underwent CE-MR. MR images were used only for research; all imaging-based decisions relied on CE-CT and US at the discretion of the treating physician. Inability to provide informed consent and contraindications to CE-MR imaging were exclusionary criteria. Following the ED visit, two fellowship-trained abdominal radiologists independently interpreted each CE-MR examination following anonymization and randomization of order. They were blinded to results of US and CE-CT, as well as all clinical information except that patients were undergoing CE-CT for evaluation of possible appendicitis. They evaluated the images using a standardized case report form inquiring about the presence of common gynecologic pathology (ovarian cyst or torsion, tubo-ovarian abscess, oophoritis/salpingitis, free pelvic fluid, endometrial/uterine mass, etc.). They rated their confidence in the presence of each of these findings on a five point scale, with a score of 4 or 5 considered positive. The research MR images were compared to clinical US reads, which were interpreted with full knowledge of clinical data including CT interpretation if already resulted. A reference standard of surgical/pathological interpretation was used if available, while a chart review plus one month follow-up phone call was used if unavailable. If multiple diagnoses were present, they were analyzed as separate cases. Results: The study cohort included 41 women with a mean age of 27.6 (SD ± 10.8) years. While the accuracy for any diagnosis visualized was tabulated, ovarian cyst was the most common diagnosis present at 27% (n=11). Sensitivity, specificity, and positive and negative predictive values (with 95% confidence intervals) were, respectively, 62% (38-82%), 81% (58-95%), 76% (56-89%), and 68% (54-79%) for US and 80% (64-91%), 65% (50-79%), 67% (57-75%), and 79% (66-88%) for CE-MR. Conclusion: CE-MR performed comparably to US and should be considered as a primary imaging modality in the evaluation of acute pelvic pain, particularly in women who may otherwise undergo both US and CE-CT.

EXAMINING RELATIONSHIPS BETWEEN SMOKING, POVERTY AND RACE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Mentor: Christie M. Bartels, MD, MS

Support: Shapiro Summer Research Program; Department of Medicine

Introduction: Systemic lupus erythematosus (SLE) is a multi-organ disease where minority patients have increased incidence, severity, and mortality. Patients with SLE live 5-10 years less than peers primarily due to premature cardiovascular disease (CVD), yet 25% of US patients still smoke. Smoking is also linked to cutaneous and serologic SLE, features emphasized in the new Systemic Lupus Collaborating Clinics (SLICC) classification criteria vs. the older American College of Rheumatology (ACR) criteria. Thus, we sought to validate a WI SLE cohort, examine predictors of smoking in SLE including race and poverty, and study the effects of smoking on SLE criteria.

Methods: We manually abstracted electronic records of adults with SLE codes into a REDCap database. Definite SLE was classified as meeting 4 of 11 ACR or 4 of 17 SLICC criteria. Smoking history included current or former smokers. Zip codes were linked to an area deprivation index (ADI), a published neighborhood poverty marker. We used descriptive statistics and multivariable logistic regression (Odds Ratio (OR), 95% Confidence Interval) to examine the prevalence and sociodemographic predictors of smoking, and the relationships between classification criteria and smoking history.

Results: Of 897 reviewed cases, 620 met definite SLE criteria. 91% were female, mean age of 54 ± 15 years. 43% had a smoking history, 58% of males, 41% females (p=0.01); 43% White, 54% Black (p=0.001). The strongest predictors of smoking were Black race (OR=5.8, 1.8-18.5) and the worst 2 ADI quartiles (OR=2.9, 1.7-5.1; 2.4, 1.3-4.1). Yet, there was a protective interaction between Black race and a lower ADI poverty quartile (OR=0.03, 0.003-0.36). Smoking did not correlate with mean total SLICC or ACR criteria. However, discoid lupus, chronic cutaneous lupus, thrombosis, lupus anticoagulant, psychosis, and neuro-lupus were more common in smokers. Limitations include a single-center cohort with low diversity. ADI was absent for 63 patients.

Conclusion: SLE patients who smoked were equally likely to meet SLICC and ACR criteria. Consistent with prior literature, smokers met more cutaneous and thrombotic criteria. New associations were noted between neuropsychiatric criteria and smoking. Black race and poverty predicted smoking, identifying smoking as a modifiable target to reduce outcome inequities in WI SLE patients. Creation of a diverse multicenter cohort is underway to examine effects of smoking on chronic SLE damage.
INTRATUMOR INJECTION OF TUMOR-SPECIFIC ANTIBODY AND IL2 TRIGGERS IN SITU VACCINATION FOLLOWING LOCAL RADIATION THERAPY

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**Mentors:** Zachary S. Morris, M.D. Ph.D., Paul M. Sondel, M.D. Ph.D.

**Support:** Shapiro Summer Research Program; Department of Human Oncology

**Background:** In murine models of GD2⁺ melanoma, GD2⁺ neuroblastoma, and EGFR⁺ head and neck cancer, we have reported a cooperative interaction between radiation and intratumor (IT) injection of tumor-specific antibody (anti-GD2 hu14.18K322A or anti-EGFR cetuximab). Consistent with a process mediated by antibody-dependent cell-mediated cytotoxicity, this interaction required the Fc portion of the antibody, host Fcγ receptor, NK cells, and tumor expression of the antibody-targeted antigen. In this GD2⁺ melanoma model, combined treatment with RT + IT - hu14.18-IL2 immunocytokine (a fusion protein of hu14.18 antibody and IL2) markedly enhanced response compared to radiation or IT-IC alone, radiation + IT-hu14.18 antibody, or radiation + intravenous-IC. In those studies, radiation + IT-IC induced an in situ vaccine effect, resulting in a tumor-specific memory T cell response. Here we test whether IT administration of non-fused tumor-specific antibody and IL2 may elicit an in situ vaccination response following local radiation.

**Methods:** C57BL/6 mice were flank engrafted with syngeneic GD2⁺ B78 melanoma and 5-week tumors (~200 mm³) were treated with single fraction 12 Gy radiation, IT-IL2 (150,000U), and/or IT-hu14.18K322A (50µg). IT injections were given daily on days 6-10 after radiation. Outcomes included tumor response and rates of complete regression, overall survival, tumor-specific memory (tested in disease-free mice by contralateral flank injection with B78 melanoma >90 days after radiation), and immunohistochemistry on tumors resected at day 12 after radiation.

**Results:** The combination of local radiation + IT-hu14.18K322A + IT-IL2 resulted in greater tumor regression compared to radiation + IT-hu14.18K322A or radiation + IT-IL2 [50% (19/38) aggregate complete tumor regression vs 0% (0/11) and 25% (3/12), respectively, p<0.001]. No mice were rendered disease-free with these IT-treatments in the absence of radiation. Kaplan-Meier analysis demonstrated improved survival with radiation + IT-hu14.18K322A + IT-IL2 compared to radiation + IT-hu14.18K322A and radiation + IT-IL2 (log-rank p<0.0001; 80% alive at day 65 vs 0% and 50%, respectively). Thus far, 100% (6/6) of mice rendered disease-free by combined radiation + IT-hu14.18K322A + IT-IL2 have rejected subcutaneous B78 re-implantation at >90 days after radiation, compared to 0/10 naïve control mice. Preliminary immunohistochemistry analyses suggest that IT-IL2 may increase tumor infiltrating CD8⁺ T cells in this preclinical model. **Conclusions:** We present evidence of a cooperative anti-tumor effect with the combination of local radiation and IT injection of both tumor-specific antibody and IL2. Given the widespread availability of tumor-specific antibodies, this may offer a viable approach to pursuing in situ tumor vaccination in many diverse types of cancer using off-the-shelf reagents.
INSURANCE STATUS AND RACE AFFECT TREATMENT AND OUTCOME OF SEVERITY STRATIFIED TRAUMATIC BRAIN INJURY

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Support: Shapiro Summer Research Program; Department of Surgery

Background: Socioeconomic status and race has been shown to increase the chance of being afflicted by a Traumatic Brain Injury (TBI) and result in worse post-hospitalization outcomes.¹³ There is a paucity of data on how severity of TBI mediate these treatment and outcome factors. The goal of this study is to determine the effect disparities have on in-hospital mortality, discharge to inpatient rehabilitation, hospital length of stay (LOS), and TBI procedures performed based on insurance status and race/ethnicity throughout the range of TBI severity. Methods: This was a retrospective cohort study using the National Trauma Data Bank (2012-2015) analyzing patients with closed head injuries. Univariate and multivariate logistic/linear regression models were performed to determine the impact of race/ethnicity and insurance status on in-hospital mortality, discharge to inpatient rehabilitation, LOS, and TBI procedures performed in groups stratified by head Abbreviated Injury Scale (AIS). Results: We analyzed 708,261 TBI patients 76.6% white, 30% private insurance, 13% uninsured, the distribution of severity was 1.3% AIS of 1, 28.3% of AIS of 2, 30.1% of AIS of 3, 30.4% of AIS of 4, 9.9% of AIS of 5. As compared to privately insured patients, uninsured patients experienced greater mortality with increasing AIS, beginning from an AIS of 3 (OR = 1.01, p < 0.001) increasing to an AIS of 5 (OR = 1.11, p < 0.001). As compared to privately insured patients, uninsured patients were less likely to be discharged to rehabilitation with increasing AIS as seen beginning from an AIS of 2 (OR = 0.98, p < 0.001) increasing to an AIS of 5 (OR = 0.84, p < 0.001). As compared with white patients, black patients had a longer LOS as their AIS increased, which started from an AIS of 2 (0.16 days, p < 0.001) increasing to an AIS of 5 (2.44 days, p < 0.001). As compared with non-Hispanic patients, Hispanic patients had a longer LOS with increasing AIS, which started with an AIS of 2 (0.11 days, p < 0.001) to the longest LOS at an AIS of 5 (1.124 days, p < 0.001). Compared with privately insured patients, Medicaid patients had a longer LOS in all AIS stratifications from an AIS of 1 (0.55 days, p < 0.001) and increased to an AIS of 5 (5.52 days, p < 0.001). Conclusion: Disparities lead to differences in mortality, procedures performed, and discharge to inpatient rehabilitation for uninsured patients in higher ranges of TBI severity. Also, disparities lead to differences to LOS for black, Hispanic and Medicaid patients throughout the entire spectrum of TBI severity. The most vulnerable populations and minorities with the highest TBI severity seem to have the greatest disparities in treatment and outcome factors.

HOSPITALIZATIONS AND EMERGENCY DEPARTMENT USE DUE TO DEVICE COMPLICATIONS FOR CHILDREN WITH MEDICAL COMPLEXITY

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Background: Children with medical complexity (CMC) have health conditions affecting multiple organ systems and commonly rely on invasive medical devices, e.g., gastrostomy, tracheostomy tubes. Although these devices support essential body functions, device complications can lead to unplanned and potentially preventable hospital or emergency department (ED) use. The objectives of this study were to characterize device use associated with hospitalizations or ED visits due to device complications; and to identify specific patient and clinical characteristics that predict these encounters. Methods: Retrospective cohort study of patients enrolled in the UW Pediatric Complex Care Program between 4/1/2014 and 4/30/16 who were dependent on at least 1 medical device. All hospital and ED encounters in the year prior to enrollment were rated on a 0-3 scale for likelihood of being due to a device complication. Ratings for the first 100 random encounters were conducted by 3 blinded independent reviewers. Interrater reliability was calculated using Kappa statistics. Device-complicated hospitalizations or ED visits were dichotomized as those rated 3 vs <3. Bivariate followed by multivariate logistic regression clustered by patient identified associations between demographic, clinical and device characteristics associated with device-complicated ED or hospital visits. Results: Among 98 patients, median number of devices was 2/patient (IQR 1-4), and interrater reliability was 0.92. Device-complicated encounters represented 17% of 258 hospitalizations and 30% of 228 ED visits. The highest fraction of hospitalizations due to a specific device complication was nasogastric tube (40.0%). The highest fraction of ED visits due to a specific device complication was central venous catheter (47.1%). In adjusted analyses, gastrojejunostomy (OR 3.9, 95% CI 1.6-9.6) or tracheostomy (OR 4.1, 95% CI 1.0-17.2) were associated with device-complicated hospitalizations; while central venous catheters (OR 2.2, 95% CI 1.0-5.1) were associated with device-complicated ED visits. General demographic, social and clinical variables were poor predictors of device-related hospitalizations or ED visits. Conclusion: ED and hospital visits due to device complications, much of which may be preventable, are common among CMC enrolled in our program. Future interventions targeting these devices may be an effective strategy to reduce CMC hospital and ED use.
EVALUATION OF THE COORDINATION OF CANCER CARE BY MULTIDISCIPLINARY TEAMS AND EFFECT ON PATIENT EXPERIENCE

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Background: Multidisciplinary teams (MDTs) for treatment of oncology patients are increasingly used nationwide, and studies have shown that MDTs improve patient clinical outcomes, including survival. However, the process by which MDTs determine and communicate a treatment plan for new oncology patients is highly variable. Few studies have assessed patient preferences for the MDT process. We aimed to improve the quality of the integration of new cancer patients at the University of Wisconsin Carbone Cancer Center (UWCCC) by assessing patient preferences via a nationwide survey and examining the provider perspective at the UWCCC. Methods: A survey of experience with navigation to a treatment plan was posted in six online national cancer support groups. In addition, qualitative, semi-structured interviews were conducted with members of UWCCC MDTs to assess provider perceptions of the MDT process for new cancer patients. Interviews were analyzed via content analysis. Results: A total of 156 patients and caregivers responded to the survey. Of these, 39% were unclear on next steps after they received their cancer diagnosis, 35% did not know whom to contact with questions, and 69% had no interaction with a nurse navigator prior to their first oncology appointment. Furthermore, 78% wanted to discuss the treatment plan within one week of receiving their diagnosis, but only 41% had done so. Additionally, 62% met with the different providers over multiple days to discuss the treatment plan, but 63% actually expressed a preference to meet with all members of the care team on the same day. Four nurse navigators and three oncology fellows from UWCCC MDTs were interviewed. There was general agreement that the period from the initial cancer diagnosis to the first appointment discussing the treatment plan is a confusing time for patients, and that patients prefer to discuss the treatment plan soon after diagnosis. The interviewees identified challenges for patient integration with the MDT including variability in access points for new patients, time required to obtain additional patient records and diagnostic studies, difficulty determining which diagnostic tests and which types of providers each patient needs, and limitations in provider availability. Major themes for improving patient integration into the MDT process were the importance of nurse navigators for patient coordination and questions, and a desire to create standardized processes for connecting new cancer patients with the correct providers more efficiently. However, the interviewees emphasized the difficulty of standardization given the differences in patient needs at the time of access to the MDT process. Conclusion: Overall, balancing patient preferences with logistical and provider needs is key to improving new patient integration into the MDT process. Analysis examining timing of UWCCC MDT integration and barriers to access for new cancer patients is ongoing.
EXAMINING SYSTEMIC APPROACH TO DETECTING THE DIAGNOSIS OF DEMENTIA USING ELECTRONIC MEDICAL RECORDS

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Background: The prevalence of dementia among patients over 70 years of age is over 14.7%, with over $157 billion in monetary cost per year [1]. There is a growing need for earlier detection and management of dementia and its wide-ranging disease complications, in the acute settings such as the Emergency Department as well as for research. One of the current methodology of automatically detecting dementia patients for research purposes is by identifying International Classification of Disease (ICD) codes for dementia and dementia-related conditions. However, dementia is often underdiagnosed and underreported in the electronic medical records (i.e. patient does not reflect dementia-related ICD codes when being billed). Recent efforts to develop a natural language system to flag for dementia resulted in a sensitivity of 63% as compared to a physician reviewing the charts [2]. Our objective is therefore to compare ICD automated flagging for dementia with a manual comb of the electronic medical records using the same database of patients to assess sensitivity and specificity of the automated process.

Methods: A cohort of patients over 65 years old was created comprising of those who presented to University of Wisconsin Hospital and Clinic (UWHC) ED between September of 2012 to September of 2015 with a chief complaint of acute chest pain. Patients within the cohort was then scanned for ICD – 9th Edition (ICD-9) codes related to dementia and flagged. As a comparison, abstractors also analyzed each patient’s electronic health records to determine the diagnosis of dementia, with the use of natural language query into HealthLink’s search bar. The abstractors’ criteria for determining the presence of dementia was either the diagnosis of dementia or dementia-related conditions in any Encounter Notes prior to the ED visit or if the patient had ever taken dementia-related medication prior to the ED visit (e.g. donepezil, rivastigmine, galantamine, or memantine). After the manual reviewing, sensitivity and specificity calculations were performed.

Results: The initial cohort consisted of 1,609 patients, with the automated ICD-9 process flagging 182 patients positive and 1,427 patients negative for dementia. Of the 182 patients, the manual review determined 164 true positives and 18 false positives. Of the 1,427 patients, the manual review determined 1,342 true negatives and 85 false negatives. This came out to a sensitivity of 65.9% and specificity of 98.7%, with a positive predictive value of 90.1% and negative predictive value of 94.0%. Conclusion: The ICD-9 automated process had high specificity but poor sensitivity. More research is needed to refine the ICD automated process to improve sensitivity of detecting dementia. Likewise, future work includes attempting to automate the natural language process for ease and comparing this new process with a gold standard such as the Clinical Dementia Rating.

Sources:
DEPRESSION SEVERITY IN ADOLESCENT MALE AND FEMALE ATHLETES FOLLOWING SPORTS-RELATED CONCUSSION

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Support: Shapiro Summer Research Program; National Athletic Trainer Association

Introduction: Concussions are a growing concern in adolescent sports medicine, with over 300,000 high school athletes experiencing a sports-related concussion (SRC) each year. However, there is no prospective data demonstrating an association between sustaining an SRC and long-term depressive symptoms in adolescents. The objective of this study was to prospectively assess clinically relevant changes in depressive symptoms in high school athletes the six months following an SRC. Methods: This longitudinal cohort study consisted of n=1701 adolescent athletes (grades 9-12) who were monitored for SRC. Of those, 99 athletes sustained a concussion during the study period (n=38 females, n=61 males). Participants completed the Patient Health Questionaire-9 (PHQ-9) survey to measure depressive symptoms at the following time points: baseline (at time of enrollment, pre-SRC), within 24-72 hours post-SRC, and 7 days, 3 months, and 6 months post-SRC. Clinically relevant depressive symptoms were defined as a PHQ-9 score >4, or some depressive symptoms most days and most of each day. Linear mixed-effect models adjusting for sex and time were used to assess changes in PHQ-9 scores from baseline; least-square means and standard errors are reported. GEE models assuming a binomial distribution and logit link were used to model the association between depressive symptoms and time since concussion, stratified by sex. Results: When compared to baseline, females reported PHQ-9 scores that were, on average, 1.53(0.56) points higher at 24-72 hours post-SRC and 1.62(0.57) points higher at 7 days post-concussion than at baseline (p=0.007; p=0.004). PHQ-9 scores were lower (i.e. better) than baseline for both males and females at 3 months (M: -1.19(0.48); p=0.01, F: -1.14(0.66); p=0.09) and 6 months (M: -1.43(0.51); p=0.005, F: -1.28(0.80), p=0.11). Additionally, females are 7.6 times more likely to have a PHQ-9 >4 at 24-72 hours post-concussion (95% CI: 1.47, 39.08) than they were at baseline (p=0.02) and 10.36 times more likely at 7 days post-concussion (95% CI: 1.90, 56.59) than at baseline (p=0.007). By 3 months and 6 months, no difference from baseline is noted. There is no evidence to suggest that males experience a shift in clinically relevant depressive symptoms over time compared to baseline. Conclusions: We found no evidence that SRCs have a long-lasting impact on depression symptoms and severity in both males and females. However, in the week following an SRC, both males and females experience a transient increase in depressive symptoms which resolve by the time the player returns to unrestricted play. Furthermore, females are more likely to experience a clinically relevant burden of depressive symptoms at 24-72 hours and 7 days post-SRC compared to male athletes at the same timepoints. It is essential for athletes, parents, coaches, and academic staff to be aware of these transient changes in the athlete's mental health as to better support these students through their SRC recovery.
IDENTIFYING PREDICTORS OF PROLONGED LEVOTHYROXINE DOSE ADJUSTMENT AFTER THYROIDECTOMY

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Support: Surgery T35 Summer Research Program

Introduction: Synthroid (LT4) is one of the most prescribed drugs in the US. Despite its widespread use and multiple dosing schemes, many patients struggle to achieve euthyroidism after thyroidectomy and suffer symptoms of hyper- or hypothyroidism. The objectives of this study are to describe time required for dose adjustment prior to achieving euthyroidism and to identify predictors of prolonged dose adjustment (PDA+ after thyroidectomy. Methods: This is a retrospective cohort study of patients from a single institution who achieved euthyroidism with LT4 therapy between 2007 and 2017 after undergoing total thyroidectomy or completion thyroidectomy for benign disease. PDA+ was defined as needing at least 3 dose adjustments top quartile (prior to achieving euthyroidism. We compared patient characteristics of PDA+ patients to the remaining patients PDA- using Wilcoxon Rank Sum test or Chi-squared test where appropriate. Multivariate logistic regression was used to identify predictors of PDA+. Results: The 605 patients in this study achieved euthyroidism in a median of 116 days (range 14 - 863 and 1 dose adjustment (range 0 - 7. The 508 (83.97%) patients who were PDA- achieved euthyroidism in a median of 101 days (range 14 - 627 and 1 dose adjustment) range 0 - 2. The 97 (16.03%) patients who were PDA+ achieved euthyroidism in a median of 271 days (range 52 - 863 and dose adjustments) range 3 - 7. PDA+ patients required more than twice the median number of days to achieve euthyroidism 271 vs. 101 days, p<0.001. PDA+ patients were more likely to have chronic renal insufficiency 5.2% vs. 1.6%, p=0.026. More than three times as many patients in the PDA+ group were taking iron 6.2% vs. 1.8%, p = 0.010. Similarly, nearly twice as many patients in the PDA+ group were taking multivitamin with minerals 22.7% vs. 11.6%, p = 0.003. When controlling for all other factors, iron supplementation OR = 4.4, 95% C.I. = 1.43 - 13.55, p = 0.010 (and multivitamin with mineral supplementation OR = 2.4, 95% C.I. = 1.3 - 4.3, p = 0.004 were independently associated with PDA+. However, plain multivitamins were not associated with PDA+. Age, gender, preoperative thyroid disease, and co-morbidities did not independently predict PDA+. Conclusion: After thyroidectomy at a high-volume center, achieving euthyroidism can take nearly four months. Iron and mineral supplementation are associated with PDA+. This information can be useful when counseling patients preoperatively and suggests that education about proper LT4 administration and interfering supplements may expedite achieving euthyroidism.
BARRIERS TO APPROPRIATE SURGICAL HAND ANTISEPSIS IN A TERTIARY CARE HOSPITAL

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Support: Shapiro Summer Research Program; Department of Medicine

Background: Surgical hand antisepsis (scrub) is an integral component of surgical site infection prevention; however compliance is variable, despite institutional policies. A systems approach to better understand reason for this variation may be useful. We undertook a mixed methods study to evaluate surgical staff’s adherence to institutional policy for surgical hand antisepsis, and identify barriers to correct performance of surgical scrub in a tertiary care hospital. Methods: Direct observations and semi-structured interviews of staff performing surgical scrubs during 7/1/- 7/15/17 at University of Wisconsin Hospital. Results categorized with deductive coding using the Systems Engineering Initiative for Patient Safety (SEIPS) model, which has five components: person, tasks, tools/technology, environment, and organization. Results: We conducted 45 direct observations in 17 different operating rooms and interviewed 14 staff. Hand antisepsis was performed in accordance to the institutional policy in 2/34 (6%) of the alcohol-based scrubs, and 1/11 (9%) of the water-based scrubs. Major barriers to correct performance in the five SEIPS categories were: 1) Person: unawareness of correct technique, or institutional policy or available video on how to perform a surgical scrub correctly. Most staff relied on knowledge acquired during their school training or upon initial hire. 2) Task: the 3-5 minutes time recommended for water-based scrub was considered too long, with staff’s preference for alcohol-based scrubs instead. 3) Tools and technology: soap or alcohol dispenser pumps not working properly; antiseptic products judged to be “too harsh” on the skin. 4) Physical environment: sink water pressure and temperature too high or too low; antiseptic dispensers not always easily accessible. 5) Organization: lack of oversight; no sustained emphasis on training and auditing staff’s surgical scrub techniques. Conclusion: We discovered suboptimal adherence to institutional surgical hand antisepsis policy, with most staff missing or incorrectly performing one or more elements of the surgical scrub. Implementing interventions to address the barriers identified in our study may improve performance.
INVESTIGATING THE USE OF EDUCATION ON DIET AND MEDICAL COMORBIDITIES TO REDUCE CATARACT SURGERY SCREENING FAILURE IN A RURAL COMMUNITY IN IMO STATE, NIGERIA

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Support: Shapiro Summer Research Program, Department of Pediatrics, Mezu International Foundation

Background: Cataracts are among the leading causes of preventable blindness worldwide. Mezu International Foundation (MIF), a non-profit organization that provides humanitarian aid in rural Imo State, Nigeria, collaborated with University of Wisconsin Shapiro Research Program to do a community health needs assessment. A study showed that lack of finances to afford surgery and poor health practices were major contributory risk factors to early cataracts in the community. MIF collaborated with Combat Blindness International (CBI) to provide free cataract surgeries; only 10 out of 100 patients screened qualified for same-day surgery due to untreated medical comorbidities like hypertension, diabetes, glaucoma, and anemia. This study seeks to investigate the influence of dietary habits and socioeconomic status (SES) on chronic conditions in order to develop a vision education program focused on early management of medical comorbidities.

Methods: A cross-sectional study using a questionnaire was administered to 83 patients aged 45 to 85 years old with a diagnosis of mature cataracts. All subjects underwent detailed medical and ocular exam to identify comorbidities. An Institutional Review Board (IRB) was obtained from a collaborating local institution, Federal University of Technology, Owerri. Diet diversity, SES, and quality of life (QOL) scores were determined. Results: 40 male and 43 females aged 45-85 years were surveyed. 74% of subjects had hypertension (n=61), 42% had anemia (n=35), 16% had diabetes (n=13), and 51% had glaucoma (n=42). Drinking bottled water or having a personal bore hole was associated with hypertension (P=0.0373). There was a significant positive association between SES and QOL score (P=0.021). People who consumed foods high in vitamins and minerals were more likely to have higher numbers of chronic diseases (P=0.0048). There was no association between QOL scores and percentage of carbohydrates, protein, vitamins/minerals, or fats/oils in the diet (P>0.05). Conclusion: A higher SES and being able to afford clean water source was associated with hypertension, likely indicative of access to poorer health choices. A diet high in vitamins and minerals was associated with higher numbers of chronic diseases, likely due to lower diet diversity. Education on diet diversity and management of chronic illness could empower patients to make better health practices and ultimately lead to higher cataract screening success rates in the community.
ASSOCIATION OF GENDER WITH THE UTILIZATION OF PERITONEAL DIALYSIS

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Support: Shapiro Summer Research Program; Department of Medicine

Background: Peritoneal dialysis (PD) is underutilized in the United States compared to other countries despite being a cheaper modality of dialysis with a better quality of life. We analyzed data from the United States Renal Data Services (USRDS) and US census to assess the association between gender and initial dialysis modality to determine whether gender might impact PD utilization. We also investigated gender-specific associations of age, race/ethnicity, median household income, employment status, cause of End-Stage Renal Disease (ESRD) and number of comorbidities on the incidence of PD. Methods: We estimated the proportion of USRDS patients utilizing PD as their initial modality between 2000-2014, adjusting estimates to the mean value of all covariates (age, race, ethnicity, cause of ESRD, comorbidities, incidence year, income and employment status) and compared these estimates for women and men. Additionally, we used effect modification analysis to compare the effects of these covariates on PD use within each gender. Results: 108,022 patients (45% women) initiated PD and 1,267,803 patients (44% women) initiated hemodialysis during this time period. On average, women were more likely than men (OR: 1.12, 95% CI 1.10-1.14) to utilize PD as their initial dialysis modality. In our effect modification analysis, we found that black women (OR Female 0.65; OR Male 0.59; p-value <0.001), women with "other" as the cause of ESRD (OR Female: 0.89; OR Male: 0.82; p-value 0.002) and employed women all have higher odds of PD than their male counterparts (OR Female: 2.41; OR Male 2.24; p-value <0.001). In comparison, men with diabetes (OR Female: 0.84; OR Male: 0.97; p-value <0.001) and glomerulonephritis (OR Female: 1.08; OR Male: 1.18; p-value 0.004) as the cause of ESRD, men with any number of comorbidities (OR Female w/ 1 Comorbidity: 0.70; OR Male: 0.77; p-value <0.001) and men with no referral have higher odds of PD than women in the same group (OR Female: 0.22; OR Male 0.25; p-value <0.003). Conclusion: Our results indicate that on average, women in the US were more likely than men to utilize PD as their initial modality, but this association varies between demographic group and cause of ESRD. Most interestingly, women with a greater number of comorbidities are less likely to be on PD than their male counterparts, indicating that a bias may exist in that providers see only healthier women as candidates for PD. This study emphasizes the role gender may play in medical decision making and highlights the need to further investigate the factors that influence patients of each gender to choose PD.
ESTIMATING THE IMPACT OF POST-PRESCRIBING REVIEW ON THE QUALITY OF ANTIBIOTIC PRESCRIBING IN SKILLED NURSING FACILITIES

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Department: Department of Medicine

Mentor: Christopher Crnich, MD

Support: Shapiro Summer Research Program, Department of Medicine

Background: Almost half of all antibiotic courses prescribed in nursing homes (NHs) are unnecessary, and even when clinically indicated, the antibiotics used are often excessively broad-spectrum or used for a longer durations than necessary to eradicate the infection. While most interventions to counteract this trend have focused on reducing initiation of antibiotics, there may be additional opportunities to reduce inappropriate antibiotic use through efforts that promote review and modification of existing antibiotic orders. The purpose of this study is to estimate the frequency and types of de-escalation opportunities associated with antibiotic courses initiated for treatment of suspected urinary tract infection (UTI) in Wisconsin NHs. Methods: Data was extracted in a standardized case report form from the clinical and pharmacy records of 364 subjects being treated for suspected UTI in five Wisconsin NHs in order to evaluate opportunities for potentially 1) stopping treatment (urine cultures negative and/or lack of clinical symptoms), 2) shortening treatment (duration of therapy >7 days), and 3) streamlining treatment (switching to a non-fluoroquinolone alternative if indicated by urine culture susceptibility results). Results: Of the 353 UTI treatment courses identified in which abstracted data permitted evaluation for at least one de-escalation opportunity, 234 treatment courses (66%) would have potentially benefited from at least one antibiotic de-escalation intervention. Antibiotic discontinuation (n = 223) was the most common de-escalation opportunity identified; however, treatment was stopped appropriately in only 32 (14%) of these cases. 265 cases were analyzed for appropriateness of duration of effective therapy; 86 (32%) of these cases could have potentially benefited from a shorter duration of therapy. 94 cases of fluoroquinolone use were studied; fluoroquinolone use was required in only 14 (15%) of these cases. Based on urine culture susceptibility results, 80 subjects could have potentially been switched to a more narrow-spectrum alternative; 64 (80%) of these cases were not streamlined adequately. Conclusions: Our study shows that over two-thirds of antibiotic courses initiated for treatment of suspected UTI in NHs were amenable to some form of post-prescribing optimization. Future studies are needed to determine how to best implement post-prescribing optimization interventions in this setting.
TIMELY EVALUATION AND MANAGEMENT OF PRIMARY HYPERPARATHYROIDISM IN PATIENTS WITH KIDNEY STONES

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Background: Kidney stones are a common manifestation of primary hyperparathyroidism (PHPT), and a strong indicator for surgical treatment of PHPT. Effective detection and treatment of PHPT is critical for managing the risk of recurrent stone disease and other complications of unmanaged PHPT. In this study, we examined predictors of kidney stones in PHPT patients and determined how effectively the diagnosis of PHPT is made in patients who first present with stones. Methods: We performed a retrospective analysis of surgically treated PHPT patients, comparing 247 patients who were kidney stone-formers (SF) and 1,047 patients with no stones (NS). We identified 51 SF patients who presented with a stone before their PHPT diagnosis, and whose stone evaluation and treatment was completed entirely within our health system for further analysis. Extracted data included clinical assessment and treatment of stones as well as timing of PHPT evaluation. Results: Compared to NS patients, SF patients were more likely to be male (28.6% vs 19.7%, p=0.002) and to be normocalcemic (26.6% vs. 16.9%, p=0.001) than the NS patients. SF patients also had higher alkaline phosphatase (92 IU/L vs. 85 IU/L, p=0.012) and higher 24-hour urinary calcium levels (342 mg/day vs 304 mg/day, p=0.005). On multivariate analysis, being male and having a higher 24-hour urine calcium and alkaline phosphatase were independently associated with a greater incidence of kidney stone formation. Despite these differences, 52.7% of SF had 24-hour urinary calcium levels within the normal range at the time of surgery. Of the 51 SF patients with full chart available for review, 72.5% (n=37) had a serum calcium drawn within 6 months of the first stone episode. Hypercalcemia was present in 43.2% of these patients (n=16), but only 10 (62.5%) of these patients had a serum parathyroid hormone (PTH) ordered within 3 months of their elevated calcium. Patients that had both a calcium and PTH drawn within 9 months of their first episode of kidney stones had a significantly shorter time from their first stone to surgical treatment than the other patients (median 8.5 months vs. 49.1 months, p=0.001). Conclusion: SF patients were found to be stronger excreters of calcium, but elevated urinary calcium and serum alkaline phosphatase levels did not identify the majority of PHPT patients at risk of forming kidney stones. Many patients with kidney stones had normal serum calcium levels and normal urinary calcium levels highlighting the need to carefully evaluate all SF for the possible treatable cause of hyperparathyroidism. Timely consideration of PHPT as well as prompt serum calcium and PTH evaluation significantly reduces time to treatment and minimize the risks of complications of longstanding PHPT.
EARLY BACTEREMIA AFTER SOLID ORGAN TRANSPLANTATION IS ASSOCIATED WITH LOWER 10-YEAR SURVIVAL

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Background: Patients who have undergone organ transplantation are at increased risk of developing opportunistic infections due to the immunosuppression they receive to prevent graft rejection. This immune suppression is designed to suppress the adaptive immune response to foreign tissue antigens, but may also have unintended, profound effects on innate immunity. Few studies have investigated how the innate arm of immune response is altered by transplant immunosuppression. Susceptibility to bacteremia does not depend on adaptive immune function; thus, bacteremia is a useful measure of innate immune functionality. This study investigated whether one or more agents used for induction immunosuppression (basiliximab, alemtuzumab or thymoglobulin/anti-thymocyte globulin) is associated with an altered risk of bacteremia within 90 days after transplant. Methods: We used a retrospective cohort study design to identify episodes of bacteremia among 4,030 individuals who received a kidney, liver, pancreas, or kidney-pancreas transplantation at the University of Wisconsin between January 2004 and June 2014. We used univariate analysis to identify independent risk factors for bacteremia by comparing induction immune suppression regimen, maintenance immune suppression regimen (mycophenolate and tacrolimus or non-standard), age, gender, race, white blood cell count, organ type, donor type (deceased or live), transplant year, biopsy-proven rejection, and weight among bacteremia cases and controls. Categorical variables were compared using chi-squared or Fisher’s exact test. Continuous variables were compared using the two-sample t test. All potential risk factors with a p value of < 0.10 in the univariate analysis were then included in a multivariate logistic regression model to identify independent predictors of bacteremia. Kaplan-Meier estimates were used to compare overall patient survival and graft survival in patients with and without bacteremia, using the log-rank test for significance. Results: There were 163 episodes of bacteremia, 51% due to Gram-positive organisms, 44% due to Gram-negative organisms, and 5% due to multiple bacterial pathogens. 18% of episodes were due to a multidrug resistant organism. Bacteremia occurred in 3% (64/2,123) of the basiliximab group, 3% of the thymoglobulin group (12/469), 4% of the alemtuzumab group (26/734), and 9% of the “no induction” group (61/699) (χ²=48.4, p<0.001). In the multivariate analysis, liver transplant was independently associated with bacteremia compared to kidney transplant (OR 7.74, 95% CI 4.66-12.87, p<0.001). Receipt of an organ from a donor who suffered cardiac death as compared to a live donor was also independently associated with bacteremia (OR 1.92, 95% CI 1.09-3.63, p=0.023). No particular induction regimen was associated with an altered risk of bacteremia. Patients with 90-day bacteremia had significantly worse survival up to 10 years after transplant compared to controls (p<0.0001). As previously reported, alemtuzumab (p<0.0001) and thymoglobulin (p=0.013) were associated with decreased graft survival compared to basiliximab. Conclusion: These preliminary data show that there is no particular advantage of one induction regimen over another in terms of reducing risk of 90-day bacteremia. However, bacteremia within 90 days of transplant strongly predicted reduced long-term survival. In the near future, we will further this analysis by examining an additional induction immune suppression group – those persons receiving heightened immune suppression because of a high level of donor-specific antibodies. We hypothesize that this group will also be at increased risk for bacteremia.
RELATIONSHIP BETWEEN CD4/CD8 RATIO AND VIREMIA IN INCARCERATED PATIENTS

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Background: Of the 1.57 million people incarcerated in the United States, about 1.3% are currently living with an HIV diagnosis1. Although most of these individuals receive structured highly active antiretroviral therapy (HAART) while in prison, almost all inmates face the challenge of acquiring medications when reentering the community. A study has shown that only 5.4% of inmates filled their antiretroviral prescriptions within 10 days of release from prison, 17.7% within 30 days, and 30% within 60 days2. This lack of adherence to HAART medications causes poor virologic control and increased incidence of viremic episodes. The reintegration of prisoners into society represents a high risk time period both for possible transmission of HIV as well as for death of the former inmate. How to mitigate these risks is unclear. The purpose of this study is twofold: first, we hypothesized prolonged incarceration would lead to reversal in a marker for HIV-mediated immunodysregulation known as the CD4/CD8 ratio. Secondly, we hypothesized that an increased CD4/CD8 ratio would be protective of viremia post-release. Methods: A retrospective chart review was performed on 95 patients who were currently or previously incarcerated through the Wisconsin Department of Corrections. Results: Of the 95 patients in our cohort, we found that 78 patients experienced an increase in their CD4/CD8 ratio. We also found that the relative rise in ratio is directly related to the length of incarceration as those incarcerations greater than 730 days lead to larger relative increases in the ratio (p-value equal to 0.038; significant at p < 0.05). Additionally, of the 95 patients in our cohort, we were able to extract post-release viremia data on 30 with 20 of these patients also having CD4/CD8 ratio data. Six of these 20 patients experienced no change or a decrease in their CD4/CD8 ratios while imprisoned with 4 of the 6 becoming viremic following release from prison (p-value equal to 0.0048; significant at p < 0.05). Of these 4 patients, 2 experienced viremic episodes less than 100 days after release. Conclusion: Incarcerated patients experience increases in their CD4/CD8 ratio relative to their length of incarceration with longer incarcerations leading to larger relative increases in the ratio. The data further suggests that increases in the ratio may be protective of viremic episodes, however, more data is needed to substantiate this claim.


THE EFFECTS OF PROLACTIN ON THE CHONDROGENIC POTENTIAL OF BONE MARROW-MARROW DERIVED MESENCHYMAL STEM CELLS

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Background: Prolactin (PRL) is present in all mammals and has widespread function beyond lactation. PRL was recently identified as a soluble bone marrow factor that primes bone marrow-derived mesenchymal stem cells (BMSCs) for osteochondral differentiation in vitro. PRL may also play a role in diseases like osteoarthritis. To date, PRL studies have not mirrored physiologic concentrations nor timing. This study aims to answer how different concentrations of PRL given during different in vitro culture processes (proliferation, differentiation, or both) affect BMSC chondrogenesis. Methods: BMSC were harvested from the iliac crest of donors and cultured in low-glucose DMEM + 10% FBS. BMSCs were differentiated in chondrogenic media + TGF-β1 for 21 days. BMSCs were treated with 0, 10 (physiologic), or 100 ng/mL (supraphysiologic) PRL during proliferation and again with either 0, 10, or 100 ng/mL PRL during differentiation. Chondrogenesis was evaluated by DNA normalized glycosaminoglycan (GAG) production and by qRT-PCR for chondrogenic gene expression (Col-1, Col-2, Col-10, Aggrecan, and SOX9). All data was collected in triplicate and analyzed by two tailed t-test with Bonferroni correction.

Results: Both the 100, 0 (expansion culture [PRL], differentiation culture [PRL]) and 100, 100 samples expressed significantly less GAG/DNA than the 0, 0 samples (p=.006, p=.008). The 10, 0 and 10, 10 samples expressed slightly more GAG/DNA than the 0, 0 group, but the difference was not statistically significant (p=.08). PRL supplementation had more effect on GAG production when given during BMSC proliferation than during differentiation. qRT-PCR data was largely inconclusive and requires further workup, but initial results suggest the addition of 10 ng/mL PRL seemed to promote chondrogenic gene expression and 100 ng/mL decreased expression. Specifically, the 0, 10 samples expressed 1.21 fold more SOX9 than 0, 0 (p=.29) and 3.71 fold more SOX9 than 0, 100 (p=.018). PRL supplementation had considerable effect on gene expression during both proliferation and differentiation; however, the trends and degree of response were variable. Conclusions: Our data supports prior studies suggesting that PRL in a physiologic range promotes BMSC chondrogenesis. Interestingly, pathologic PRL levels may directly inhibit BMSC chondrogenesis and lead to disease process. Experimentation needs to be repeated in at least 2 more biologic replicates to confirm trends and, with improved technique, reduce standard error.