UCSF Multidisciplinary Resident Research Symposium

Sponsored by CTSI Resident Research Training Program
and the Molecular Medicine Pathway

We are pleased to offer a combined clinical and translational research and molecular medicine symposium dedicated to the research accomplishments of our residents. The mission of CTST, the training component of CTSI, is to create a pipeline and training system that enhances the number, quality, and cross-disciplinary skills of clinical and translational researchers at UCSF. The Molecular Medicine Pathway aims to enrich the residency experience with opportunities to engage with clinician-scientists and peers, to engage with current scientific literature, and to develop mentoring relationships in order to support career development.

The primary goal of the CTSI **Resident Research Training Program** (RRTP) is to create opportunities for all residents to gain fundamental knowledge in clinical and translational research methods and evidence-based medicine skills. Additionally, we aim to inspire residents to pursue future opportunities in investigation. CTST sponsors a one-month course (**Designing Clinical Research**) which provides residents with the opportunity to gain fundamental skills and to develop their own research proposal in small group sessions with close guidance from the faculty. CTST also offers two funding opportunities: the **Resident Research Funding (RRF) award,** which provides up to $2000 per academic year to UCSF residents for qualified clinical and translational research expenses not covered by their mentor or other sources; and the **Resident Research Travel (RRT) award,** which provides $600 matching funds to support travel to present research findings at a scientific meeting.

The main goal of the graduate medical education component of the **Molecular Medicine Pathway** (MMP) is to create a community of and for basic science oriented residents across all specialties in the UCSF School of Medicine and other professional schools. We are here to help these physician-scientists achieve their career goals in academia. Activities throughout the year include social gatherings, a mentoring/career-development workshop, and the annual resident research symposium co-sponsored with the CTSI.

We thank you for joining us today to celebrate the accomplishments of this year's participants.

Miriam Kuppermann, PhD, MPH
Co-Director, RRTP

Ben Cheyette, MD, PhD
Director, MMP

Alison Huang, MD, MPhil, MAS
Co-Director, RRTP

Schedule of Events

4:00 pm   **Welcome & Resident Research Program Overview**
Miriam Kuppermann and Alison Huang, Co-Directors,
*   CTSI Resident Research Training Program*

4:15 pm   **Resident Oral Papers**
Moderated by Alison Huang and Miriam Kuppermann

Speaker Name: James E. Anstey, MD
Title: Changing the Culture: Predicting Bacteremia using the Electronic Health
**   Record**
Residency Program: Internal Medicine, Categorical
Research Mentor: Sara Murray, MD, MAS

Speaker Name: Anamaria J. Robles, MD
Title: The Impact of Pro-Inflammatory States on the Fibrin-Platelet Balance
**   Following Injury**
Residency Program: Surgery
Research Mentor: Rachael Callcut, MD

Speaker Name: Randi K. Agata, PharmD
Title: Impact of a Discharge Alert Tool on Pharmacist Discharge Medication
**   Review**
Residency Program: Pharmacy
Research Mentor: Kathy Ghomeshi, PharmD, MBA, BCPS, CPPS

Speaker Name: Joseph T. Patterson, MD
Title: LMWH Does Not Prevent Clinically Important VTE after Fracture Surgery
**   Below the Knee**
Residency Program: Orthopaedic Surgery
Research Mentor: Saam Morshed, MD, PhD

Speaker Name: Vaibhav Upadhyay, MD, PhD
Title: Exploration of Novel Autoantigens in Patients with Idiopathic Pneumonia
**   with Autoimmune Features**
Residency Program: Internal Medicine, Categorical
Research Mentor: Anthony Shum, MD

5:30 pm   **Mentor of the Year Award**
Clinical and Translational Recipient: Joshua Woolley, MD, MS, Psychiatry

5:45 pm   **Poster Viewing and Reception**
MH-1400

Mentor of the Year Award

It is well-recognized that mentoring is a critical factor in academic success. The success of residents embarking on a research project is highly influenced by the quality of their mentorship. Thus, we would like to recognize the contributions of the many faculty who have assisted with the research endeavors presented today.

Today we are recognizing a faculty mentor for outstanding excellence in mentoring. This year's awardee was selected from many outstanding nominations.

Clinical and Translational Mentor
Joshua Woolley, MD, MS

"Dr. Woolley has gone out of his way to support my taking on this project, despite its complexity and clear challenges. He has been unwavering in how he has championed my work on this high-risk high-reward project that has become the core of my residency experience and has opened up incredible career doors for me. It's hard to imagine that many other mentors would allow a resident to write a trial protocol and implement the study the way that I have been able to do under his guidance."

Abstracts:

Oral Presentations

UCSF Multidisciplinary Resident Research Symposium

Monday, June 11th, 2018

Mission Bay, Mission Hall, MH-1401/1402

Abstract title: Changing the Culture: Predicting Bacteremia using the Electronic Health Record

Resident's name: James E. Anstey, MD
Name of program: Internal Medicine, Categorical

Purpose: Blood cultures are frequently ordered in hospitalized patients, often to work up undifferentiated fever or leukocytosis. This leads to low rates of positive cultures and high burden of false positive results resulting in avoidable interventions and waste. A recent study in hospital medicine patients identified several predictors of blood stream infection (BSI), but the sample size was small and generalizability was limited. In the era of the Electronic Health Record (EHR), we are collecting a multitude of clinical data that can be leveraged to address this question on a larger scale. We used EHR data to investigate predictors of BSI in patients hospitalized on the medicine service at a large academic medical center.

Methods: Using EHR derived data, we created a retrospective cohort of all patients with blood cultures ordered during 2016 on the hospital medicine service. We excluded all culture episodes ordered in the ED or ICU. Blood cultures were initially adjudicated based on organism. Possible non-pathogenic results then underwent expert review to further characterize true and false positive cultures. Predictors of interest included vital signs, white blood cell count, lactate, admission diagnosis, age, central line presence, immunosuppression, and recent antibiotics. We then calculated likelihood ratios of each predictor for BSI.

Results: 3,131 blood cultures were ordered on the hospital medicine service in 2016, of which 165 were true positives and 59 false positives (contaminated). Significant predictors of true BSI included transient hypotension (LR 1.72, 95% CI 1.04-2.83), central venous access (LR 3.26, 95% CI 2.90-3.65), age <65 (LR 1.69, 95% CI 1.53-1.87) and admission diagnosis of bacteremia/intravascular infection (LR 2.98, 95% CI 1.26-7.05). We did not find a relationship between recent antibiotics, fever, or leukocytosis and BSI. When stratified by admission diagnosis, we did find lower rates of BSI in patients with pneumonia, urinary tract infection, or skin/soft tissue infection although confidence intervals crossed one in these small groups.

Conclusions: This is the first study to leverage clinical EHR data on a large scale to investigate predictors of BSI. We demonstrated that commonly referenced factors (fever, leukocytosis) are not predictive of blood stream infection, while other factors (admission diagnosis, hypotension, age <65 years, and presence of a central line) are associated with increased likelihood of BSI. This suggests a change in blood culture ordering practices may be indicated. We conclude that these objective and readily available EHR data can be used as predictors to create clinical decision support to help clinicians identify patients at high or very low risk of BSI.

Abstract title: The Impact of Pro-Inflammatory States on the Fibrin-Platelet Balance Following Injury

Resident's name: Anamaria J. Robles, MD

Name of Program: Surgery

Purpose: In non-injured patients, aging and HIV infection are both known to induce chronic pro-inflammatory milieus with associated hypercoagulable states. Studies have demonstrated that both elderly patients and HIV patients have increases in pro-coagulant factors and decreases in anti-coagulant factors. Although antiretroviral therapy (ART) decreases viral replication for the HIV patients, low-level inflammation and immune activation are known to persist. Overall, the impact of the pro-inflammatory states of aging (>=55 years) and HIV infection on post-injury coagulation is unknown. We hypothesized that these patients demonstrate hypercoagulable states following even severe injury.

Methods: Data were prospectively collected on 1671 injured patients from 2005-2016. Citrated rapid thromboelastography (CRT), functional fibrinogen levels (FLEV), and standard coagulation measures were performed. Patients on anti-coagulant/anti-platelet medications were excluded from analysis. Multiple regression analysis was performed to determine the independent associations of age and HIV infection on coagulation.

Results: Amongst 1671 patients enrolled, 22% were age >=55 years and 39 (3%) were HIV positive amongst the 1349 in whom their HIV status was known. Older patients were more severely injured (ISS 21 vs 12) and had lower initial hemoglobin (13 vs 14 g/dL) and platelet counts (231 vs 275 k/uL; all $p<0.01$) compared to their younger counterparts. 18 of the HIV patients (46%) were on ART, with 24 (69%) having history of ART treatment; the median CD4 count was 399 (227-536 cells/mm3). HIV infected patients trended towards being older (43 vs 37 years, $p=0.05$) and had significantly lower BMI (24 vs 26 kg/m2 $p<0.01$) compared with HIV-negative patients. They also had lower initial hemoglobin (13 vs 14 g/dL, $p<0.01$), platelet counts (239 vs 269 103/μL, $p<0.01$), and WBC (7.8 vs 9.8 103/μL, $p=0.01$). In multiple logistic regression, older patients were hypercoagulable with increased speed of clot formation (CRT alpha angle +2.34 deg, $p=0.03$), increased levels of functional fibrinogen (FF FLEV +45.57 mg/dL, $p=0.01$), but lower platelet contributions to clot strength (-3.80%, $p<0.01$). Similarly, in multiple logistic regression, HIV infected patients were also hypercoagulable with an increased speed of clot formation (CRT alpha angle +4.90 deg, $p=0.02$). However, in contrast to the older cohort, they had decreased levels of functional fibrinogen (FF FLEV -67.30 mg/dL, $p=0.04$), and higher platelet contributions to clot strength (+9.03%, $p=0.02$).

Conclusions: Following injury, pro-inflammatory states including aging and HIV infection have independent associations with hypercoagulability and alterations in the fibrin-platelet balance. Identifying fibrin-platelet imbalances following injury is critical, as targeted treatment may require shifts in resuscitation and thromboprophylaxis in at-risk populations including those with chronic pro-inflammatory states.

Abstract title: Impact of a Discharge Alert Tool on Pharmacist Discharge Medication Review

Resident's name: Randi K. Agata, PharmD

Name of program: Pharmacy

Purpose: Medication discrepancies may occur when patients are discharged from the hospital. Medication reconciliation identifies and resolves medication discrepancies, and the review of a patient's medication list is the first step of medication reconciliation. Recent evidence suggests that pharmacist review of discharge medications is associated with decreased medication discrepancies and adverse events associated with drug therapy issues, and decreased readmission rates. The purpose of this study is to evaluate the impact of a pharmacy discharge alert tool on the number of pharmacist discharge medication reviews completed, and to determine whether a pharmacist intervention was performed during after-visit summary (AVS) medication review.

Methods: This retrospective study utilized data from the electronic health record (EHR) to identify patients 18 years of age and older discharged from the inpatient medicine service of an academic medical center. Study exclusions were patients who left against medical advice, expired during hospitalization, transferred to another hospital, or discharged to hospice or jail/prison. Data collected included patient age, date and time of discharge, discharge disposition, discharge pharmacy activities (including AVS medication review completed and intervention performed on the AVS), total number of medications on the AVS, and the presence of a high-alert medication (anticoagulant, opioid, or insulin) on the AVS medication list. The primary outcome is the proportion of patients with AVS medication review completed by a pharmacist before and after implementation of the discharge alert tool. Secondary outcomes include the number of pharmacy interventions at AVS medication review and the number of patients discharged with a high-alert medication and AVS medication review completed.

Results: The proportion of patients with pharmacist AVS medication review completed pre-implementation of the discharge alert tool was 20 percent versus 29 percent post-implementation (P equals 0.138). After the implementation of the discharge alert tool, the proportion of AVS medication reviews with a pharmacist intervention increased from 11 percent to 18 percent (P equals 0.159). The proportion of patients with a high-alert medication and AVS medication review completed by a pharmacist pre-implementation of the discharge alert tool was 33 percent versus 67 percent post-implementation (P equals 0.036).

Conclusions: There was no statistically significant increase observed in the number of pharmacist discharge medication reviews completed before and after the implementation of a discharge alert tool. The discharge alert tool resulted in an increased number of patients on high-alert medications with pharmacist discharge medication review completed. While the discharge alert tool did not significantly increase pharmacist discharge medication review, there is potential utility of the tool to improve pharmacist visibility of the AVS medication list.

Abstract title: LMWH Does Not Prevent Clinically Important VTE after Fracture Surgery Below the Knee

Resident's name: Joseph T. Patterson, MD

Name of program: Orhthopaedic Surgery

Purpose: Orthopaedic practice has shifted from therapeutic anticoagulation of any lower extremity venous thromboembolism (VTE) to only thromboses with risk of proximal extension or embolization – clinically important VTE (CIVTE). Isolated operative fractures below the knee are associated with low-to-intermediate VTE risk. There is wide variability in the choice to prophylactically anticoagulate as well as anticoagulant. We sought to evaluate the role for chemoprophylaxis of VTE and CIVTE in these injuries by meta-analysis of Level I evidence.

Methods: Two orthopaedic surgeons systematically reviewed randomized controlled trials describing chemoprophylaxis of VTE after operative management of fractures below the knee published in English, Chinese, French, and German in MEDLINE, Biosis, and EMBASE from 1988 to 2016. Chemoprophylaxis regimen, VTE, CIVTE, and major bleeding events were recorded. Study quality was assessed with regard to randomization, outcome assessment allocation and treatment concealment, and commercial funding.

Results: Independent review of 1,502 citations yielded five studies (1,181 patients) meeting inclusion criteria. A random effects model meta-analysis determined that chemoprophylaxis with a low molecular weight heparin (LMWH) compared with placebo or no intervention significantly reduced the risk of any VTE (pooled RR = 0.696, 95% CI [0.490-0.989], p = 0.043; homogeneity p = 0.818, I2 = 0%). However, chemoprophylaxis with a LMWH compared with placebo did not significantly reduce the risk of CIVTE (relative risk = 0.865, 95% confidence interval [pooled RR 0.112-3.863, p = 0.790; homogeneity p = 0.718, I2 = 0%). No major bleeding events occurred. Funnel plots did not suggest publication bias. The number need to treat was 31 patients treated with chemoprophylaxis using a LMWH to prevent one VTE.

Conclusions: Meta-analysis of Level I evidence suggests routine prophylactic postoperative anticoagulation after surgical management of an isolated fracture of the tibia or distally in patients without risk factors for VTE is unlikely to provide a clinical benefit, based on the absence of a treatment effect for preventing VTE warranting therapeutic anticoagulation.

Abstract title: Exploration of Novel Autoantigens in Patients with Idiopathic Pneumonia with Autoimmune Features

Resident's name: Vaibhav Upadhyay, MD, PhD

Name of program: Internal Medicine, Categorical

Purpose: Individuals with idiopathic pneumonia with autoimmune features (IPAF) are a group of patients who present with lung autoimmunity and who lack disease specific markers. A unique disease pattern characterized by a high titer of anti-nuclear antibody (ANA), a non-specific interstitial pneumonia pattern of lung injury, and clinical hallmarks of autoimmunity such as Raynaud's phenomenon, have led to a hypothesis that people with IPAF suffer from a break in tolerance leading to circulation of currently unknown auto-antibodies.

Methods: We are utilizing a novel screening technology enabling profiling of serum from patients against DNA encoded targets spanning all open reading frames of the human genome; similar technology has previously been successfully used to identify novel autoantigens.

Results: 30 patients were identified as screening candidates for our IPAF study from a database of 3270 total patients enrolled in the UCSF interstitial lung diseases program. Fourteen out of 30 patients have a positive ANA without positive known nuclear target (i.e. negative dsDNA, SSA, SSB, Sm, RNP) indicating they have an autoantibody against a nuclear target of unknown etiology. An additional 14 patients have a combination of known autoantibody targets but do not fit into a specific diagnosis of known connective tissue diseases. The remaining two patients have high titer ANA and have demonstrated improvement after treatment with Rituximab (n=1) and a BAFF inhibitor (n=1). Additionally, several patients with a lung specific form of autoimmunity (the 'COPA' syndrome) will be screened. Positive targets will be validated.

Conclusions: Further work completing the screening process and validation will be undertaken to determine if disease specific markers can be established for this disease using genomic targets.

Resident Research Training Program
CTSI Resident Research Funding Award 2017 Recipients

Name	Program	Mentor
Ashish Agrawal	Anesthesia and Perioperative Care	Debbie Madhok
Brian Anderson	Psychiatry	Josh Woolley
Scott Bauer	Internal Medicine, UC Primary Care	Stacey Kenfield
Polly Fu	Internal Medicine, Categorical	Vanessa Jacoby
Jin Ge	Internal Medicine, Categorical	Jennifer C. Lai
Nicole Jiam	Otolaryngology	Charles Limb
David Klein	Obstetrics, Gynecology and RS	Karen Smith-McCune
Sara LaHue	Neurology	Vanja Douglas
Gopal Lalchandani	Orthopaedic Surgery	Igor Immerman
Stephen Magill	Neurological Surgery	David Raleigh
Stefana Morgan	Psychiatry	Susan Voglmaier
Audrey Nguyen	Plastic Surgery	Jason Pomerantz
Ryan Rampersaud	Psychiatry	Owen Wolkowitz
Eva Raphael	Family and Community Medicine	Rita Hamad
Jessica Ristau	Internal Medicine, UC Primary Care	Celia Kaplan
Diana Robles	Obstetrics, Gynecology and RS	Vanessa Jacoby
Jae Ho Sohn	Radiology and Biomedical Imaging	Thienkhai Vu
Vaibhav Upadhyay	Internal Medicine, Categorical	Anthony Shum
Connie Wang	Internal Medicine, Categorical	Jennifer Lai
Emily Williams	Psychiatry	Joshua Woolley

Abstracts:
Poster Presentations

UCSF Resident Research Symposium

Monday, June 11th, 2018

Selected Poster Presentations

Name	Residency Program	Mentor	Abstract Title
Ashish Agrawal	Anesthesia and Perioperative Care	Debbie Madhok	Comparison of Two Techniques to Measure Optic Nerve Sheath Diameter in Patients at Risk for Increased Intracranial Pressure
Alfredo Aguirre	Internal Medicine, Categorical	Anandi Sheth	Persistent Low-Level Viremia Is Associated with Low Protease Inhibitor Levels in Hair
Brian Anderson	Psychiatry	Josh Woolley	Psilocybin-assisted Group Therapy for Demoralization in Long-term AIDS Survivors
Scott Bauer	Internal Medicine, UC Primary Care	Stacey Kenfield	Heart Healthy Dietary Patterns and Erectile Dysfunction in the Health Professionals Follow-up Study
Jonathan Cheah	Orthopaedic Surgery	Erik Hansen	Does Intrathecal Morphine in Spinal Anesthesia Have a Role in Modern Multimodal Analgesia for Primary Total Joint Arthroplasty?
Ivan de Kouchkovsky	Internal Medicine, Categorical	Margaret Fang	Periprocedural Anticoagulation Management in Patients with Venous Thromboembolism: A Systematic Review
Polly Fu	Internal Medicine, Categorical	Alison Huang	Increased Anxiety and Depressive Symptoms Associated with Abnormal Cardiac Autonomic Function in Peri- and Postmenopausal Women with Hot Flashes
Jin Ge	Internal Medicine, Categorical	Jennifer Lai	Waitlist Candidates who Travel for Liver Transplantation and the Donor Organs They Receive
Trevor Grace	Orthopaedic Surgery	Derek Ward	Predictors of Financial Loss for Femoral Neck Fracture Patients Undergoing Hip Replacement in the Bundled Payments for Care Improvement (BPCI) Initiative
Ryan Guinness	Preventive Medicine	George Rutherford	Low-Intensity Outreach to Increase Uptake of HIV Pre-Exposure Prophylaxis Among Patients with Sexually Transmitted Infections
Nghiem Ha	Internal Medicine, Categorical	Mindie Nguyen	Natural Disease Presentation and Progression in Nonalcoholic Fatty Liver Disease among Different Gender
Matthew Kan	Pediatrics	Atul Butte	Tracing diagnoses trajectories over millions of California inpatients reveals association between schizophrenia and rhabdomyolysis
Daniel Kwon	Internal Medicine, Categorical	Katherine Van Loon	Peri-Procedural Management of Patients Undergoing Liver Resection or Embolotherapy for Neuroendocrine Tumor Metastases
Gopal Lalchandani	Orthopaedic Surgery	Igor Immerman	Patient Outcomes and Costs After Isolated Flexor Tendon Repairs of the Hand
Joseph Leach	Radiology and Biomedical Imaging	Michael Hope	MRI-Based Stress Analyses of Abdominal Aortic Aneurysms With Resolved Intraluminal Thrombus Heterogeneity

Name	Residency Program	Mentor	Abstract Title
Stefana Morgan	Psychiatry	Susan Voglmaier	Training Healthcare Professionals to Identify and Respond to Victims of Human Trafficking
Dustin Nash	Pediatrics	Akash Patel	Methadone Use in Children: Assessment of Cardiotoxicity
Sara Nunnery	Internal Medicine, Categorical	Rebecca Olin	Efficacy and cost-effectiveness of Clo-HiDAC for treatment of R/R AML
Michelle Peng	Ophthalmology	Jay Stewart	Feasibility Of Detecting RNA Expression in Human Vitreous
Eva Raphael	Family and Community Medicine	Rita Hamad	Health Status of Refugee, US-Born and Immigrant Patients, ZSFG Family Health Center
Brooke Rosen	Psychiatry	Marina Tolou-Shams	Pregnancy Attitudes and Intentions Among First-Time Offending Youth
Nicholas Satariano	Orthopaedic Surgery	Igor Immerman	Incidence of Corrective Procedures after Non-Operatively Managed Distal Radius Fractures in the Elderly
Timothy Simpson	Internal Medicine, Categorical	Nelson Schiller	Mitral Annular Peak Systolic and Diastolic Velocities are Characteristic of Healthy Hearts: A Doppler Tissue Imaging Study
Emma Steinberg	Pediatrics	Anisha Patel	Leveraging School-Based Food Pantries to Promote Health
William Temple	Pediatrics	Katherine Matthay	Association of Image-Defined Risk Factors with Clinical Features, Histopathology, and Outcomes in Neuroblastoma
Martin Thelin	Pediatrics	Thomas Serwold	Enrichment of Diabetogenic T Cells in Vivo Using Implantable Scaffolds
Evan Walker	Internal Medicine, Categorical	Rebecca Sudore	Advance Care Planning Documentation Practices and Accessibility in the Electronic Health Record
Melody Xu	Radiation Oncology	Katherine Van Loon	Predictors of Radiation Therapy Incompletion among Esophageal Cancer Patients in Tanzania

Abstract title: Comparison of two techniques to measure optic nerve sheath diameter in patients at risk for increased intracranial pressure

Resident's name: Ashish Agrawal, MD

Name of program: Anesthesia and Perioperative Care

Purpose: Elevated intracranial pressure (ICP) over 20mmHg is associated with poor neurologic prognosis, but measuring this pressure requires an invasive procedure by a neurosurgeon. Dilation of the optic nerve sheath seen on axial ultrasound of the eye has been associated with elevated ICP, but optimal cutoffs have been inconsistent possibly because of artifacts in the measurement technique. An alternative coronal measurement technique has been studied on healthy volunteers but not on patients with high ICP. We compared two measurement techniques (axial and coronal) in patients with suspected high ICP due to bleeding, tumor, or infection in the brain.

Methods: We conducted a prospective study of adult patients admitted to a tertiary care center or academic trauma center intensive care unit expected to need an extraventricular drain (EVD) for high intracranial pressures. Ultrasound measurements of each optic nerve were taken in both axial and coronal views prior to placement of an EVD. Two predictor variables (average or highest of left and right optic nerve diameters) and two outcome variables (first measured ICP or highest measured ICP in 24 hours) were prespecified. Analysis included Wilcoxon signed-rank test, variance ratio test, area under receiver operating characteristic (AUROC), and sensitivity and specificity calculations.

Results: 16 patients were analyzed in this interim analysis. Coronal measurements showed smaller differences between measurements in each eye than axial measurements (mean difference 0.3mm vs. 1.1mm, p=0.005) as well as narrower standard deviations (0.3 vs. 0.8mm, p=0.002). Both mean and highest coronal measurements showed fair test characteristics when compared to first ICP measurement (AUROC 0.73 and 0.71, respectively) and highest ICP measurement (AUROC 0.66, 0.64) within 24 hours. Mean and highest axial measurements showed better association with first (AUROC 0.83, 0.92) and highest ICP measurement (AUROC 0.84, 0.94) within 24 hours. A cutoff of highest axial measurement in either eye greater than 6.2mm or mean axial measurement between eyes of 5.6mm had a sensitivity of 100% in predicting high ICP over the following 24 hours.

Conclusions: Coronal measurements showed better consistency of measurement between eyes in the same patient, consistent with prior studies in healthy patients. However, our study is the first to look at this measurement technique in patients with high ICP, and the axial technique has superior test characteristics. We identified test cutoffs that identify 100% of patients with high ICP in our population. This comparison should inform larger studies that attempt to set test cutoffs for measurement of optic nerve sheath diameter by ultrasound.

Abstract title: Persistent Low-Level Viremia Is Associated With Low Protease Inhibitor Levels In Hair

Resident's name: Alfredo Aguirre, MD

Name of program: Internal Medicine, Categorical

Purpose: HIV-infected patients on combination antiretroviral therapy (ART) may experience episodes of low-level viremia (LLV). Persistent LLV is associated with antiretroviral (ARV) drug resistance and regimen failure, but its etiology and optimal management are unclear. We evaluated the association between LLV and ARV concentration in hair, a measure of long-term ARV exposure.

Methods: HIV-infected women in the Women's Interagency HIV Study receiving proteaseinhibitor (PI)-containing ART for ≥1 year with plasma viral load (VL) <500 copies/mL were evaluated during semiannual visits from 2002-2014 for persistent LLV (≥2 consecutive detectable VL <500 copies/ml), transient LLV (detectable VL <500 copies/mL on nonconsecutive visits), or sustained viral suppression (VS, all VL below limit of detection). Participants with virologic failure (any VL ≥500 copies/ml) were excluded. Concentrations of lopinavir, atazanavir, and darunavir were measured from hair samples using liquid chromatography/tandem mass spectrometry and divided into quartiles by drug. Multivariable logistic regression and generalized linear mixed models examined factors associated with persistent or transient LLV (versus VS) including age, race, enrollment site, year of first ART, pre-regimen VL, self-reported adherence, and hair ARV quartile.

Results: Among 730 participants contributing 6266 person-visits of follow-up, 90 (12%) had persistent LLV and 167 (23%) experienced transient LLV. Maximum VL during follow-up was similar for women with persistent and transient LLV (median 132 [IQR 78, 240] and 119 [IQR 119, 210] copies/mL, p=0.12). In models including the above factors except hair ARV quartile, only non-Hispanic African American race was associated with persistent LLV (OR 1.9, 95%CI 1.2–3.0) and transient LLV (OR 1.8, 95%CI 1.0–3.3). Among 440 participants with hair PI levels, mean hair ARV concentration was lowest in the persistent LLV group for all 3 drugs (Figure 1). After adjusting for self-reported adherence, race, and the above factors, hair ARV quartile was significantly associated with persistent LLV (OR 2.5, 95%CI 1.1–5.8) but not transient LLV (OR 1.5, 95%CI 0.8–2.9).

Conclusions: In this cohort of HIV-infected women receiving PI-containing ART, 1/3rd experienced either transient or persistent LLV during >4 years follow-up. Persistent LLV was more likely to occur among women with lower hair PI levels, suggesting that improving ARV exposure could prevent persistent LLV and its adverse consequences.

Abstract title: Psilocybin-assisted Group Therapy for Demoralization in Long-term AIDS Survivors

Resident's name: Brian Anderson, MS, MD

Name of program: Psychiatry

Purpose: Long-term AIDS Survivors (LTAS) are peole living with HIV (PLWH) who were diagnosed prior to the advent of combined antiretroviral therapy. Compared to HIV seronegative peers, LTAS (like older PLWH more generally) suffer higher rates of depression, anxiety, trauma exposure, substance use and risky sexual behaviors (High, 2012; Greene, 2015). Demoralization is a syndrome common in palliative care patients and it is characterized by a sense of helplessness, hopelessness and a loss of meaning and purpose in life (Robinson, 2016). Psilocybin is a 5HT2A agonist and classic psychedelic that can improve depression and anxiety in cancer patients when combined with individual psychotherapy (Griffiths, 2016), possibly by enhancing patients' sense of meaning in life.

Methods: We are conducting an on-going open-label Phase I trial of psilocybin-assisted group therapy for gay-identified LTAS >50 years old who suffer from moderate-to-severe demoralization; participants are recruited from the community. Primary outcomes include adverse events and feasibility of combining a brief course of group therapy with a single psilocybin administration visit (0.3mg/kg po) half-way through the course of therapy. Secondary outcomes include self-report measures of demoralization, complicated grief, depression, PTSD and shame. Safety and preliminary efficacy are evaluated with descriptive statistics. This trial is approved by the FDA, DEA and UCSF IRB.

Results: To date, six participants have completed the trial, retention is 100%, and no related serious adverse events occurred. Average pre/post-psilocybin self-report scores include: Demoralization Scale-II 17.8 / 3.2 (>8 = moderate); Inventory for Complicated Grief 25.8 / 13 (>25 = significant functional impairment); CESD-R 32.3 / 11.2 (>25 = MDD likely); PCL-5 25.2 / 6.3 (>33 = PTSD likely). Inferential statistics were not conducted due to the small sample size.

Conclusions: This is the first trial to demonstrate the safety and feasibility of administering psilocybin as an adjunct to group (vs individual) psychotherapy for palliative care patients with psychiatric distress. Preliminary results resemble prior findings of rapid and significant improvement in mood and anxiety symptoms in cancer patients. This trial is the first to test psilocybin-assisted psychotherapy specifically in PLWH, and the data suggest that psilocybin-assisted group therapy may have a rapid and significant positive impact on mood and trauma-related disorders in PLWH.

References:

Greene, M., et al.: Geriatric Syndromes in Older HIV-Infected Adults. J AIDS 2015; 69(2):161-167.

Griffiths, R.,, et al.: Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. J Psychopharm 2016; 30(12):1181-1197.

High, K, et al.: HIV and Aging: State of Knowledge and Areas of Critical Need for Research. A Report of the NIH Office of AIDS Research by the HIV and Againg Working Group. J AIDS 2012; 60(Supp 1):S1-S18.

Robinson, S., et al.: Refinement and revalidation of the Demoralization Scale: The DS-II-Internal Validity. Cancer 2016; 122(14):2251-2259.

Abstract title: Heart Healthy Dietary Patterns and Erectile Dysfunction in the Health Professionals Follow-up Study

Resident's name: Scott R. Bauer, MS, MD

Name of program: Internal Medicine, UC Primary Care

Purpose: Erectile dysfunction (ED) affects more than half of men over age 70 and leads to decreased quality of life. Non-pharmacologic treatments, such as smoking cessation and weight loss, are attractive options because they are inexpensive, well tolerated, and have additional health benefits, such as decreased cardiovascular risk. However, it remains unknown if heart healthy dietary patterns are associated with ED.

Methods: We conducted a prospective analysis of 21,469 men aged 40 to 75 years old enrolled in the Health Professionals Follow-Up Study. Dietary data was self-reported on validated food-frequency questionnaires completed every 4 years and used to calculate Mediterranean Diet and Alternative Health Eating Index (AHEI) scores. ED was assessed with questionnaires in 2000, 2004, and 2008. Multivariable adjusted cox proportional hazards models were used to compute hazard ratios (HR) for incident ED (N = 7,322).

Results: Higher Mediterranean Diet and AHEI scores were both associated with decreased risk of incident ED. Men in the highest, compared to the lowest, category of Mediterranean Diet score had a 12% lower risk of developing ED (HR = 0.88; 95% CI 0.83 - 0.93). Similarly, men in the highest quintile of AHEI score were 0.82 times less likely to develop ED (HR = 0.82, 95% CI 0.76 – 0.88), compared to men in the lowest quintile. When associations with individual score components were examined, higher intakes of legumes, fruit, vegetables, and fish were associated with decreased risk of ED. Conversely, total and processed meat, monounsaturated and trans fat intakes were positively associated with risk of ED. Other score components, including dairy, grains, alcohol, and polyunsaturated fat, were not associated with ED.

Conclusions: Heart health dietary patterns, specifically Mediterranean Diet and AHEI, are associated with decreased risk of ED in this prospective cohort study. Additional research is needed to determine if dietary interventions are effective for the prevention or treatment of ED among older men.

Abstract title: Does intrathecal morphine in spinal anesthesia have a role in modern multimodal analgesia for primary total joint arthroplasty?

Resident's name: Jonathan W. Cheah, MD

Name of program: Orthopaedic Surgery

Purpose: Intrathecal morphine (ITM) combined with bupivacaine spinal anesthesia can improve postoperative pain, but has potential side effects of postoperative nausea/vomiting (PONV) and pruritus. With the use of multimodal analgesia and regional anesthetic techniques, postoperative pain control has improved significantly to a point where ITM may be avoided in total joint arthroplasty (TJA). We hypothesize that the use of ITM would be associated with decreased PO/IV opioid consumption, but with increased symptoms of PONV and pruritus that would contribute to perioperative complications such as poor mobilization and extended inpatient length of stay.

Methods: We performed a retrospective study of primary TJA patients who underwent a standardized multimodal recovery pathway and received bupivacaine neuraxial anesthesia with ITM versus bupivacaine neuraxial anesthesia alone (control). Postoperative clinical outcomes and side effects were assessed; visual analog scale (VAS) pain scores, morphine equivalents (MEQ) consumption, distances walked on postoperative day 1, the incidence of PONV, length of hospitalization stay.

Results: 598 patients were identified (131 control, 467 ITM) with similar demographics. On postoperative day 0 (POD 0), ITM patients had significantly lower mean VAS scores (1.5 ± 1.6 vs. 2.5 ± 1.9, $p<0.001$) and consumed less oral MEQ (10.5 ± 25.4 vs. 16.8 ± 27.2, $p=0.013$). ITM patients walked further compared to controls by POD 1 (133.6 ± 159.6 vs. 97.3 ± 141 meters, $p=0.028$) and were less likely to develop PONV during their entire hospital stay (38.5% vs. 48.6%, $p=0.043$). No significant differences were seen for total MEQ consumption, rate of discharge to care facility, length of stay, and 90-day readmission rates.

Conclusions: Our findings suggest that ITM has a significant analgesic benefit in the early POD 0 time period. This improved analgesia highlights the potential advantages of using ITM as part of a modern multimodal recovery pathway, as it was associated with a significant reduction in opioid consumption and VAS scores on POD 0. Improved POD 0 pain control was followed with a subsequent improvement in POD 1 mobilization, while also creating an early opioid-sparing effect with less consumption of oral/IV opioids. This early reduction in oral/IV opioid consumption may also limit the subsequent development of opioid-induced PONV on POD 1. This reduction in PONV with ITM was an unexpected finding in our study and is likely due to the fact that patients who received ITM required less early oral/IV opioid doses for postoperative pain control. In the setting of our multimodal pathway, the data is suggestive that the risk of PONV with intrathecal morphine is offset by the benefits of less early oral/IV consumption of opioids. In the setting of a modern regional anesthesia and multimodal analgesia recovery plan for total joint arthroplasty, ITM can still be considered for its benefits.

Abstract title: Periprocedural Anticoagulation Management In Patients With Venous Thromboembolism: A Systematic Review

Resident's name: Ivan de Kouchkovsky, MD

Name of program: Internal Medicine, Categorical

Purpose: Vitamin K antagonists (VKA) remain widely used in the treatment of venous thromboembolism (VTE). During surgical interventions, the prevention of recurrent VTE must be weighed against the increased bleeding risk conferred by anticoagulation. There is a lack of strong evidence to guide the optimal periprocedural management of anticoagulation in patients with prior VTE, and in particular to identify those who would benefit from short-acting parenteral "bridging" therapy. We performed a systematic review to describe the risk of recurrent VTE and bleeding in patients with prior VTE, comparing periprocedural bridging with short-acting anticoagulants to VKA interruption without bridging.

Methods: We performed a systematic review of original articles in the Pubmed and EMBASE databases from inception through September, 2017 to identify studies reporting thrombotic or bleeding outcomes in patients on chronic VKA for secondary VTE prevention who required temporary interruption for an elective procedure. Two reviewers screened titles, abstracts, and appropriate full texts, and abstracted data on study design, patient characteristics, bridging strategies, and rates of recurrent VTE and major bleeding. We then qualitatively synthesized the outcomes of patients receiving periprocedural bridging and those who were not bridged.

Results: Out of 2,476 articles screened, we identified 16 non-randomized studies and 0 randomized trials, for a total of 6,692 procedures. The estimated risk of VTE recurrence in included participants was reported in 11 of the 16 studies, ranging from low to very high. The incidence of VTE or major bleeding outcomes was directly compared across patients receiving periprocedural bridging and non-bridged patients in only 6 studies. Recurrent VTE events occurred in 26 of 3,141 (0. 8%) procedures in bridged patients (30-day VTE risk ranging from 0 to 7. 7%) and in 16 of 3,539 (0. 5%) procedures in non-bridged patients (30-day VTE risk 0 to 1. 1%). Major bleeding rates were available in 6 studies and occurred in 32 of 1,462 (2. 2%) procedures in bridged patients, and 13 of 2,208 (0. 6%) procedures in non-bridged patients.

Conclusions: Our systematic review found only sparse observational data to guide the optimal periprocedural management of patients anticoagulated for VTE. Studies included heterogeneous populations and often lacked control groups. We found that the 30-day incidence of VTE recurrence during temporary anticoagulant interruption was low, even in patients who did not receive periprocedural bridging. High-quality randomized trials are needed to further clarify the role of short-acting anticoagulation during periods of VKA interruption.

Abstract title: Increased Anxiety and Depressive Symptoms Associated with Abnormal Cardiac Autonomic Function in Peri- and Postmenopausal Women with Hot Flashes

Resident's name: Polly Fu, MD

Name of program: Internal Medicine, Categorical

Purpose: The menopause transition is marked by an increased prevalence of mood symptoms in midlife women, including anxiety and depression. Prior research in non-menopausal population has suggested that both anxiety and depression may be associated with alterations in cardiac autonomic function. Increased sympathetic and decreased parasympathetic activation have in turn been associated with adverse cardiovascular outcomes and higher rates of chronic diseases that increase incidence of cardiovascular disease, such as obesity, diabetes, and hypertension. We aim to examine whether anxiety and depressive symptoms are associated with an adverse cardiac autonomic profile among midlife women with hot flashes.

Methods: The Menopausal Treatment Using Relaxation Exercise (MaTURE) trial was a parallel-group, single-blinded, randomized trial of slow-paced respiration for treatment of hot flashes in peri- and postmenopausal women, age 40 to 59 years old, with at least four hot flashes reported per day. Main predictors of anxiety and depressive symptoms were assessed as continuous scores using validated self-administered questionnaires. State anxiety (i.e., fluctuating, transitory emotional state to perceived threats) and trait anxiety (i.e., stable individual tendency towards perceived threats) were measured using the Spielberger State Trait Anxiety Inventory (STAI). Cognitive anxiety (i.e., mental component of anxiety associated with fear of future adverse events) was assessed using the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS). Depressive symptoms were assessed using Beck Depression Inventory-II (BDI-II) and the depression subscale of HADS. Perceived stress (i.e., degree to which situations in one's life are appraised as stressful) was measured using the Perceived Stress Scale (PSS). Main outcomes of cardiac autonomic function included pre-ejection period (PEP) and respiratory sinus arrhythmia (RSA), both measured during resting period at baseline and 12 weeks using impedance cardiography and electocardiography. PEP, the time from the start of cardiac ventricular depolarization to the opening of aortic valve, is a marker of sympathetic activity. RSA, the variability of the heart rate during the typical respiratory cycle, is a marker of parasympathetic activity. Multivariable repeated measures linear regression models examined associations between anxiety, depressive symptoms, and cardiac autonomic markers, adjusted for age and body mass index.

Results: Among the 121 participants, the mean scores on questionnaire measures evaluating anxiety, depressive symptoms, and perceived stress were within the normal ranges with no significant differences detected between the paced respiration and the music control groups at baseline. Resting cardiac autonomic parameters were similar at baseline and at 12 weeks with no significant between-group differences. Greater state anxiety was associated with shorter PEP, reflecting higher sympathetic activity (β=-0.24, p<0.01). Greater trait anxiety, cognitive anxiety, and perceived stress were associated with lower RSA, reflecting decreased parasympathetic activity (β=-0.03, p<0.01 for STAI Trait Anxiety; β=-0.06, p=0.01 for HADS Anxiety Subscale; β=-0.03, p=0.03 for PSS). Greater depressive symptoms were also associated with lower RSA (β=-0.03, p=0.02 for BDI-II; β=-0.06, p=0.02 for HADS Depression Subscale).

Conclusions: Among peri- and postmenopausal women with hot flashes, greater self-reported anxiety and depression were associated with lower levels of cardiac vagal tone, while greater state anxiety was associated with higher resting sympathetic nervous system activation. Findings suggest that midlife women with increased anxiety and depressive symptoms as well as perceived stress may have an unfavorable cardiac autonomic profile with potential implications for their overall cardiovascular risk.

Abstract title: Waitlist Candidates who Travel for Liver Transplantation and the Donor Organs They Receive

Resident's name: Jin Ge, MBA, MD

Name of program: Internal Medicine, Categorical

Purpose: Geographic disparities in access to liver transplantation (LT) has led to candidates seeking LT outside their home UNOS region ("Travelers"). Little is known about their socio-economic profiles, migration patterns, and donor organ quality.

Methods: We analyzed all 2010-2014 US non-status 1 adult LT candidates. Travelers were defined as those listed ≥2 regions away from their home region (identified by home state). "Non-Travelers" were listed in their home region. We explored migration patterns, used linear regression to associate travel with donor quality, and Cox regression to evaluate transplant outcomes.

Results: Of 83,352 candidates, 2,036(2.4%) Travelers listed ≥2 regions from their home. Compared to non-Travelers, Travelers were more likely to be older (56 vs 58y), non-Hispanic White (77 vs 69%), male (71 vs 64%), privately (62 vs 57%) or VA insured (15 vs 1%). They had higher median listing allocation MELD (aMELD; 17 vs 15), received more HCC exceptions (22 vs 20%), more likely to receive LT (55 vs 41%), less likely to have died (16 vs 22%)[p<0.01 for each].

Of the 2,036 Travelers, 1,040(51%) traveled to a region with a median aMELD ≥5 less than their home region: 57% from high aMELD regions 1, 5, or 9; 70% to lower aMELD regions 2, 3, 10. 90/126(71%) centers listed Travelers, but 62% listings and 66% LTs were at 6/126(5%) centers. Travelers received a greater % of DCDD (9 vs 5%) or nationally-shared livers (8 vs 3%), and had shorter cold ischemic times (5.9 vs 6.0h)[p<0.01 for each]. Travelers vs non-Travelers received organs with a median DRI(IQR) 1.48(1.19-1.82) vs 1.44(1.19-1.75)[p<0.01].

Nationwide, Traveler status was associated with DRI 0.02 [p=0.05] points higher than non-Travelers. Significant differences existed by region: Travelers from region 5 received livers at a median aMELD24 that were 0.09 [p<0.01] DRI points higher than non-Travelers from region 5 at aMELD34. Travelers from region 9 received livers at a median aMELD25 that were 0.24 [p<0.01] DRI points lower than non-Travelers from region 9 at aMELD31. Travelers had 20% decreased mortality post-transplant (HR 0.80, 95%CI 0.67-0.95, p=0.01) compared to non-travelers in multivariable analysis.

Conclusions: The benefits of traveling were largely utilized by candidates who were older, White, male, and privately insured. Traveling for LT is associated with higher rates of LT at lower aMELDs at a small cost in donor quality, except for those originating from region 9.

Abstract title: Predictors of Financial Loss for Femoral Neck Fracture Patients Undergoing Hip Replacement in the Bundled Payments for Care Improvement (BPCI) Initiative

Resident's name: Trevor Grace, MD

Name of program: Orthopaedic Surgery

Purpose: Patients undergoing hip replacement (HR) for femoral neck fracture (FNF) are a higher-risk population with a greater magnitude of comorbidity than patients undergoing replacement for Degenerative Joint Disease (DJD). There is concern that reimbursement targets are improperly risk-adjusted for the FNF population in the Bundled Payment for Care Improvement (BPCI) Initiative, but the factors that drive these costs have not been fully defined.

Methods: Institution-specific Medicare claims data were collected and analyzed for patients undergoing hip replacement for either DJD or FNF at a single tertiary care center. Patient demographics were collected along with surgical and inpatient data. Episode payments from the index hospitalization to 90 days postoperatively were aggregated as well as the target reimbursement established by the Diagnosis Related Group (DRG) assignment. Demographic, surgical, and inpatient data were compared between the FNF and DJD cohorts, whereas univariate and multivariate logistic regression analyses were used to assess how fracture status, DRG assignment, discharge to skilled nursing, length of stay, and readmission affect the likelihood that total payments exceed the target reimbursement for a given episode of care.

Results: A total of 183 patients undergoing HR were included for analysis including 152 patients with DJD and 31 patients with FNF. The FNF cohort was found to be older ($p < 0.001$) and have a higher mean Charlson Comorbidity Index ($p < 0.001$) than the DJD cohort. Fracture patients were also more likely to be discharged to a skilled nursing facility ($p < 0.001$), stay longer in the hospital ($p < 0.001$), and be readmitted ($p = 0.009$). On univariate logistic regression analysis, costs for episodes involving a FNF that were assigned to DRG 470 were over 9 times more likely to exceed the target reimbursement (OR 9.51; 95% CI 3.23-28.0, $p < 0.001$), which would result in a loss in the bundle. However, on multivariate logistic regression analysis, this pattern was mitigated ($p = 0.188$) when discharges to skilled nursing facility, readmissions, and longer lengths of stay were accounted for.

Conclusions: Assigning FNF patients who undergo hip replacement into MS-DRG 470 risks financial loss within BPCI, although this risk is mitigated when accounting for discharges to skilled nursing facilities, longer lengths of stay, and readmissions. While there are likely opportunities for improvement in clinical outcomes for FNF patients, significant financial costs may not be completely avoidable for patient safety. Reimbursement targets should be carefully evaluated for this complex population.

Abstract title: Low-intensity outreach to increase uptake of HIV pre-exposure prophylaxis among patients with sexually transmitted infections

Resident's name: Ryan R. Guinness, MD

Name of program: Preventive Medicine

Purpose: Patients with rectal sexually transmitted infections (STIs) and syphilis are at substantial risk for acquiring HIV, yet many are not using pre-exposure prophylaxis (PrEP). Prior outreach interventions to increase PrEP uptake among high-risk individuals found fewer than 1% initiating PrEP. We assessed the feasibility of low-intensity outreach to increase linkage to PrEP care.

Methods: We identified all HIV-uninfected adult members of a large integrated healthcare system, Kaiser Permanente (KP), in San Francisco and Oakland, who had diagnoses of rectal gonorrhea, rectal chlamydia, or syphilis and were not on PrEP during January-July 2017. These patients received a secure, password protected email message through the KP message center or a letter if email was not available. They were given general information about PrEP, as well as information about how to access PrEP at KP, including a direct phone number for self-referral or to obtain additional information. We assessed the proportion of patients linked to PrEP care in the following three months, using Fisher's exact tests to compare those who were and were not linked.

Results: A total of 126 HIV-uninfected patients had a rectal STI (56.4%) or syphilis (43.7%). Of these, 119 (94.4%) were cismale, four (3.2%) were ciswomen, and three (2.4%) were transwomen. The median age was 36 years (interquartile range, 28-52 years); 48 (38.1%) were White, 36 (28.6%) Latino, 18 (14.3%) Asian, 19 (15.1%) African-American, and 5 (4.0%) Other. We sent a one-time secure email to 97 (77.0%) or letter to 29 (23.0%) individuals with information about PrEP and how to access it at KP. Of those sent a secure email, 78 (78.8%) read the message, 12 (12.4%) were linked to PrEP care, and 11 (11.3%) filled a PrEP prescription. Among those sent a secure email, Latinos were more likely to be linked to PrEP care (32.0%) than White (4.8%) or Black (0.0%) individuals (P=0.019), while age, gender, and type of STI were not associated with linkage to PrEP care. No individuals sent letters were linked to PrEP care (p=0.07).

Conclusions: A one-time email to patients with recent STIs was a feasible intervention to increase PrEP uptake in this population at risk for acquiring HIV, particularly among Latinos, while letters did not increase PrEP linkage. The lack of linkage to PrEP care seen for African Americans, however, suggests that emails may be insufficient to overcome barriers to PrEP uptake in some populations. Further studies are urgently needed to evaluate the feasibility and effectiveness of scalable interventions to increase PrEP uptake in high-risk populations.

Abstract title: Natural Disease Presentation and Progression in Nonalcoholic Fatty Liver Disease among Different Gender

Resident's name: Nghiem B. Ha, MD, MAS

Name of program: Internal Medicine, Categorical

Purpose: Nonalcoholic fatty liver disease (NAFLD) is associated with higher risk of liver-related complications and mortality. Data on natural history remains limited, especially among different gender groups. We aim to examine disease presentation and long-term disease progression of NAFLD among different gender.

Methods: Retrospective study of 1,702 consecutive NAFLD patients (919 female and 783 male) seen at a university medical center from 1999-2014. NAFLD was diagnosed by imaging/histological evaluation. Exclusion criteria: viral/drug-induced hepatitis, heavy alcohol use, or inflammatory/genetic liver disease. Advanced fibrosis/cirrhosis was determined by histological/clinical evidence and/or noninvasive fibrosis scoring systems. Advanced disease progression included development of nonalcoholic steatohepatitis (NASH), advanced fibrosis based on noninvasive marker panels, cirrhosis, decompensation, and hepatocellular carcinoma. Noninvasive marker panels include AST to-Platelet ratio, Fibrosis-4 score, and NAFLD Fibrosis Score.

Results: The majority of patients were Caucasian (n=837 or 49%) followed by Asian (n=474 or 28%) and Hispanic (n=391 or 23%). Prevalence of female were higher among Hispanics (68% vs. 32%, p<0.001) and Caucasians (52% vs. 48%, p=0.02), while male were more prevalent in Asians (54% vs. 46%, p<0.001). Females were older (50±15 vs. 46±14 years, p<0.001) with higher BMI (32.5±8.0 vs. 31.3±6.3 kg/m2, p<0.001). More female had diabetes (58% vs. 42%, p=0.02) compared to male; however, similar rates were observed in metabolic syndrome (55% vs. 45%, p=0.32), hypertension (54% vs. 46%, p=0.85), hypercholesterolemia (53% vs. 47%, p=0.60), and coronary artery disease (49% vs. 51%, p=0.12). Advance fibrosis/cirrhosis was more prevalent among female (61% vs. 39%, p=0.045). Median follow-up was 67 (6-274) months. Female and male has similar 12-year cumulative incidence rates of disease progression from simple steatosis to NASH (4.7% vs. 4.4%, p=0.53), advanced fibrosis/cirrhosis (23.6% vs. 19.8%, p=0.45), hepatic decompensation (4.9% vs. 2.7%, p=0.08), and hepatocellular carcinoma (0.7% vs. 0.7%, p=0.84). In multivariate Cox proportional hazard models also inclusive of sex, ethnicity, hypertension, and hypercholesterolemia, older age (HR=1.05, 95%CI=1.04-1.07, p<0.001), higher BMI (HR=1.08, 95%CI=1.05-1.11, p<0.001), and diabetes (HR=2.51, 95%CI=1.68-3.75, p<0.001) were significantly associated with advanced liver disease progression.

Conclusions: Despite differences in initial disease presentation at diagnosis among different genders, natural disease progression from simple steatosis to nonalcoholic steatohepatitis, advanced fibrosis/cirrhosis, hepatic decompensation, and hepatocellular carcinoma were similar among females and males, with increased risk of disease progression among older patients with elevated BMI and diabetes.

Abstract title: Tracing diagnoses trajectories over millions of California inpatients reveals association between schizophrenia and rhabdomyolysis

Resident's name: Matthew J. Kan, MD, PhD

Name of program: Pediatrics

Purpose: In the recent era of "big data," it has been technically feasible to create longitudinal representations of individual health across large data sets, from hospitals to entire countries, but to date there have been few successes using these techniques to identify novel disease associations. Here, we created the first large-scale longitudinal disease network of inpatient admissions in the U.S., creating a "map" of disease progressions and used this network to identify previously unknown disease associations.

Methods: Using the California State Inpatient Database (CA SID) from the Healthcare Cost and Utilization Project (HCUP), we analyzed inpatient admission data collected between 1980 and 2010 from 350 California hospitals representing 10.4 million ethnically diverse individuals. Using principal inpatient diagnoses, we identified temporal correlations between disease pairs and concatenated these correlations using a greedy algorithm to create a network representation of "disease trajectories," from initial hospitalization until death. On reviewing the network through literature review and expert curation, we discovered a previously unappreciated relationship between inpatient admissions for schizophrenia, a psychiatric disorder, and re-admission for rhabdomyolysis, a rare disease of muscle breakdown. We validated this finding using the Amino database, which collects U.S. health insurance claims from over 220 million patients. We further extended this finding by performing a case review of patients at University of California, San Francisco (UCSF) with schizophrenia treated for rhabdomyolysis.

Results: We created a longitudinal representation of disease progressions that maps over 300 common disease trajectories, revealing a previously unknown association between schizophrenia and rhabdomyolysis. 2.6% of inpatients with schizophrenia were found to be hospitalized for rhabdomyolysis, which has a general population incidence of 1 in 10,000. We validated this association is also true among outpatients using the Amino database, which collects U.S. health insurance claims from over 220 million patients, and five years of electronic health records from over 830,000 patients treated at UCSF, demonstrating similar incidences of 2.0-2.4%. A case review of patients with schizophrenia treated for rhabdomyolysis at UCSF between 2011-2018 (n=29) demonstrated that 35% of these cases were due to drug ingestions, 12% were from fractures/falls, but 53% were of idiopathic origins, suggesting there are both preventable risk factors and potential biological predisposition for rhabdomyolysis with underlying schizophrenia.

Conclusions: Through a combination of informatics and expert review, we identified a previously unrecognized association between schizophrenia and rhabdomyolysis. As detailed records (labs, notes) are not available from HCUP, an institutional case review demonstrated both preventable (drug ingestion) and potential biological links between these two diseases, which are avenues for future investigation and improvement of patient care. Together, these findings demonstrate the power of using public disease registries in combination with electronic medical records to discover novel disease associations and explore their etiologies, and inform clinical practice.

Abstract title: Peri-procedural management of patients undergoing liver resection or embolotherapy for neuroendocrine tumor metastases

Resident's name: Daniel H. Kwon, MD

Name of program: Internal Medicine, Categorical

Purpose: To describe the peri-procedural management of patients with well-differentiated neuroendocrine tumors (NETs) with hepatic metastases who underwent liver-directed procedures.

Methods: A retrospective review of clinical data of all consecutive patients with metastatic NETs who underwent liver resection, ablation, or embolotherapy at a single tertiary referral center from 2012-2016 was performed. Primary outcome was occurrence of either carcinoid crisis (CC) identified based on clinical documentation or hemodynamic instability (HDI) defined as ≥10 min of SBP <80 or >180 mmHg or pulse >120 BPM in anesthesia records.

Results: We identified 75 patients who underwent liver resection/ablation (n=38) or embolotherapy (n=37). Twenty-four (32%) patients experienced CC or HDI (CC/HDI); CC occurred in 3 patients. No clinicopathologic or procedural factors, including procedure type, pre-procedural octreotide or long-acting somatostatin analogue use, and history of carcinoid syndrome, were associated with CC/HDI. Forty-two percent of patients who experienced CC/HDI had Clavien-Dindo grade 2-4 complications versus 16% who did not (p<0.05).

Conclusions: A significant portion of patients developed CC/HDI, and these patients were more likely to develop severe post-procedural complications. Peri-procedural octreotide use was not associated with lower CC/HDI occurrence, but continued use is advised given its safety profile until additional studies definitively demonstrate lack of benefit.

Abstract title: Patient Outcomes and Costs after Isolated Flexor Tendon Repairs of the Hand

Resident's name: Gopal R Lalchandani, MD

Name of program: Orthopaedic Surgery

Purpose: While substantial progress has been made in both flexor tendon repair technique and rehabilitation over the past decades, overall treatment of flexor tendon injuries remains a challenge. This study aimed to quantify the reoperation rate after flexor tendon repair and determine the impact of demographics and hand therapy utilization on reoperation rate and costs of care. We hypothesized there would be a correlation between utilization of post-operative therapy and decreased reoperation rate and costs.

Methods: A commercially available database (PearlDiver, Colorado Springs, CO) was utilized to access insurance claims data filed for 20.9 million patients, with 13.1 million patients active for at least 1 year in the US from 2007 to 2015. Patients undergoing primary flexor tendon repair were included and followed for 1 year. Patients with fractures, vascular injuries, or digit replantation were excluded. We studied the reoperation rate, post-operative rehabilitation utilization, and costs. Chi-Square analysis was used to assess effects of rehabilitation utilization on reoperation rate and costs.

Results: The one-year reoperation rate was 11.4 percent at a median time of 100.0 days amongst 1129 patients undergoing primary flexor tendon repair. There was variation in reoperation rate in different age groups, with peaks of highest reoperation in patients aged 30 to 59 (p = 0.008), but there was no difference in reoperation rate between genders. The rate of reoperation in patients who had no post-operative therapy was 5.2%, which was significantly lower than the reoperation rate of patients who received therapy, 12.2% (p = 0.005). Increased number of rehabilitation visits was correlated with a higher reoperation rate (p < 0.001), particularly amongst those who had more than 21 visits in a year. Insurance reimbursement over one year following primary flexor repair was approximately $14,533 per patient, but $27,870 if patients went on to reoperation.

Conclusions: The one-year reoperation rate after primary flexor tendon repair is 11 percent. Higher utilization of therapy was associated with higher reoperation rate, possibly due to patients with worse outcomes being more likely to attend additional therapy and pursue secondary surgery. As expected, there was a much higher cost of care when patients had secondary procedures after flexor tendon repair.

Abstract title: MRI-based stress analyses of abdominal aortic aneurysms with resolved intraluminal thrombus heterogeneity

Resident's name: Joseph Leach, MD, PhD

Name of program: Radiology and Biomedical Imaging

Purpose: Abdominal aortic aneurysms (AAA) are common, and their rupture is often fatal. Much work has focused on assessing rupture risk for individual patients using finite element wall stress estimations incorporating aneurysm features from medical imaging, principally computed tomography (CT). CT cannot resolve the material heterogeneity of the intraluminal thrombus (ILT) common in larger aneurysms, and the disparate stiffnesses of distinct thrombus layers, known from specimen testing, have not been incorporated in a patient-specific fashion. Using a T1-weighted black-blood fast spin echo acquisition as part of an MRI protocol for comprehensive AAA evaluation, we delineate ILT layers in 7 AAA patients and study the effects of explicitly modeling ILT heterogeneity in computational stress analyses.

Methods: Seven AAA patients undergoing MRI surveillance were selected for having significant ILT burden with two distinct layers on T1-weighted black-blood imaging: low signal in thrombus adjacent to the lumen and high signal closer to the vessel wall. Geometric boundaries of different ILT layers were segmented manually from black blood imaging, while CE-MRA and post-contrast VIBE imaging were used to segment the flow lumen and vessel wall, resulting in a set of 3-dimensional surfaces that served as the basis for computational mesh generation. Finite element analysis was performed in three different paradigms of ILT material stiffness distributions: 1) very disparate stiffness between layers; 2) lower disparity, both relatively stiff; and 3) lower disparity, both relatively weak. A fixed-point iterative technique was used to estimate the unloaded geometry of each AAA, with subsequent pressurization to 120 mmHg. Vessel displacements at the inlet and outlets were constrained to be radially oriented. Von Mises stress distributions and spatial maps of rupture potential index were analyzed in different ILT stiffness paradigms, and results compared using the Wilcoxon signed rank test.

Results: In each ILT stiffness paradigm, explicitly modeling ILT heterogeneity as derived from MRI resulted in no significant difference in peak aneurysm wall stress ($p = 0.22$) when compared to models assuming homogeneously stiff ILT. Peak stresses were significantly lower when heterogeneous ILT was considered compared to models with homogeneously weak ILT ($p = 0.016$). Global peak rupture potential index for each case followed a similar trend, although local maxima showed spatially complex patterns of variation between modeling paradigms, tied to the distribution of different ILT layers.

Conclusions: Explicit modeling of ILT heterogeneity is unlikely to significantly change the most important results of AAA finite element stress modeling compared to models assuming homogeneous ILT, so long as the stiffest ILT layer is represented in the model.

Abstract title: Training Healthcare Professionals To Identify and Respond to Victims of Human Trafficking

Resident's name: Stefana Morgan, MD

Name of program: Psychiatry

Purpose: Our goal is to develop, evaluate and disseminate an online module to train health professionals to identify and respond to human trafficking (HT) victims. We aim to evaluate provider knowledge about HT before and after watching the module and plan to assess module efficacy and user-friendliness. The module will be housed on the UCSF website and disseminated throughout the UCSF community.

Methods: We conducted a series of focus groups with a variety of health professionals to do a needs assessment. We curated the online module content using a multidisciplinary team including various medical specialties, legal experts, service providers and technological leads. We are currently working with our technical lead to fit this content in the pre-existing web platform. We piloted the content of the module at the lead author's Senior Talk at the UCSF Department of Psychiatry and collected data on provider knowledge of HT before and after the talk.

Results: By relying on our multidisciplinary team, we came up with consensus learning objectives for the online module. After watching the module, learners should be able to 1) recognize who is vulnerable, 2) use proper interview techniques 3) know about the possible interventions, including rescue, education about rescue, attending to medical and mental health needs and addressing basic shelter, food and safety needs. When we piloted the content of the module during the first author's senior talk, we found that the learners ability to define HT increased from 65% agree or strongly agree prior to the talk to 92% after the talk. We found similar improvements for the learners ability to recognize victims of human trafficking, to find more information about human trafficking, and to make referrals.

Conclusions: The content curated to create an online module to educate health professionals about HT was effective at increasing knowledge during a pilot presentation of the content. The online module has the potential to improve knowledge of HT across UCSF. Next steps include, disseminating the module to providers at the department of psychiatry (residents, nurses, social workers, attending physicians) who will watch the module and evaluate it via Qualtrics.

Abstract title: Methadone Use in Children: Assessment of Cardiotoxicity

Resident's name: Dustin B. Nash, MD

Name of program: Pediatrics

Purpose: Methadone exposure carries the risk of QT prolongation with associated torsade-de-pointes (TdP) and sudden death (SCD) in adults. Recent guidelines regarding screening ECGs exist despite the limited data regarding methadone use and its cardiac effects in children. We hypothesized that Methadone use in children does not result in clinically significant cardiotoxicity.

Methods: A retrospective cohort study was performed from January 2014 to August 2016 at a tertiary children's hospital evaluating measures of cardiotoxicity in all pediatric patients (< 18 yrs) on methadone. Measures of cardiotoxicity analyzed included prolongation of QTc interval, documented TdP, and SCD.

Results: A total of 118 patients (50% male) received methadone with a median age of 1.9 (IQR: 0.2 - 11.5) years and weight of 10.0 (IQR: 4.5 - 37.6) kgs. The primary indications included pain (57%), opioid withdrawal/sedation wean (41%), and opioid addiction (2%). ECGs were obtained prior to treatment in 60% of patients (n=71) with a mean QTc of 423 ± 26 msec and on treatment in 42% of patients (n= 49) with a mean QTc of 426 ± 29 msec (p=.19). The mean change in QTc observed after methadone initiation among patients with baseline and on treatment ECGs (n=35, 30%) was 8 ± 8 msec (421 ± 25 to 429 ± 32 msec, p=0.12). The mean change in QTc observed during treatment among patients with serial ECGs (n=30, 25%) was 24 ± 16 msec (428 ± 32 [first ECG on treatment] to 452 ± 29 msec [max QTc on treatment, p=0.004]). At baseline (n = 71), 23% of patients had an QTc ≥ 450 to 499 msec and 4% with QTc ≥ 500 msec. There was no significant change in risk on treatment stratified by QTc group. There were no arrhythmias or death documented while on therapy.

Conclusions: Methadone was not associated with clinically significant cardiotoxicity in children despite suboptimal ECG compliance to guidelines. Further data and compliance is warranted as a 20-43% of children receiving methadone had baseline or on-treatment QTc prolongation.

Abstract title: Efficacy and cost-effectiveness of Clo-HiDAC for treatment of R/R AML

Resident's name: Sara E. Nunnery, MD

Name of program: Internal Medicine, Categorical

Purpose: There is no standard reinduction regimen for adults with relapsed/refractory acute myeloid leukemia (R/R AML). Clofarabine with high-dose cytarabine (Clo-HiDAC) is commonly used, but limited data exists to support its efficacy. Its cost-effectiveness over other non-clofarabine based regimens is also controversial.

Methods: We performed a single-center, retrospective cohort study evaluating 71 adult patients with R/R AML treated with Clo-HiDAC (cytarabine dose > 1 g/m2 x5 days) between July 2012 and June 2017. The primary outcome was complete remission (CR). Secondary outcomes included overall response rate (ORR; defined as CR + CR with incomplete neutrophil and/or platelet recovery), event free survival (EFS) and overall survival (OS). We analyzed the cost-effectiveness of this regimen based on wholesale drug acquisition costs.

Results: Median age in this cohort was 54 years (range 21-75). Median number of prior lines of therapy was 1 (range 1-5), and 24% had prior allogeneic transplant. The CR rate was 30% and ORR was 42%. In responders, median duration of response was 18.8 months. For the overall cohort, median EFS was 1.4 months, and median OS was 12.2 months. There was no difference in CR, ORR, EFS, or OS by age (<55 vs ≥55 years), primary refractory vs relapsed disease, prior lines of therapy (1 vs >1) or prior allogeneic transplant. Using wholesale drug acquisition costs, the cost per patient of Clo-HiDAC is $25,083 using generic clofarabine and $57,724 using brand name clofarabine for a cost/CR of $83,610 and $192,413 respectively. Cost per patient of non-clofarabine based regimens MEC, FLAG-Ida, and CLAG-M are $924, $2679, and $3,094 respectively. Using CR rates from literature, cost/CR for MEC, FLAG-Ida, CLAG-M, are $1,422-$5,133, $4,252, and $5,838 respectively.

Conclusions: Our analysis found rates of CR and ORR (30% and 42% respectively) to be comparable to prior report. We compared the efficacy (based on literature review), cost per patient and cost per CR of common AML reinduction regimens and found Clo-HiDAC not to be cost-effective. The poor cost effectiveness of Clo-HiDAC may limit its utility to patients who cannot receive anthracycline. Future work will include a retrospective review of patients receiving anthracycline-based reinduction at our institution.

Abstract title: Feasibility of detecting RNA expression in human vitreous

Resident's name: Michelle Y. Peng, MD

Name of program: Ophthalmology

Purpose: Vitreoretinal conditions are often due to a complex interplay of risk factors and molecular events which have not been well elucidated.

Methods: We aim to qualitatively identify known markers for diabetes: vascular endothelial growth factor (VEGF), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1) in human vitreous specimen from patients at UCSF and San Francisco General Hospital. RNA extraction, reverse transcription, and quantitative polymerase chain reaction (QPCR) for VEGF, IL-6, and MCP-1 were performed.

Results: Five vitreous specimens from proliferative diabetic retinopathy (PDR) patients and 10 with vitreous opacities (VO) or epiretinal membrane (ERM) were analyzed. RNA expression of VEGF, IL-6, MCP-1 was higher in eyes with PDR in comparison with VO and ERM.

Conclusions: This is the first reported study of RNA isolation from human vitreous samples. Qualitatively, we demonstrate increased expression of genes known to play a part in pathogenesis of patients with PDR.

Abstract title: Health Status of Refugee, US-Born and Immigrant Patients, ZSFG Family Health Center

Resident's name: Eva Raphael, MD, MPH

Name of program: Family and Community Medicine

Purpose: The purpose of this study is to elucidate disease burden in refugee, immigrant and US-born patients at the Family Health Center at ZSFG. About 85,000 refugees came to the US in 2016. Although they compulsorily go through medical screens, little is known about disease burden in this population compared to US-born patients.

Methods: This is a retrospective cohort study of refugee, immigrant and US-born patients seen at the FHC over 3 years (2014-2017). Demographic characteristics and presence of selected chronic diseases, infectious diseases, and mental health disorders were abstracted from patient medical records.

Results: We examined records of 308 refugees, 242 immigrants, and 135 US-born patients seen at the FHC. The mean age for refugee patients was 35, immigrant patients 47 and US-born patients 38 years. There were 85 (62%) women in the US-born group, compared to 142 (60%) women in the immigrant group, and 164 (53%) women in the refugee group. In the refugee group, 83 (26%) were from China, 40 (12%) from El Salvador, 29 (9%) from Guatemala, and 18 (6%) from Honduras, country of origin was unknown for 3 (1%) patients. In the immigrant group, 29 (12%) were from Mexico, 24 (10%) from Guatemala, 23 (9%) from El Salvador and 21 (9%) from China, country of origin was unknown in 67 (28%) patients. Diabetes was present in 52 (21%) immigrant patients and 21 (15%) US-born patients, whereas only 13 (4%) refugee patients had diabetes ($p<0.05$). Seventy-eight (32%) immigrant patients and 42 (31%) US-born patients had hypertension compared to 20 (6%) refugee patients ($p<0.05$). Refugee patients and US-born patients had similar prevalence of HIV with 5 (1%) and 3 (2%) in each group, respectively. Eighteen (7%) immigrant patients had tuberculosis, compared to 1 (0.3%) of refugee patients and 3 (2%) US-born patients ($p<0.05$). Depression was present in 33 (24%) US-born patients, 56 (23%) immigrant patients and 49 (16%) refugee patients. Post-traumatic stress disorder was present in 41 (13%) refugee patients, 8 (3%) immigrant patients and 3 (2%) US-born patients ($p<0.05$). In US-born patients, 21 (15%) smoked and 12 (9%) had substance use disorders, compared to 17 (7%) and 3 (1%) immigrant patients and 26 (8%) and 2 (0.6%) refugee patients, respectively. Alcohol use was present in 9 (6%) US-born patients, 15 (6%) immigrant patients and 7 (2%) refugee patients.

Conclusions: Preliminary results show different disease burden between refugees, immigrants and US-born patients. The refugee patient population at the FHC, despite being younger and having less chronic diseases, is just as affected by infectious diseases and mental health disorders than immigrant and US-born patients. These results highlight a need for further research on disease burden in refugees and the need to appropriately focus resources for the different patient groups at the FHC.

Abstract title: Pregnancy attitudes and intentions among first-time offending youth

Resident's name: Brooke Rosen, MD

Name of program: Psychiatry

Purpose: Adolescent pregnancy has significant long-term socioeconomic, developmental, and physical and mental health consequences for teenage parents as well as their offspring. Substantial racial/ethnic and geographic disparities in adolescent pregnancy mirror those of youth involvement in the juvenile justice system. Furthermore, children of teen parents are more likely to be incarcerated during adolescence and are at higher risk of teen pregnancy themselves, thus perpetuating intergenerational cycles of incarceration, early childbearing, and poverty. With rates of teen pregnancy in juvenile detention reaching up to 30%, this system presents a critical opportunity for interrupting these cycles. However, literature on this topic remains limited and exclusively focuses on detained youth, even though up to 80% of justice-involved youth are non-incarcerated. Therefore, the aims of this study are three-fold: 1) Characterize pregnancy attitudes and intentions (PAI) in a sample of first-time offending, court-involved, non-incarcerated (FTO-CINI) youth; 2) Examine the relationship between PAI and high-risk sexual behaviors; and 3) Identify associations between psychiatric symptoms and PAI in FTO-CINI youth.

Methods: Data are from an observational cohort of 423 FTO-CINI youth, recruited from a large Family Court in the Northeast and followed over a period of 24 months to examine trajectories of substance use, HIV/STI risk behavior, psychiatric symptoms and recidivism. The current study uses youth baseline self-report data (collected using Audio Computerized Assisted Self-Interview (ACASI) software) from the following measures: Pregnancy Attitudes and Intentions scale, the AIDS Risk Behavior Assessment (sexual risk behavior), and the Behavior Assessment System for Children-2 (psychiatric symptoms).

Results: Data presented here address Aim 1 (analysis for Aims 2 and 3 remains ongoing). This sample includes 187 girls and 218 boys, with a mean age of 14.6 (±1.5) years. Of these youth, 34% of males and 27% of females reported some degree of "pregnancy intention" (defined as either likelihood of or plans for pregnancy) within the next four months. While the vast majority (>88%) reported no plans for pregnancy, one-third of sample reported potential likelihood of pregnancy. On a Likert scale (1 to 5), both female and male teens rated their overall pregnancy intentions as very low (M = 1.31, SD 0.57). Comparatively, overall attitudes toward pregnancy differed as a function of gender, with male youth endorsing more positive attitudes toward pregnancy (M = 2.10, SD = 1.08) than their female counterparts (M = 1.72, SD = 1.00); t(399) = 3.65, p < 0.0005.

Conclusions: At least one-third of first-time offending youth endorse some likelihood of pregnancy within the next four months, with males endorsing more positive attitudes toward pregnancy than females. These initial findings indicate a critical opportunity for pregnancy screening, education, and counseling at first contact with the system. Ongoing analyses will further examine the relationships between pregnancy attitudes and intentions and high-risk sexual behaviors and psychiatric symptoms.

Abstract title: Metabolic Acidosis Resolution in Premature Neonates

Resident's name: Nicholas P. Satariano, MD

Name of program: Orthopaedic Surgery

Purpose: Distal radius fractures in the elderly present an increasingly common burden on the healthcare system. While recent studies have suggested that non-operative management yields functional results equivalent to operative treatment, malunion remains an appreciable complication of conservative therapy, with controversy as to whether it is associated with higher rates of disability or need for a subsequent procedure. Currently, the true incidence of distal radius malunion in the elderly requiring corrective surgery is unknown. We hypothesized that although the majority of elderly patients with distal radius fractures could be successfully managed non-operatively, there would be a significant cohort of patients requiring additional wrist surgery within a 2 year follow-up period.

Methods: A commercially available database (PearlDiver, Colorado Springs, CO) was utilized to access insurance claims data for 2.3 million patients in the Medicare 5% sample. ICD-9 and CPT codes were employed to select patients aged 65 and older undergoing non-operative treatment of distal radius fractures with a minimum 2 year follow-up. Rates of subsequent wrist surgery were determined. Chi square test and multivariate regression analysis were used to determine the relationship between subsequent corrective surgery and patient age, gender, and geographic region.

Results: 11,203 patients with nonoperatively treated distal radius fractures with a mean age of approximately 78 years were included. Over a 2-year follow-up, 91 patients (0.8%), underwent subsequent wrist surgery at a median time of 167 days (5.4 months) post-injury. There was a significantly higher rate of subsequent wrist surgery amongst patients aged 65 to 69 years old, with a reoperation rate of 1.5% ($p < 0.001$). There was no significant difference in the incidence of corrective procedures between gender or region in the U.S. When patients did undergo corrective procedure, 43% had a nonunion repair, while 57% had a variety of other procedures including osteotomy, external fixation, open reduction internal fixation, and arthrodesis.

Conclusions: The aim of this study was to determine the percentage of elderly patients that require subsequent corrective wrist surgery after the initial non-operative treatment of a distal radius fracture. The results demonstrate that within 2 years of conservative management, only a small percentage (0.8%) undergo corrective wrist surgery, and that this specific population includes significantly more patients aged 65 to 69 years old (1.5%). The data supports nonoperative management in a large majority of elderly patients, however a small subset of patients remain at risk for requiring additional surgery. Further research should aim to identify risk factors, including radiographic markers, predictive of need for reoperation in the younger cohort.

Abstract title: Mitral Annular Peak Systolic and Diastolic Velocities are Characteristic of Healthy Hearts: A Doppler Tissue Imaging Study

Resident's name: Timothy F. Simpson, MD, PharmD

Name of program: Internal Medicine, Categorical

Purpose: As systolic and diastolic dysfunction frequently coexist but are assessed in isolation, a simple and reproducible quantitative measurement of combined systolic and diastolic function is desirable. We hypothesize that the absolute sum of lateral mitral annular systolic and early diastolic peak velocities are predictive of overall cardiac function.

Methods: Lateral mitral annular systolic (S') and early diastolic (E') peak velocities were measured in healthy subjects collected from the prospectively enrolled Health eHeart Study, and compared to subjects with progressive degrees of systolic and diastolic dysfunction sequentially selected from the University of California, San Francisco clinical echocardiography database using keyword searches. Exclusion criteria included age greater than 75 or less than 30 years, severe mitral pathology (regurgitation, prolapse, or calcification) and non-sinus rhythm. Myocardial velocities were measured using standard pulse-wave Doppler technique, and S' and E' measured from the lateral mitral annulus in all subjects in isolation from other measurements and thus generally blinded to the remainder of the echocardiogram. To assign a quantitative expression of global cardiac function, we applied an integer value of 0-3 points to progressively severe systolic and diastolic dysfunction using standard guideline definitions. A receiver operating characteristic (ROC) curve was constructed for the absolute S' + E' values, and the area under the ROC curve was calculated as a measure of the discriminative ability of the model to identify normal compared with abnormal function.

Results: A total of 149 subjects (56% male, mean age 48 years) were enrolled and stratified according to global cardiac function; 76 normal, 40 mild-moderate dysfunction, and 33 moderate-severe dysfunction. Subjects with a S' + E' score < 20 cm/s were more likely to be older, hypertensive, and diabetic than those with score > 20 cm/s. Adjusting for baseline differences, univariate analysis showed mean S'+ E' values were significantly different between subjects with normal, mild-moderate, and moderate-severe global cardiac function (27 cm/s, 17 cm/s, 13 cm/s; p< 0.001 for all comparisons). Overall there was a strong correlation between S' + E' scores and global cardiac function (R = -0.75). The absolute sum of S'+ E' ≥ 20 cm/s identified normal global cardiac function with a sensitivity of 95%, specificity of 85%, and ROC area under the curve of 0.924.

Conclusions: In a cohort of subjects with varying levels of combined systolic and diastolic function, we report the novel finding that the easily obtained, combined sum of absolute S' + E' peak velocities is highly discriminatory among degrees of global cardiac function. Additional studies should be considered for validation in additional populations.

Abstract title: Leveraging School-Based Food Pantries to Promote Health

Resident's name: Emma Steinberg, MD

Name of program: Pediatrics

Purpose: While food assistance programs attempt to provide nutritious food to families many families lack the skills to use these foods to prepare healthy and appealing meals. In our recent needs assessment, school-based pantry users indicated a need for support and resources to eat more healthfully. Therefore, this project aims to fill this gap by piloting a healthy cooking and nutrition curriculum for school-based food pantries. The objectives are to:

1) Develop a curriculum for school-based food pantries that is evidence-based, culturally appropriate, and economically relevant.

2) Test the feasibility and acceptability of the curriculum with school-based food pantries users.

Methods: Our pilot will include a modified version of a validated 6-week community-based healthy cooking and nutrition curriculum augmented by the use of a smartphone application designed for food pantry patrons. The curriculum will be modified by a dually trained chef/MD to better incorporate nutrition principles, recipes, and meal planning strategies that are directly relevant to school-based food pantry users. Pre- and post-session surveys as well as interviews with participants will be used to evaluate the impact of the pilot on fruit and vegetable consumption, healthy food preparation skills, food literacy, and food insecurity. Participant feedback from the initial six weekly sessions will drive frequency and content of subsequent classes, which will be led by community members.

Results: Expected results of this pilot curriculum planned for Summer 2018 include:

- Eight to ten participants per session
- Participants will attend at least four of the initial six weekly sessions
- Increased fruit and vegetable consumption
- Increased confidence in healthy food preparation and management
- Improved food literacy
- Reduced food insecurity

Conclusions: We believe that our approach will lead to the development of an effective, culturally appropriate, and economically relevant curriculum that fills a known community need. If this project is successful, we believe it could lead to more widespread use of school-based food pantries as an access point not only for nutrition counseling but also for other public health interventions to promote health.

Abstract title: Association of image-defined risk factors with clinical features, histopathology, and outcomes in neuroblastoma

Resident's name: William C. Temple, MD

Name of program: Pediatrics

Purpose:

Clinical and histopathologic features guide treatment for neuroblastoma, but obtaining tumor tissue may cause complications and is subject to potential sampling error due to tumor heterogeneity. The association of specific imaging characteristics of neuroblastoma with clinical features, histopathology, and outcomes is unclear.

Methods: We performed a retrospective cohort study of patients with neuroblastoma or ganglioneuroblastoma enrolled on the Children's Oncology Group biology study (ANBL00B1) between 2000-2015 at UCSF Benioff Children's Hospitals in San Francisco and Oakland. Data collected included clinical features (age, stage, primary tumor site, surgical complications); histopathology (MYCN status, ploidy, mitosis-karyorrhexis index [MKI]); detailed radiographic review of diagnostic CT scans for image-defined risk factors (IDRFs); and event-free survival (EFS). IDRFs were evaluated in five separate binary variable categories: extension within multiple body compartments, vascular encasement, airway compression, infiltration of adjacent organs/structures, and intraspinal extension.

Results: Our analytic cohort included 68 patients. Fifty-three patients (78%) had tumors with IDRFs. Of the clinical and surgical variables, tumors with IDRFs compared to tumors without IDRFs are associated with INSS stage 4 disease (43% vs. 13%, p=0.033), abdominal/retroperitoneal primary tumor location (73% vs. 43%, p=0.038), and the presence of surgical complications (59% vs. 0%, p=0.001). When analyzing histopathologic features, the presence of IDRFs compared to the absence of IDRFs is associated with MYCN amplification (28% vs. 0%, p=0.031) and undifferentiated/poorly differentiated grade (94% vs. 73%, p=0.026) Using backward elimination regression, individual IDRFs correlated with clinical, surgical, and histopathologic variables. The presence of the IDRF vascular encasement correlates with surgical complications (95% CI, 0.131 – 0.523, p=0.002), undifferentiated/poorly differentiated grade (95% CI, 0.291 – 0.915, p=< 0.001), and possibly INSS stage 4 disease (95% CI, - 0.001 – 0.401, p=0.051). The presence of the IDRF organ infiltration is associated with MYCN amplification (95% CI, 0.203 – 0.611, p=< 0.001) and high MKI (95 % CI, 0.148 – 0.629, p=0.002). The 10-year EFS was 66.7% (95% CI, 49.9 – 79.0) in patients with IDRFs compared to a 10-year EFS of 85.7% (95% CI, 53.9 - 96.2) in patients without IDRFs (p=0.23).

Conclusions: The presence of the IDRF vascular encasement correlates with surgical complications (95% CI, 0.131 – 0.523, p=0.002), undifferentiated/poorly differentiated grade (95% CI, 0.291 – 0.915, p=< 0.001), and possibly INSS stage 4 disease (95% CI, - 0.001 – 0.401, p=0.051). The presence of the IDRF organ infiltration is associated with MYCN amplification (95% CI, 0.203 – 0.611, p=< 0.001) and high MKI (95 % CI, 0.148 – 0.629, p=0.002). The 10-year EFS was 66.7% (95% CI, 49.9 – 79.0) in patients with IDRFs compared to a 10-year EFS of 85.7% (95% CI, 53.9 - 96.2) in patients without IDRFs (p=0.23).

Abstract title: Enrichment of diabetogenic T cells in vivo using implantable scaffolds

Resident's name: Martin A. Thelin, MD, PhD

Name of program: Pediatrics

Purpose: Type 1 diabetes (T1D) is the most common chronic autoimmune disease in children and its prevalence is increasing globally. When a child is diagnosed with T1D, the immune system has already eradicated a great number of the insulin producing cells and subsequently a life-long insulin replacement therapy is required. T cells are known to play an essential role in the development of T1D both in humans and non-obese diabetic (NOD) mice. A major roadblock in the study of T1D is that the T cells that promote T1D, while abundant in the pancreas, are exceedingly rare in the blood. Currently, there is no efficient way of capturing T cells during the development of T1D without removing the pancreas. In order to enable the study of rare β-cell specific T cells, we developed an implantable scaffold to enrich for diabetogenic T cells.

Methods: To determine whether scaffolds recruit populations of T cells that are similar to the T cell populations found in the pancreas, we loaded the scaffolds with beta cell lysates and implanted them subcutaneously onto the backs NOD mice. After 2 weeks, the scaffolds were harvested and autoimmune T cells were analyzed.

Results: We found that antigen-specific T cells become enriched within scaffolds containing their cognate antigens. These T cells induced diabetes after adoptive transfer, indicating their pathogenicity. Furthermore, T-cell receptor (TCR) sequencing identified many expanded TCRs within the β-cell scaffolds that were also expanded within the pancreata of NOD mice.

Conclusions: These data demonstrate the utility of biomaterial scaffolds loaded with disease-specific antigens to identify and study rare, therapeutically important T cells.

Abstract title: Advance care planning documentation practices and accessibility in the electronic health record

Resident's name: Evan J. Walker, MD

Name of program: Internal Medicine, Categorical

Purpose: Documenting patients' advance care planning (ACP) wishes is essential to providing value aligned care, as is having this documentation readily accessible. Little is known about current ACP documentation practices. In this cross-sectional study, we describe ACP documentation practices and accessibility of documented ACP discussions in the electronic health record (EHR).

Methods: Participants were recruited from outpatient clinics at the San Francisco VA, were ≥60 years old, with ≥2 chronic/serious conditions and ≥2 primary care visits in the past year. ACP documentation was abstracted from the EHR in 2013-2015 and included any prior legal forms/orders and ACP discussions documented within the prior five years. Frequency and type of ACP documentation was calculated using percentages and means. For discussions, author discipline and location of documentation was determined. Discussions were deemed "accessible" if documented in a designated ACP posting location or "not easily accessible" if recorded as free text in progress notes.

Results: The mean age of 414 participants was 71 years (SD ± 8), 9% were women, 43% were non-white, and 51% had documented ACP including 149 (36%) with ACP forms and 138 (33%) with ACP discussions. Seventy-five (54%) discussions were documented by social workers and 48 (35%) by primary care providers. However, 76 (55%) discussions were not easily accessible. For 27 (18%) participants with advance directives, subsequent discussions documented a change in treatment preferences. Nineteen (70%) discussions reporting a change in wishes were not easily accessible.

Conclusions: Half of chronically ill, older patients had documented ACP wishes, including a third with documented ACP discussions. Most discussions were documented by social workers and were not easily accessible, although discussions often represented changes from prior advance directives. Clinician education and EHR changes to ensure documented discussions are accessible are important patient-safety and quality improvement targets to ensure patients' wishes are honored.

Abstract title: Predictors of Radiation Therapy Incompletion among Esophageal Cancer Patients in Tanzania

Resident's name: Melody Xu, MS, MD

Name of program: Radiation Oncology

Purpose: East Africa hosts a disproportionately high incidence of esophageal cancer. In Tanzania, radiation therapy (RT) is routinely offered for definitive and palliative therapy. However, many patients do not complete RT or expire shortly afterward. This study aims to characterize RT treatment patterns in Tanzania and identify predictive factors for RT incompletion.

Methods: A retrospective chart abstraction was performed for esophageal cancer patients treated with RT at a national referral cancer center in Tanzania from 2011-2013. Definitive intent was defined as RT prescriptions with at least 20 fractions with concurrent chemotherapy; other fractionation regimens were considered palliative. Wilcoxon rank-sum tests, Chi-squared tests, and logistic regression models were utilized to identify factors associated with palliative or definitive RT incompletion.

Results: A total of 300 patients (202 male and 98 female) were identified with median age of 60 years (interquartile range, IQR 48-70). Nearly 100% (299 of 300) reported dysphagia to solids and 54% reported dysphagia to liquids (155 of 288). The median duration of symptoms prior to presentation was 4 months (IQR 2-6) and the median time from diagnosis to RT was 1.2 months (IQR 0.8-1.9). Overall, 23% were unable to complete RT due to death or clinical decompensation. Palliative treatment was given to 149 patients and 26% did not complete RT; definitive treatment was given to 151 patients and 20% did not complete RT (p=0.24). Patients younger than 60 years were less likely to complete palliative RT (Odds Ratio [OR] 2.4, p=0.02). Tobacco use (OR 2.7, p=0.04) and RT initiation within 30 days of diagnosis (OR 3.5, p=0.004) were associated with incomplete definitive RT.

Conclusions: In Tanzania, approximately 23% of patients expire or decompensate prior to completing esophageal RT. Patients younger than 60 years were less likely to complete palliative RT. Tobacco use and RT initiation within 30 days of diagnosis was associated with definitive treatment incompletion, perhaps reflecting differences in cancer biology or pace of disease. Further understanding of how these factors contribute to RT incompletion may inform supportive care resource allocation and patient selection for esophageal RT in Tanzania and similar resource-limited settings.

NOTES