35th Annual Research Forum

Friday, April 28, 2017
8:00am to 9:30am
208 Light Hall

Established and Sponsored by the Vanderbilt University House Staff Advisory Council

VANDERBILT UNIVERSITY

MEDICAL CENTER

Vanderbilt University Medical Center's Research Forum provides an opportunity for non-faculty VUMC personnel to present research conducted at Vanderbilt. This Forum is open to all Vanderbilt University House Staff and Medical Students.

Research must have been performed at Vanderbilt. Unpublished work is eligible and encouraged. Work already published, or presented at another meeting, is also eligible and encouraged. All submitted abstracts are published in the Vanderbilt University Medical Center Research Forum book.

Abstracts are reviewed and selected for either an oral or a poster presentation by a panel of Vanderbilt School of Medicine faculty members who are actively involved in clinical and basic science research. The top three abstracts will be selected for oral presentation. The oral presentations will be judged by non-scientifically/non-medically trained professionals and will be judged grossly on the ability to effectively communicate to a lay audience. Following the oral presentations at the Forum, the best overall project will be awarded an Elliot V. Newman Award.

The Grant W Liddle Award, which honors a faculty member who demonstrates exemplary leadership in the promotion of scientific research at Vanderbilt University Medical Center, is presented annually at the Forum.

THIRTY-FIFTH ANNUAL RESEARCH FORUM

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Department of Medicine—Division of Pulmonary and Critical Care

GRANT W. LIDDLE AWARD

The Grant W. Liddle Award was established in 1983 by the Vanderbilt University Medical Center house staff to recognize faculty members who demonstrate exemplary leadership in the promotion of scientific research at the Vanderbilt University Medical Center.

A native of American Folk, Utah, Dr. Liddle graduated first in his class from the University of Utah in 1943. After obtaining an M.D. degree from the University of California, San Francisco, in 1948, he served as a post-doctoral fellow at the newly formed Metabolic Research Unit at the NIH. In 1956, Dr. Liddle was recruited by Dr. Hugh J. Morgan to become Director of Endocrinology at Vanderbilt University. He was named Chairman of the Department of Medicine in 1968, a position he held until 1983.

Dr. Liddle's career was marked by commitment to excellence in research, patient care, and the teaching of house staff and medical students. His research accomplishments include developing the dexamethasone suppression test and metyrapone test for assessing pituitary-adrenal gland function; describing a new form of hypertension, pseudohypoaldosteronism (Liddle's Syndrome); developing spironolactones as useful aldosterone antagonists; and systematically improving methods for treating Cushing's disease. In 1982, he was elected to the National Academy of Sciences and to the Royal College of Physicians in England.

Past Recipients of the Grant W. Liddle Award are:

2017	Donald H. Arnold, MD MPH
2016	Michael F. Vaezi. MD, PhD, MS
2015	Keith T. Wilson, MD, AGAF
2014	Jonathan G. Schoenecker, MD, PhD
2013	Terence S. Dermody, M.D.
2012	Russell Rothman, M.D., MPP
2011	Alfred L. George, Jr., M.D.
2010	Harold L. Moses, M.D.
2009	D. Brent Polk, M.D.
2008	Dennis Hallahan, M.D.
2007	Nancy J. Brown, M.D.
2006	Adrian Jarquin-Valdivia, M.D., R.D.M.S.
2005	Marshall L Summar, M.D.
2004	Denis M. O'Day, M.D.
2003	Herbert S. Schwartz, M.D.
2002	John A. Zic, M.D.
2001	Kathryn M. Edwards, M.D.
2000	R. Michael Rodriguez, M.D.
1999	David H. Van Buren, M.D.
1998	Charles Wright Pinson, M.D., M.B.A.
1997	Steven Leach, M.D.
1996	Jason D. Morrow, M.D.
1995	Robert H. Ossoff, M.D., Ph.D.
1994	William O. Richards, M.D.
1993	Barney S. Graham, M.D.
1992	Gordon Bernard, M.D.
1991	Achilles Demetrious, M.D., Ph.D.
1990	David Robertson, M.D.
1989	Robert Collins, M.D.
1988	Stanley Cohen, Ph.D.

THE ELLIOT V. NEWMAN PRIZE

Elliot Voss Newman was a distinguished cardiologist, scientist, medical scholar and teacher. A graduate of Harvard College and Medical School, Dr. Newman came to Vanderbilt from Johns Hopkins University in 1952 to establish a program of clinical physiology and research. The author of the electrocardiography chapter in Harrison's Textbook of Medicine and of the renal physiology chapter in Cecil and Loeb's textbook, Dr. Newman was a pioneer in the development of medical engineering and the use of applied mathematics and computer science for clinical problems. Dr. Newman was the first Joe and Morris Werthan Professor of Experimental Medicine at Vanderbilt and was founder of the Clinical Research Center, which bears his name. He was a friend and mentor to medical students and house officers alike and helped to promote the scientific careers of many.

Recent Elliot V. Newman Award recipients:

2016

Brian T. Craig, MD— Resident, General Surgery "Induced Differentiation Inhibits Sphere Formation in Neuroblastoma"

2015

Paul Whiting, MD—*BMI as a predictor of perioperative complications following Orthopaedic Trauma Surgery: An ACS-NSQIP analysis.*

2014

Emily Zern, B.A., VMS III - *B cell responses to HIV antigen are a potent correlate of viremia in HIV-1 infection and improve with PD-1 blockade*

Ciara M. Shaver, M.D., Ph.D. – *New-onset atrial fibrillation is independently associated with increased mortality in critically ill patients*

2013

Bobak Parang, B.A.— VMS II, *BVES Suppresses Inflammatory Carcinogenesis*

Young Min Lee, B.S.P.H.— VMS III, *Recovery from Sports-Related Concussion: Days to Return To Neurocognitive Baseline in Adolescents vs. Young Adults*

2012

Jonathan Kropski, M.D.– Clinical Fellow, Allergy, Pulmonary & Critical Care Medicine
"*Murine Herpesvirus-68 Infection Exacerbates Endoplasmic-reticulum Stress in Alveolar Epithelial Cells and Acts As a "second-hit" in the Development of Lung Fibrosis"*

Patrick C. Drayna, M.D. – "*Ketamine Sedation is not Associated with Clinically Meaningful Elevation of Intraocular Pressure"*

2011

Stephen Tourjee, B.A. - *The Impact of Nerve Blocks on Opioid Use and Hospital Length of Stay in Patients with Traumatic Lower-Extremity Injury"*

Yong I. Cha, M.D., Ph.D. - "*Sensitivity of HPV (+) Oropharyngeal Head and Neck Cancers to Poly (ADP-ribose) Polymerase, PARP, Inhibition, Due to Defective DNA Damage Response"*

2010

Daniel J. Moore, M.D., Ph.D. - Clinical Fellow, Pediatrics and Microbiology & Immunology
"*Targeting the Nuclear Import Shuttle Resolves Insulitis and Arrests Type 1 Diabetes"*

Joyce P. Granger, M.D. - "*Reliability of End Tidal CO2 Monitoring in Acute Pediatric Asthmatic Attack"*

2009

James M. Dies, M.D. - *"Parental Knowledge and Use of Preventive Asthma Care Measures"*

THIRTY-FIFTH ANNUAL
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8:00 **WELCOME**……Rebecca Swan, MD

INTRODUCTION OF FORUM MODERATOR……. …Nichelle Winters, MD, PhD

FORUM MODERATOR…….……Michael F. Vaezi, MD, PhD, MS

8:05 **Systolic Blood Pressure within 24 Hours After Thrombectomy for Acute Ischemic Stroke Correlates with Outcome**
Akshitkumar Mistry, Eva Mistry, Michael Froehler, Rohan Chitale, Robert James, Matthew Fusco, John Volpi

8:25 **Alterations in intestinal sulfur assimilation metabolism regulate iron homeostasis**
Andrew Hale, Benjamin Hudson, Ryan Irving, John York

8:45 **Enhanced recovery after surgery in microvascular autologous tissue-based breast reconstruction: Should it become the standard of care?**
Christodoulos Kaoutzanis, Nishant Ganesh Kumar, Dillon O'Neill, Blair Wormer, Kent Higdon

9:05 **Excuse Judges for Deliberation**……. …Michael F. Vaezi, MD, PhD, MS

9:10 **Poster Presentation Awards**……Nichelle I. Winters, MD, PhD

9:15 **Grant W. Liddle Award**…….....J.P. Arroyo, MD, PhD.
Donald H. Arnold, MD, FAAP, MPH ***(Award Winner)***

9:20 **Elliot V. Newman Awards**……..……...…….Michael F. Vaezi, MD, PhD, MS

2017 ORAL PRESENTERS

(Alphabetically by presenter's last name)

ANDREW HALE
Medical Student
Medical Scientist Training Program

AKSHITKUMAR MISTRY, MD
Resident
Department of Neurosurgery

DILLON O'NEILL
Medical Student
VMS3

BASIC SCIENCE RESEARCH ABSTRACTS

2017 Basic Science Research Abstracts

Page #:

Inhibition of Endothelial Nitric Oxide Synthase Modulates Inflammatory Signaling in Human Endothelial Cells

Eric Mace, Stephen Koch, Ryan Stark

OBJECTIVES:
Severe infections induce significant vascular inflammation that is a major cause of morbidity and mortality in the ICU setting. One such mechanism of vascular inflammation is via toll-like receptor (TLR) activation, which leads to widespread inflammation, vasodilation, and organ failure. Nitric oxide (NO), produced by endothelial (eNOS) nitric oxide synthase, has been postulated to play an important role in the propagation of the inflammatory reaction. The aim of this study was to elucidate the effect of eNOS on TLR4 signaling and evaluate its role in infection-mediated vascular dysfunction.

METHODS:
Pooled human microvascular endothelial cells (HMVECs) were plated at a concentration of 30,000 cells/well and exposed to either control (scrambled) siRNA or eNOS siRNA for 16 hours, Afterwards, the media was replaced with complete media (5% FBS) for an additional 56 hours. Cells were then exposed to LPS (100ng/mL), Poly I:C (10mg/mL), or vehicle controls (media). After a 16 hour exposure, supernatants were then collected and IL-6 and IP-10 levels were measured via ELISA.

RESULTS:
HMVECs that had reduced eNOS expression produced significantly greater amounts of IL-6 in response to both LPS and Poly I:C. Endothelial cells exposed to LPS in the control siRNA group produced a mean IL-6 of 1853pg/mL ± 90.69 whereas those in the eNOS siRNA group produced 4356pg/mL ± 360.8 ($n=4$ per group, $p<0.05$). Likewise, in HMVECs exposed to Poly I:C, the control siRNA group produced a mean IL-6 concentration of 965.3pg/mL ± 139.5, while the eNOS siRNA group produced 2075pg/mL ± 152.9 ($n=4$ per group, $p<0.05$). In the control siRNA group, Poly I:C produced 5222pg/mL ± 489.9 vs. 9974pg/mL ± 1475 in the eNOS siRNA group ($n=4$ per group, $p<0.05$).

CONCLUSIONS:
These results suggest that inhibition of endothelial nitric oxide signaling results in increased TLR-mediated inflammation in human endothelial cells. This finding has important implications for understanding the pathogenesis of severe infections and the associated vascular dysfunction.

Toll like receptor 4 contributes to drug reward behavior and synaptic physiology

Daniel T. Kashima, Brad A. Grueter

OBJECTIVES:
Substance use disorders remain as significant problems in society. Drugs of abuse alter excitatory synapses within the nucleus accumbens (NAc) suggesting a role in dependence/addiction. The NAc is primarily made up of medium spiny neurons (MSN) expressing either D1 or D2 dopamine receptors. These cells differentially modulate reward behavior.
Neuron-mediated regulation of excitatory synapses within the NAc are well-studied. Evidence also suggests that the brain's innate immune system shapes motivated behavior. Specifically, toll-like receptor 4 (TLR4), a pattern-recognition molecule of the innate immune system, has been implicated in drug-reward learning. Despite these observations, mechanistic examination of how the innate immune system contributes to NAc synaptic physiology in relation to drug-reward behavior has not been pursued. We tested the hypothesis that cocaine experience remodels excitatory synapses within the NAc in a TLR4-dependent manner.

METHODS:
We used a combination of behavioral and *ex vivo* slice electrophysiology assays on wild type (WT), TLR4 knockout (TLR4.KO), and microglial TLR4.KO (mTLR4.KO) mice. We performed cocaine-induced locomotor sensitization and conditioned place preference (CPP) assays to test drug reward learning. Open field and novel object recognition tests were used to control for basal locomotor activity, anxiety, and working memory.
To examine synaptic function, we performed cell-type specific voltage-clamp recordings from NAc MSNs in WT and TLR4.KO mice under naïve and cocaine-treated conditions.

RESULTS:
TLR4.KO animals exhibit significant attenuations in cocaine reward learning. Importantly, there were no differences in basal locomotor activity, anxiety, or working memory. mTLR4.KO animals exhibit a deficit in acquisition of cocaine locomotor sensitization.
Slice electrophysiology revealed weaker synaptic strength in TLR4.KO animals in both D1 and D2 MSNs. Additionally, we found altered synaptic strength on D2 MSNs in TLR4.KO mice following drug experience.

CONCLUSIONS:
Alterations of the reward system are a characteristic of many neuropsychiatric conditions including substance use disorders. Despite their high prevalence and cost, effective treatments are lacking in part due to an incomplete understanding of the underlying pathology. Using behavioral assays and transgenic animal models, we found that TLR4 participates in drug reward behavior and shaping of NAc physiology. Future experiments will determine signaling mechanisms which may uncover novel therapeutic targets to mitigate neuropsychiatric conditions.

Effect of Interleukin-12 of T cell Receptor Repertoire Diversity

Chinonso Opara, Mark Pilkinton, Louise Barnett, Greg Wilson, Spyros Kalams

INTRODUCTION:

HIV rapidly adapts to immune pressures exerted by CD4+ and CD8+ T cells. There are potentially more than 107 different T-cell receptors (TCRs) in an individual. An HIV vaccine that exploits this diverse potential may be more likely to prevent infection.

In HIV Vaccine Trials Network (HVTN) 087, subjects were primed with HIV plasmid DNA and varying doses of IL-12 plasmid (pIL-12), followed by a vesicular stomatitis virus (VSV) boost expressing HIV-gag. pIL-12 had no effect on the frequency of CD4 responses, nor on the magnitude of those responses as determined by intracellular cytokine staining (ICS). Similarly, pIL-12 had no effect on the frequency of CD8 responses, but did increase the magnitude of positive responses. The effect of pIL-12 dose on Gag-specific TCR repertoire diversity is unknown.

OBJECTIVE:

We will determine the correlation between antigen-induced expression of surface activation markers, which can be used to identify and sort live antigen-specific cells, with ICS, which requires fixation, and therefore not suitable for live sorting. We will then determine if the dose of pIL-12 during the DNA prime increases HIV Gag-specific TCR diversity.

METHODS:

Peripheral blood mononuclear cells (PBMCs) from vaccinated subjects were stimulated overnight with a pool of HIV Gag peptides. The next day PBMCs were stained for markers of activation. Activated CD4+ T cells, defined by co-expression of CD69 and OX40, and activated CD8+ T cells, defined by co-expression of CD69 and CD137, were sorted for TCR analysis. Spearman rank was used to determine the correlation between the frequencies of cytokine-producing cells, and frequencies of cells expressing surface activation markers in response to HIV Gag peptides.

CONCLUSION FUTURE DIRECTIONS:

CD69 and OX40 identify HIV-gag-specific CD4+ cells, while CD69 and CD137 identify HIV -gag-specific CD8+ cells and correlate with ICS responses. TCR ß chain sequencing will be performed to assess TCR repertoire diversity. HIV gag-specific CD4 and CD8 TCR ß chain diversity after VSV-gag boost will be compared among individuals receiving varying doses of IL-12. Furthermore, in individuals who generated both CD4 and CD8 responses, HIV Gag-specific CD4 and CD8 TCR ß chain diversity will be directly compared. These results will inform studies to more completely evaluate cellular immune responses in future vaccine trials.

Investigating the effect of CDK4/6 and MDM2 inhibition on antitumor immune defenses

Lauren Slesur, Anna Vilgelm, Ann Richmond, Sheau-Chian Chenn, Rami Al-Rohil

OBEJCTIVES:
Investigate how MDM2 and CDK4/6 inhibition affects immune surveillance *in vivo* in *CDKN2A*-deleted melanoma tumors. We hypothesized that combined therapy would increase tumor-infiltrating lymphocytes (TILs) by inducing T cell-recruiting chemokine expression.

METHODS:
C57BL/6J mice (n=40) were injected into both flanks with 50,000 B16F0 cells, a *CDKN2A*-deficient mouse melanoma line. After one week mice were randomized into treatment groups: vehicle (0.5% methylcellulose), palbociclib 100 mg/kg, RG7388 150 mg/kg, and combination palbociclib + RG7388. Drugs were given daily via oral gavage, and tumors were measured every 2-3 days. Tumors were excised and weighed after two weeks of therapy. Four tumors per group were randomly selected for H&E to evaluate necrosis and IHC for CD3 (T cell marker), Ki67 (proliferation marker), and caspase 3 (apoptosis marker). Slides were quantified by a pathologist blinded to the groups. Five tumors per group were randomly chosen for RT-PCR analysis of T cell-recruiting chemokines CCL5, CXCL9, and CXCL11. A mixed-effects model was used to compare tumor growth rate and tumor weights to account for correlation among tumors from the same mouse. Kruskal-Wallis and post-hoc Wilcoxon were used for other analyses.

RESULTS:
Tumor growth rate was reduced in palbociclib ($p<0.001$), RG7388 ($p=0.0012$), and combination groups ($p<0.001$) compared to the vehicle. Tumor weight was reduced in RG7388 ($p=0.0281$) and combination ($p=0.0412$) groups. There were more CD3-positive cells in the vehicle group than the RG7388 group ($p<0.05$). The RG7388 group had less Ki67-positive cells than the vehicle ($p<0.05$) and combination group ($p<0.01$). There was no difference in caspase 3 expression or necrosis. There was also no difference in CCL5, CXCL9, or CXCL11 expression.

CONCLUSIONS:
Each treatment reduced tumor growth rate. Palbociclib-treated tumors did not weigh less than control tumors due to rapid initial growth. Despite this, analysis of apoptosis and necrosis did not indicate treatments induced cell death. Only MDM2 inhibitor-treated tumors had reduced proliferation. It may be that palbociclib and the combination regimen reduced growth by other means, or the Ki67 stain detected non-tumor cells. Palbociclib and the combination did not increase TILs or chemokines as expected. Limitations include that only one slide was evaluated per tumor, and timing of samples may have failed to detect change. Experiments should be repeated with earlier time points, alternative drugs that may be more immunogenic, and alternative cells with *CDKN2A* mutations.

The lipopolysaccharide-elicited cytokine response does not predict the host response to infection

Benjamin Fensterheim, Yin Guo, Edward Sherwood, Julia Bohannon

OBJECTIVES:

Immune function in critically ill patients is commonly assessed by the magnitude of the cytokine response to lipopolysaccharide (LPS, also known as endotoxin). A suppressed response, known as endotoxin tolerance, is associated with higher morbidity and mortality in patients, yet contradictory studies show that endotoxin tolerance-inducing toll-like receptor 4 (TLR4) ligands protect animals from infection. A novel hypothesis to resolve this contradiction is that the magnitude of the LPS-elicited cytokine response is not relevant to, and thus does not predict, the host response to live infection. The objective of this study was to assess the whether the LPS-elicited cytokine response predicts the host response to infection.

METHODS:

To address this objective, the ability of diverse TLR ligands (monophosphoryl lipid A (MPLA), LPS, CpG-ODN, GpC-ODN, Poly(I:C)) to alter the LPS-elicited cytokine response as well as resistance to *Pseudomonas aeruginosa* infection was assessed in mice. Additionally, bone marrow derived macrophages (BMDMs) were exposed to TLR ligands and assessed on a variety of metabolic and antimicrobial parameters long after exposure.

RESULTS:

Mice primed with the TLR ligands LPS, monophosphoryl lipid A (MPLA), and poly(I:C) had significantly reduced plasma pro-inflammatory cytokines after LPS challenge, reflecting endotoxin tolerance, whereas CpG-ODN-primed mice had significantly increased plasma pro-inflammatory cytokines after LPS challenge. In contrast, LPS, MPLA, and CpG-ODN, but not poly(I:C), improved the host response to a *P. aeruginosa* infection. Protective TLR ligands universally reduced plasma pro-inflammatory cytokines after *P. aeruginosa* infection in association with improved bacterial clearance and augmented recruitment and function of phagocytes. In bone marrow derived macrophages, protective TLR ligands induced endotoxin tolerance, while universally augmenting macrophage glycolytic rate, oxidative rate, size, granularity, phagocytosis, and respiratory burst.

CONCLUSION:

The magnitude of the LPS-elicited cytokine response is not indicative of antimicrobial immunity after exposure to TLR ligands. Further, TLR ligand prophylaxis may be an effective way to reduce the incidence of infection in critically ill patients.

Variant of ALK6 Associated with Non Alcoholic Fatty Liver Disease

Timothy Thayer, Quinn Wells, Eric Farber-Eger, Sabrina Erin Booton, Chuanmin Cheng, Daniel Perrien, Rajeev Malhotra, Charles Hong

OBJECTIVES:
One third of adults in the US have non alcoholic fatty liver disease (NAFLD), which is an independent risk factor for coronary artery disease. In unpublished data we showed that inhibition of bone morphogenetic protein (BMP) signaling in a murine model of obesity prevents the development of hepatic steatosis. Thus, we carried out a candidate gene study to assess for association of SNPs in BMP type 1 receptors expressed in hepatocytes (ALK2/3/6) and NAFLD.

METHODS:
Utilizing Vanderbilt's de-identified electronic health record, the Synthetic Derivative (SD), and the linked genetic database BioVU, we executed a logistic regression analysis of patients in the SD with BioVU data utilizing age, gender and SNPs in ALK2/3/6 to identify SNPs associated with the Phecode 571.5 (an aggregate of ICD codes for non-alcoholic and non-viral chronic liver disease). A liberal minor allele frequency cutoff of <0.0005 was selected to include rare variants. Six SNPs met this criteria, and 1 SNP in ALK6 was associated with the Phecode 571.5. Given this Phecode is not specific for NAFLD, carriers of this SNP (rs34970181_A, n=70) were matched 1:2 with noncarriers by age, sex, race, and BMI. Charts were physician reviewed to identify NAFLD while blinded to carrier status. Next, the ALK6 mutant R371Q, the product of the rs34970181 transcript variant, was transfected into C2C12BRA cells with a BMP responsive luciferase reporter and compared with wild type (WT) and a constitutively active ALK6 receptor (Q204D). Lucerifase activity was assessed with and without incubation with BMP4 for 18h.

RESULTS:
Correlation analysis shows carrying rs34970181_A confers an odds ratio of 3.3 in having Phecode 571.5 associated with a chart (P=0.0066, with Bonferroni correction P<0.008 considered significant). Physician chart review revealed carriers of rs34970181_A were >2 times as likely as noncarriers to have NAFLD (15 of 70 v 14 of 140, P=0.03). Transfection of the R371Q allele into a BMP signaling reporter line revealed the receptor is constitutively active with 3.5 fold the basal luciferase activity as WT (P=0.008), which was similar to Q204D (4.3x WT activity P=0.002, P=0.09 vs R371Q). Moreover, R371Q is hyper-responsive to BMP4 at 5 and 25 ng/ml with 2x and 2.4x the luciferase activity as WT (P=0.03 and P=0.003)

CONCLUSIONS:
A rare ALK6 variant is constitutively active with hyperresponsiveness to BMP ligands and carriers of this allele are at increased risk NAFLD. Inhibition of BMP signaling represents a novel therapeutic target in the treatment of NAFLD.

Predicting the Response of Triple Negative Breast Cancer to Doxorubicin

Matthew T. McKenna, Jared Weis, Stephanie Barnes, Darren Tyson, Michael Miga, Vito Quaranta, Thomas Yankeelov

OBJECTIVES:
Doxorubicin forms the basis of neoadjuvant chemotherapy regimens for several malignancies, including triple negative breast cancer (TNBC). Here, we present a coupled experimental/modeling approach to establish an *in vitro* pharmacokinetic/pharmacodynamic (PK/PD) model to describe how the concentration and duration of doxorubicin therapy shape subsequent cell population dynamics.

METHODS:
Whereas traditional therapy response assays are evaluated at a single timepoint following constant exposure to a drug of interest, this work focuses on a series of longitudinal fluorescence microscopy experiments that characterize 1) the temporal dynamics of doxorubicin uptake in a panel of TNBC cell lines, and 2) the response of those cells to doxorubicin over the subsequent weeks. We propose a treatment response model, fully parameterized with experimental imaging data, to describe both doxorubicin uptake and population size over time. Finally, we present a framework to predict response to experimental doxorubicin treatments.

RESULTS:
We found that doxorubicin pharmacokinetics can be described by a three compartment model, and significant differences exist in PK parameters across the panel of cell lines investigated. Further, we noted that cell population response to increasing doxorubicin concentrations and exposure times varied along a continuum, ranging from persistent exponential growth to complete population regression. Of note, this behavior was consistent across all investigated cell lines. The proposed treatment response model effectively captures cell population dynamics and translates well to a predictive framework. For example, in a representative cell line (SUM-149PT) treated for 12 hours with doxorubicin, the mean percent error of the best fit and predicted models were 14% (±10%) and 16% (±12%), which are notable considering these statistics represent errors over the 30 days following treatment.

CONCLUSIONS:
While doxorubicin has been in clinical use for several decades, to our knowledge, measurements of its cellular effects have not previously been coupled to intracellular concentrations and drug exposure times in a predictive framework. Such integrated data can populate mathematical models that can predict the *in vitro* response of a panel of TNBC cell lines to doxorubicin therapy. More generally, this work provides both a template for studies quantitatively investigating treatment response and a scalable approach toward predictions of tumor response *in vivo*.

Alterations in intestinal sulfur assimilation metabolism regulate iron homeostasis

Andrew T. Hale, Benjamin H. Hudson, Ryan P. Irving, John D. York

OBJECTIVES:
Sulfur assimilation is the process of incorporation of inorganic sulfate from the environment into sulfur-containing amino acids and sulfate-containing metabolites, and is a feature that is evolutionarily-conserved across bacteria, yeast, plants and mammals. A critical regulator of the sulfur assimilation pathway is bisphosphate 3'-nucleotidase (Bpnt1). Mice deficient for Bpnt1 (Bpnt1-/-) develop anasarca, hepatic insufficiency, impaired ribosomal biogenesis, and age-dependent alopecia, a common manifestation of anemia. Iron is a critical dietary micronutrient, and numerous disease states result from an imbalance in iron homeostasis including hereditary hemochromatosis, neurodegenerative disease and anemia. Herein, we sought to define the role of Bpnt1 in mediating iron homeostasis.

METHODS:
Bpnt1-/- mice, intestinal-specific deletion of Bpnt1 (Bpnt1-/int) mice, and the brachymorphic mouse (Papss2*bm/bm*), harboring a hypomorphic mutation in PAPS synthase 2, the gene that controls upstream production of PAP (the substrate of Bpnt1), crossed with the Bpnt1-/- mouse (Papss2*bm/bm* Bpnt1-/- - DKO) were assessed for hematologic parameters. Western blot, qPCR, RNA-seq, and immunohistochemistry were used to investigate specific targets involved in iron metabolism from whole tissue as well as isolated enterocytes.

RESULTS;
We report that loss of Bpnt1 in mice leads to iron-deficiency anemia (IDA). Independent of dietary iron content, Bpnt1-/- animals display significantly lower hemoglobin, smaller mean corpuscular volume, and reduced average cellular hemoglobin. Strikingly, using a forward genetics approach, the DKO animal specifically reduces accumulation of PAP and rescues the anemia observed in the Bpnt1 -/- animal. We hypothesized that intestinal accumulation of PAP perturbs the response to iron deficiency. Thus, we generated Bpnt1-/*int* mice, which were similarly iron deficient and display age-dependent alopecia. To understand why Bpnt1-/*int* mice were unable to respond to the low iron stress, we used an unbiased RNAseq-based approach, and show that enterocytes from Bpnt1-/*int* mice are unable to regulate key iron homeostasis factors involved in dietary iron reduction, import and transport. Interestingly, the transcriptional profile of Bpnt1-/*int* enterocytes, in part, mimic that reported from mice deficient in hypoxic-induced transcription factor, HIF-2α, which similarly develop IDA.

CONCLUSIONS:
Our studies define a new genetic basis for iron-deficiency anemia, a molecular approach for rescuing the pathophysiology and an unanticipated link between nucleotide hydrolysis in the sulfur assimilation pathway and iron homeostasis.

Glucagon-like peptide-1 receptor signaling attenuates RSV-induced type 2 responses and immunopathology

Melissa H. Bloodworth, Jian Zhang, Anne L. Hotard, Martin L. Moore, Tina V. Hartert, Kevin D. Niswender, R. Stokes Peebles Jr.

RATIONALE:
Glucagon-like peptide-1 receptor (GLP-1R) agonists are a well-accepted and safe treatment for Type II diabetes. Although GLP-1R agonists mainly act to potentiate insulin and suppress glucagon secretion, recent evidence suggests that GLP-1R signaling also has anti-inflammatory effects through unclear mechanisms. Severe RSV-associated illness is in part caused by type 2-associated immunopathology. IL-33 is a primary therapeutic target for inhibiting inflammatory lung disease given its central role in activating cells that produce type 2 cytokines. We hypothesize that GLP-1R signaling inhibits type 2-associated immunopathology of RSV 12/12-6, a strain of RSV that was isolated from a hospitalized infant with severe lower respiratory tract infection and bronchiolitis.

METHODS:
Balb/c WT mice were infected with RSV 12/12-6. GLP-1R agonist or vehicle was administered subcutaneously twice daily. Mice were euthanized and BALs (bronchoalveolar lavage) and lungs were collected for cell differentials, histopathology, AHR, ELISA, flow cytometry, or qPCR.

RESULTS:
GLP-1R agonist treatment decreased airway inflammation, airway responsiveness, and airway mucus production in RSV 12/12-6-infected mice. The GLP-1R agonist decreased total lung IL-13 and IL-33 levels, with concurrent decreases in lung IL-13-producing group 2 innate lymphoid cells (ILC2), CD4+ Th2 cells, and basophils as well as IL-33-producing epithelial cells. GLP-1R agonist treatment prevented airway inflammation, and did not impact viral load, antiviral interferon and antibody production during secondary RSV infection. Relative to the respective mock-infected groups, RSV-infected GLP-1R agonist treated mice did not have increased weight loss compared to vehicle-treated mice. A phenome-wide association study (PheWAS) identified a link between GLP-1R signaling and acute bronchitis and bronchiolitis in humans.

CONCLUSIONS:
These data suggest that a GLP-1R agonist protects against type 2-mediated immunopathology during RSV infection and are the first known FDA-approved agents to inhibit IL-33. GLP-1R signaling is associated with acute bronchitis and bronchiolitis in humans and may represent a novel treatment strategy for RSV bronchiolitis.

Real-time Identification of In-situ Pulmonary Nodule and Pathology Using Optical Coherence Tomography

Denis Gilmore, Giju Thomas, Anita Mahadevan-Jansen, Eric Grogan

OBJECTIVES:
Due to lung cancer screening and increased use of CT scans, the incidence of indeterminate pulmonary nodules (IPN) and ground glass opacities (GGO) is increasing. In lesions requiring surgical biopsy, small (<1 cm) IPN may be difficult to localize in the OR using a minimally invasive approach. Optical Coherence Tomography (OCT) utilizes interference of light waves between different layers of tissues to provide high-resolution, cross-sectional images of the internal microstructure by measuring back-reflected light. This approach can deliver video rate images of tissue structure on the micron scale in situ and can be used to scan large areas of tissue to identify nodules and provide realtime histology-like images without actual removal of tissue to detect lung lesions. OCT may aid in the localization and diagnosis of malignant lesions in patients with IPN or GGO without utilization of potentially toxic dyes or radiation.

METHODS:
Fifteen human lung tissue samples (5 malignant pathology, 5 benign pathology and 5 normal lung tissue) were obtained through an IRB approved protocol from the Cooperative Human Tissue Network thoracic oncology tissue biorepository. Tissue was fresh frozen, stored in -80C and analyzed using a 1310nm wavelength OCT system (Thorlabs Telesto, NJ). Each specimen was scanned with an area of 64-100 mm2 to a depth of 3.5mm. Image acquisition took less than one second for two dimensional and 20 seconds for three dimensional images. Specimens were analyzed by a blinded reviewer.

RESULTS:
Among the 15 samples, 100% of normal lung tissue (5/5) produced low intensity, homogenous tissue patterns. 80% benign pathology (4/5) retained the homogenous pattern of normal tissue but with higher intensity signal. In contrast, 80% (4/5) malignant samples exhibited a heterogenous cauliflower like pattern at high intensity.

CONCLUSIONS:
Utilizing OCT, real-time localization of IPN and GGO within lung tissue as well as determination of pathology can be performed prior to resection. Further optimization of this technique by potentially combining OCT with other optical imaging methods such as fluorescence or Raman spectroscopy may aid in improving sensitivity in differentiating between benign and malignant lung pathology for clinical feasibility.

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Twelve rare variants in the tissue-nonspecific alkaline phosphatase (TNSALP) gene: refining the phenotype of hypophosphatasia

Daniel Tilden, Kathryn Dahir, John Newman

OBJECTIVES:
Serum testing of alkaline phosphatase is a ubiquitous study used most commonly to diagnose liver and bone disorders. Low serum activity of this enzyme, when observed in children and symptomatic adults, is referred to as hypophosphatasia (HPP). This results from various mutations in the TNSALP gene with well-known bone and muscloskeletal manifestations. Although HPP is usually detected by a low serum alkaline phosphatase (AlkP), clinical experience suggests that this may not be a reliable indicator of disease in many patients. We hypothesized that some patients with bone or dental disease may have genotypic variants in the TNSALP gene but may not have an accompanying persistently low serum AlkP, making diagnosis more difficult.

METHODS:
We surveyed all patients in BioVU that had at least one variant in TNSALP and reviewed the de-identified medical records of patients with variants of interest along with age and gender matched controls. We then reviewed the medical records to identify bone or dental abnormalities and all recorded AlkP values. The relationships between the presence of one of the SNPs of interest and phenotypic characteristics were then analyzed.

RESULTS:
Of the 25,822 patients with sequencing data available for TNSALP, 180 patients with were identified with a total of 12 distinct, low frequency or novel variants. This represents a prevalence of 1/144, significantly higher than previously reported prevalence estimates of 1/100,000 for severe disease and 1/6,370 for more mild disease. On chart review, none of the patients with the variant alleles had been given the diagnosis of HPP. We observed significantly higher rates of orthopedic abnormalities including scoliosis (14% vs. 5% $p = 0.004$), low bone mineral density (30% vs. 20% $p = 0.02$) and dental disease (15% vs. 1% $p = 0.00002$) in patients with these variants. However, we found no clinically significant difference in the average or minimum recorded value of AlkP between the two groups.

CONCLUSIONSl
Our data show both that HPP is likely more common than previously estimated and that the chief surrogate marker used to identify cases, AlkP, is unreliable as a screening test to identify patients with the disease. In our data, clinical characteristics, especially the presence of dental disease, appears to be the most reliable disease marker. This suggests that clinicians, rather than relying on AlkP as a screening test in patients when looking for HPP are better off relying on clinical markers of disease to guide their work up and management of these patients.

Aligning In-Service Training Examinations with Competency Based Education

Michael A. Benvenuti, Mishant Ganesh Kumar, Brian C. Drolet

OBJECTIVES:
In-Service Training Examinations (ITEs) are an important assessment tool for residents across all specialties. However, it is not clear how the Accreditation Council for Graduate Medical Education (ACGME) Milestones and Core Competencies have been integrated with the ITEs. The goal of this study is to describe the distribution of specialty-specific Milestones and Core Competencies on ITEs and determine how to better integrate ITEs with competency based education.

METHODS:
Of 28 ACGME specialties, ITEs were publicly available for Plastic Surgery (PSITE) and Orthopaedics (OITE). We reviewed the 2014–2016 PSITE and 2013-2015 OITE, and mapped each question to one of the specialty-specific Milestones and to one of the six ACGME Core Competencies.

RESULTS:
There was an uneven distribution of Milestones and Core Competencies on the PSITE and OITE. Out of 36 Plastic Surgery Milestones, 9 represented more than 50% of the PSITE questions. Meanwhile, 7 of 41 Orthopaedic Milestones (17%) represented more than 50% of the OITE questions. Three Plastic Surgery and 5 Orthopaedic Milestones had no representation on the exam. Among Core Competencies, Patient Care was most common (PSITE = 62%, OITE = 59%) followed by Medical Knowledge (PSITE = 34%, OITE = 32%). A difference was noted in the distribution of the remaining Core Competencies (PSITE=4% vs OITE=9%).

CONCLUSIONS:
Despite the shift towards competency-based evaluation in residency training, the ITEs for Plastic Surgery and Orthopaedics are not yet well-integrated with ACGME competency standards. These ITEs tested a minority of the Milestones of each specialty, and focused on Patient Care and Medical Knowledge competencies. The Milestones were developed through collaboration of numerous stakeholders, and represent a validated blueprint that might be used to develop future competency-based ITE questions. Using the Milestones as template for the ITEs may help to integrate these two important evaluation systems.

Drug Allergy Training Opportunities in the United States: A Survey of Allergy and Immunology Program Directors

Michael I. Derrick, MD, Elizabeth McKinnon, PhD, Elizabeth J. Phillips, MD

OBJECTIVES:
To determine the extent to which Allergy and Immunology fellowship programs provide sufficient training in drug allergy to both meet the demand for more clinical management services and further research exposure and efforts in the United States.

METHODS:
A 15 question anonymous and voluntary e-mail survey with three reminders was distributed by the AAAAI to current Program Directors of Allergy and Immunology fellowship programs accredited with the Accreditation Council for Graduate Medical Education (ACGME) within Internal Medicine and Pediatrics in the United States.

RESULTS:
Of 49% (38/78) of program directors responding, 95% identified drug allergy training was available to fellows, and 42% rated training opportunities as outstanding. Approaches to immediate drug allergy such as desensitization, skin testing, and oral challenge were broadly available (>90% programs), particularly for testing to penicillins and cephalosporins. Fewer programs exposed fellows to testing procedures for delayed reactions such as delayed intradermal testing (42%) and multiple dose oral challenge (63%). Research and publication opportunities for fellows were largely limited to case reports (100%) and retrospective review of the literature (79%) with few programs offering clinical trial (13%), big data/dry lab exposure (16%), or wet lab basic research opportunities (8%).

CONCLUSIONS:

Although the overall standard of drug allergy training appears strong, some gaps and barriers in the depth and breadth of clinical training were identified. Survey results suggest an imperative to increase high quality research opportunities during fellowship training as necessary pre-requisites to support the next generation of clinician educators, physician scientists, and leaders driving advances in this field.

Are Gastroschisis Patients at Risk for Intestinal Ischemia Identifiable at the Time of Initial Neonatal Evaluation?

Pranit Chotai, Anna Slagle, Jose Duncan, Ajay Talati, Mauro Schenone, Max R. Langham Jr., James W. Eubanks III, Eunice Huang

OBJECTIVES:
To identify perinatal clinical factors which may be associated with intestinal ischemia in infants with gastroschisis.

METHODS:
Following IRB approval, neonates with gastroschisis managed at our institution between 1/1/2008 and 9/30/2015 were retrospectively reviewed. Patient demographics, neonatal status, such as gestational age, birth weight, Apgar scores and laboratory values within the first 4 hours of birth, maternal behavioral risk factors, indications for and mode of delivery, and hospital course and outcomes were collected. Patients with ischemic bowel at initial evaluation or on subsequent evaluations prior to abdominal wall closure were classified into the "ischemia" category (IC). All other neonates including those with atresia or perforation without ischemic bowel were classified into the "no ischemia" category (NIC). Categorization was performed by two surgical investigators followed by a third surgical investigator to reconcile disagreements. Chi-square, Student's t-test and Wilcoxon rank-sum test were used for comparison.

RESULTS:
One hundred seven (62 males and 45 female) neonates were included. The inter-rater reliability of IC versus NIC categorization was 84%. Eight patients were identified with IC at initial evaluation and 9 at subsequent evaluations (all within 1-3 days of life). There were proportionally more male patients in the IC group as compared to the NIC group ($p=0.0392$). Having a combination of non-reassuring fetal heart tones and preterm labor was more likely to be associated with IC ($p=0.0333$). In addition, having a lower pH within 4 hours of birth is also more likely to be associated with IC ($p=0.0016$).

CONCLUSIONS:
A small proportion of neonates born with gastroschisis are at risk for developing intestinal ischemia at birth or during the first days of life. Our findings indicate that male gender, fetal distress and low pH may be associated with perinatal risk for intestinal ischemia. Further collaborative work across institutions can help inform the generalizability of this trend across populations.

Surgical Informed Consent in Children: A Systematic Review

Pranit Chotai, Richard Nollan, Eunice Huang, Ankush Gosain

OBJECTIVE:
We sought to analyze current literature on surgeon and parents' understanding and role in the informed consent process for children undergoing surgery.

METHODS:
A systematic database search (Medline, EMBASE, PsycINFO, and EBM Reviews) was performed to identify manuscripts concerning any aspect of the surgical informed consent for children undergoing an invasive procedure. Articles analyzing informed consent in research studies, non-English language manuscripts, review articles, case reports/series, letters/commentaries and dentistry/nursing related articles were excluded. Articles meeting inclusion criteria were analyzed to identify common themes related to the process of informed consent.

RESULTS:
178 articles were identified on primary search, after removing duplicates and screening titles for relevance, 83 abstracts were reviewed. 32 additional abstracts were identified by secondary search. 12/115 articles met inclusion criteria. Analysis identified 5 different study themes. Information delivered during consent (Content) was studied in 5 (42%) articles, 3 (25%) studied the mechanics or delivery of the information (Delivery), 3 (25%) studied parent participation and discussion (Interchange), 6 (50%) articles discussed surgeons' perceptions or the parents' ability to understand or recall the information (Comprehension), and 5 (42%) articles evaluated surgeon or parent satisfaction or anxiety (Satisfaction). None of the articles studied all five categories.

CONCLUSIONS:
Studies of the surgical informed consent process in children are scarce. Prospective studies evaluating surgeon and parent perception regarding the Content, Delivery, and Interchange of information as well as Comprehension and Satisfaction are needed to understand barriers to the surgeon-patient relationship and to optimize the informed consent process in children undergoing surgery.

The Effect of Pre-Test Exercise on Baseline Computerized Neurocognitive Test Scores

Alec Pawlukiewicz, Aaron M. Yengo-Kahn MD, Gary Solomon PhD

OBJECTIVES:
The primary aim of our investigation was to determine the effect of pre-test exercise on baseline Immediate Post -Concussion Assessment and Cognitive Testing (ImPACT) scores in adolescent and young adult athletes. The secondary aim was to make an evidence-based recommendation as to whether to restrict strenuous exercise prior to baseline neurocognitive testing.

METHODS:
The ImPACT records of 18245 adolescent and young adult athletes were retrospectively analyzed. After application of inclusion and exclusion criteria, participants were dichotomized into groups based on a positive (n= 664) or negative (n= 6609) self-reported history of strenuous exercise within 3 hours of the baseline test. Based on age, gender, education level, concussion history and hours of sleep prior to testing, these participants were then randomly matched on a 2:1 basis with individuals from the control group in which no pre-test exercise had taken place. The ImPACT composite scores of the two groups were then compared.

RESULTS:
Significant differences were observed on the ImPACT composite scores of verbal memory (84.06 vs. 85.52, p= 0.009, Hedges' g = -0.1476728), visual memory (74.15 vs. 75.92, p=0.005, Hedge's g= -0.1356979), reaction time (0.6303 vs. 0.6137, p=0.001, Hedge's g =0.17743062), and impulse control (6.61 vs. 5.85, p=0.002, Hedge's g = 0.1702001) and in the total reported symptom score (4.86 vs. 2.84, $p < 0.0001$, Hedge's g= 0.29298033). No significant between-group difference was detected in the visual motor composite score. Further, pre-test exercise was associated with a significant increase in the overall frequency of invalid test results (4.46% vs. 2.44%, p=0.013).

CONCLUSIONS:
Our results suggest a statistically significant difference in ImPACT composite scores between individuals who report strenuous exercise prior to baseline testing versus those who do not. Since return to play decision making often involves documentation of return to neurocognitive baseline, baseline test scores must be valid and accurate. As a result, we recommend standardization of baseline testing such that no strenuous exercise takes place 3 hours prior to test administration.

The Effect of a self-reported history of seizure on baseline neurocognitive test performance in student-athletes

Brian H. Zalneraitis, Alec J. Pawlukiewicz, Aaron M. Yengo-Kahn, Gary S. Solomon

OBJECTIVES:

Baseline neurocognitive assessment such as the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) is critical in return to play (RTP) decision-making following a sport-related concussion (SRC). Many modifying factors of neurocognitive test performance have been studied; however, there has been little investigation into the effect of a self-reported history of seizure(s) on baseline testing. The objective of this investigation is to determine whether a history of self-reported seizure affects baseline ImPACT scores.

METHODS:

A retrospective analysis of 18,245 child, adolescent, and young adult athletes' ImPACT scores was performed. After application of inclusion and exclusion criteria, participants were dichotomized based on a self-reported history of seizure. Participants reporting a history of seizure (n=60) were matched1:3 based on age, gender, education level, concussion history, and hours of sleep with controls without a history of self-reported seizure. (n=180). The baseline ImPACT composite scores of the two groups were then compared using a 2-tailed t-test for scores with a parametric distribution (Visual Motor Speed) and Mann-Whitney U-Test for scores with a non-parametric distribution (Verbal Memory, Visual Memory, Reaction Time, Impulse Control, and Total Symptom Score).

RESULTS:

A significant between-group difference was observed in ImPACT visual motor composite scores (35.28 vs. 37.64, p= 0.029, hedge's g= 0.3261). No significant between-group difference was detected in the composite scores of verbal memory, visual memory, reaction time, impulse control, or total symptom score. No difference was detected in the overall frequency of invalid test results between the two groups.

CONCLUSIONS:

Athletes with a history of self-reported seizure scored significantly lower on ImPACT visual motor composite scores compared to matched controls. However, the effect size was small, and the clinical significance of this finding is unclear. Athletes with a history of self-reported seizure did not differ in any other ImPACT scores. Therefore, this analysis suggests that athletes with a history of seizure may not produce significantly different neurocognitive baseline test scores when compared with matched controls. Further investigation of self-reported seizure as a potential modifying factor for concussion assessment and management is needed.

Lenalidomide vs. Bortezomib Maintenance Choice Post-Autologous Haematopoietic Cell Transplantation (AHCT) for Multiple Myeloma

Jennifer Huang, Robert Cornell, Sharon Philips, Kyle Rawling

OBJECTIVES:

Post-AHCT lenalidomide (L) and bortezomib (B) maintenance therapy for multiple myeloma (MM) have separately been shown to improve progression-free survival (PFS) compared to placebo but have never been directly compared. We performed a retrospective study to investigate survival outcomes and toxicities of L maintenance therapy compared with B maintenance in MM patients post-AHCT.

METHODS:

This study included 156 patients who received AHCT within 12 months of MM diagnosis between 2008 and 2015 after L- or B-based induction therapy. Maintenance therapy was defined as monotherapy with either L or B. The primary outcome was PFS. Secondary outcomes were overall survival (OS) and treatment-related toxicities.

RESULTS:

92 patients received L maintenance and 64 B maintenance post-AHCT. At baseline there were no differences in ISS stage, DS stage or cytogenetic risk between maintenance cohorts. At time of analysis, 49% (n=45) on L maintenance and 52% (n=33) on B maintenance experienced disease progression. Median time to progression (1.71 vs 1.74 yrs, p=0.77) was not significantly different between cohorts. By multivariable analysis, maintenance choice was not significant for PFS. Variables significant for improved PFS were ISS stage I/II vs III (HR 1.86; 95% CI 1.11-3.12; p=0.02) and achieving at least very good partial response post-AHCT (HR 2.05; 95% CI 1.14-3.69; p=0.02). Patients on maintenance therapy for less than 2 years experienced progression earlier compared to greater than 2 years (HR 0.40; 95% CI 0.22-0.70; p<0.01). Disease response improved while on maintenance in 38% (n=24) with L and 34% (n=31) with B.

Median OS (4.28 vs 5.77 yrs, p=0.47) was not statistically different between maintenance cohorts. ISS stage I/II vs III resulted in improved OS (HR 3.87; 95% CI 1.44-10.39; p=0.01).

Secondary malignancies occurred in 7% (n=6) with L and 3% (n=2) with V. Peripheral neuropathy was more common while on B (39% vs 9%, p<0.01), while cytopenias were more common while on L (30% vs 3%, p<0.01). Median follow-up time for survivors was 33 months.

CONCLUSIONS:

These findings suggest that both lenalidomide and bortezomib are equivocal maintenance therapy options for post-AHCT MM patients. Choice of maintenance therapy post-AHCT for MM did not demonstrate a difference in survival outcomes, and based on these data, should be guided by patient-specific anticipated tolerance rather than drug type alone. ISS stage and post-AHCT disease response continue to be significant predictors for outcomes. Treatment-related toxicities were as anticipated.

Assessment of Surgical and Endovascular Re-Intervention in Pediatric Coarctation of the Aorta

Saad Rehman, Aanish Raees, Ashly Westrick, Chevis Shannon, George Nicholson, David Bichell, Bret Mettler

INTRODUCTION:
Pediatric coarctation of the aorta (CoA) is a congenital stenosis of the aorta accounting for approximately 5% of congenital heart disease. Without treatment, patients with CoA have an average life expectancy of 31 years. Despite well-documented rates of re-coarctation following repair of CoA, there are no reported methods of predicting which patients will experience a re-coarctation and which of these will require re-intervention. In the absence of this predictive capacity, disease progression may develop undetected and contribute to morbidity and mortality.

METHODS
We conducted a retrospective cohort study of pediatric patients who underwent one or more interventions for CoA at Vanderbilt Children's Hospital between 2007 and 2016. Patients were excluded if their initial intervention was performed at an outside institution or if they possessed additional heart defects. Data collected for each patient included birth history, interventional reports, echocardiographic measurements of the aortic arch, and all cardiology follow-up visits.

RESULTS
133 patients were included in the cohort; 123 (92.5%) underwent primary surgical repair while 10 (7.5%) underwent primary endovascular repair. The median age was 1.4 months [interquartile range (IQR): 0.37-51.23] for surgical intervention and 130.33 months (IQR: 1.53-163.83) for endovascular intervention. Re-interventions were required in 11 patients (8.9%) who underwent primary surgical repair and in 4 patients (40%) who underwent primary endovascular repair.

Success of initial repair was correlated with a lower rate of future re-intervention [odds ratio (OR): 0.50, 95% confidence interval (CI): 0.17-1.49], but this difference was not statistically significant. Additionally, the incidence of medically significant hypertension prior to discharge demonstrated no difference in need for future re-intervention (OR: 1.18, 95% CI: 0.40-3.53). Of the 15 patients who required re-intervention, 3 underwent surgical re-intervention, 6 underwent endovascular re-intervention, and 6 underwent both. The median time to first re-intervention was 0.54 years (IQR: 0.22-2.38).

CONCLUSION
In this single-institution retrospective cohort study, we found that re-intervention rates for CoA could not be directly compared for primary surgical repair and primary endovascular repair due to differences in patient populations. Our data suggest that the need for future re-intervention cannot be predicted by success of initial intervention or incidence of medically significant hypertension following primary repair. Additional factors must be studied to elucidate predictive factors of re-intervention for CoA.

Measuring the Value of a Clinical Practice Guideline for Children with Perforated Appendicitis

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OBJECTIVES:
Value-based surgical care (outcomes relative to costs) is frequently touted, but outcomes and costs are rarely measured together. Our main objective was to determine the incremental cost-effectiveness of a clinical practice guideline (CPG) compared to "usual care" for treatment of perforated appendicitis in children. Secondary objective was to compare cost analyses using hospital accounting system data versus data in the Pediatric Health Information System (PHIS).

METHODS:
During an 18-month period, 122 children with perforated appendicitis at a tertiary-referral children's hospital were treated using an evidence-based CPG. Clinical outcomes and costs for the CPG cohort were compared to patients in the 30-month period prior to CPG implementation (n=191 children).

RESULTS:
With CPG-directed care, intra-abdominal abscess rate decreased from 0.24 to 0.10 (aRR, 0.44 [95% CI, 0.26-0.75]). The rate of any adverse event decreased from 0.30 to 0.23 (adjusted risk ratio, 0.82 [95% CI, 0.58-1.17]). Mean total hospital costs per patient (hospital accounting system) decreased from $16,466 to $10,528 (adjusted absolute difference, (-$5,451) [95% CI, (-$7,755) - (-$3,147)]), leading to estimated adjusted total savings of $665,022 during the study period. Costs obtained from the PHIS database also showed reduction with CPG-directed care (-$6,669 [95% CI, (-$8,949) - (-$4,389)] per patient). In Bayesian cost-effectiveness analyses, likelihood that CPG was the dominant strategy was 91%.

CONCLUSIONS:
An evidence-based CPG increased the value of surgical care for children with perforated appendicitis by improving outcomes and lowering costs. Hospital cost accounting data and pre-existing cost data within the PHIS database provided similar results.

Serious Cardiovascular Morbidity and Mortality in a Cohort of Adults with Fontan Physiology

Angela Weingarten, Daniel E. Clark, Larry W. Markham

OBJECTIVES:
The morbidity and mortality in adults with single ventricular hearts who have undergone Fontan palliation is poorly defined. These patients have a high burden of arrhythmia, heart failure, and re-operation. Our objective was to characterize the burden of arrhythmia in the cohort of adults with Fontan physiology at Vanderbilt and to test the hypothesis that age and type of Fontan are associated with occurrence of arrhythmia.

METHODS:
205 patients ³ 18 years old who had undergone a Fontan procedure were identified. Those with incomplete data were excluded. Demographic, anatomic, pharmacologic, imaging, hemodynamic, and electrophysiologic data were collected. The Chi square and Mann-Whitney U tests were used to test significance defined as $p < 0.05$.

RESULTS:
Of the 205 patients identified, 59 had been lost to follow-up. Of the 146 patients (77, 53% female) actively followed 18 (12%) had died at a median (IQR) age of 27 (21-34.3); in patients alive as of 10/2016 the median age was 26 years (22-34). Fontan types were lateral tunnel (LT) (N=79, 54.1%), extracardiac (EC) (N=32, 22%), right atrial to pulmonary artery (RV-PA) (N=28, 19%), and Fontan with Bjork modification (N=4, 2.7%). Systemic left ventricle (N=96, 66%) was more common than systemic right ventricle (N=43, 30%). Of the 146 patients, 101 (69%) had significant morbidity or mortality: 86 (59%) were diagnosed with arrhythmia and 11 (8%) underwent heart transplants. Frequent procedures included: Fontan revisions/cryoablation in 28 (19%), electrophysiology studies with ablation in 73 (50%), and pacemakers in 53 (36%). Of the arrhythmia diagnoses, 57 (64%) were atrial tachyarrhythmias. RV-PA Fontan procedures were associated with significantly more atrial arrhythmia than all other Fontan types (70% vs. 30%; $P < 0.01$). There was no statistical difference in occurrence of atrial arrhythmia in adults with LT vs. EC Fontans ($p = 0.3$). While patients who had undergone RV-PA and Bjork Fontans were older with median age 34 yrs, there was no significant difference in age between LT and EC (median 24.0 and 24.5).

CONCLUSIONS:
Adult survivors of the Fontan procedure suffer from significant morbidity and mortality. The single most prevalent morbidity is atrial arrhythmia. We conclude that RV-PA Fontans, now obsolete, have the highest prevalence of arrhythmia and that there is no difference in arrhythmia burden between LT and EC Fontans. Given the high prevalence of morbidity and mortality in this population, it is imperative that they be followed by cardiologists with expertise in congenital heart disease.

Maternal Vitamin E Plasma Isoform Concentrations and Association with Child Wheezing and Asthma Outcomes

Cosby Stone Jr., Joan Cook-Mills, Tebeb Gebretsadik, Emma K. Larkin, Christian Rosas-Salazar, Alexandra Connolly, Theresa Rogers, Zhouwen Liu, Kaitlin Costello, Tina V. Hartert

OBJECTIVES:
Isoforms of vitamin E (specifically alpha- and gamma-tocopherol) have shown differential effects on in vivo mouse models of allergic inflammation and adult-onset asthma in humans. We hypothesized that maternal postpartum vitamin E isoforms would show differential associations with early life childhood respiratory outcomes.

METHODS:
We conducted a prospective nested study of the INSPIRE birth cohort of 651 children with maternal postpartum plasma vitamin E isoforms measured at study enrollment. We ascertained the outcome of recurrent wheezing requiring asthma medication at two years of life using validated questionnaires. We evaluated for association with, and for interaction between, alpha- and gamma-tocopherol concentrations and recurrent wheezing, while adjusting for covariates.

RESULTS:
Median age of the children at time of maternal sample collection was 50 days [IQR 16,81]; 47% were female and 61% were white. Children with two year wheezing (N=174; 27%) had mothers with significantly lower postpartum concentrations of plasma alpha-tocopherol (68 μmol/L [IQR:42,96]) compared to those who did not (75 μmol/L [IQR:50,106]), p=0.021. In multivariable regression analysis for interaction, the relationship of alpha-tocopherol with wheezing was modified by gamma-tocopherol concentration in tertiles (main effect of alpha tocopherol p=0.009, interaction p=0.05). At the highest tertile of gamma tocopherol, the protective association of alpha tocopherol on child wheezing was modified.

CONCLUSIONS:
In this cohort, increasing maternal postpartum plasma alpha-tocopherol isoform concentration was associated with decreased likelihood of wheezing requiring asthma medications at two years. This protective association appeared to be attenuated at high concentrations of gamma-tocopherol.

Development of Specific Electronic Phenotypes for Severe Cutaneous Adverse Drug Reactions Facilitates Genetic Discovery

Sarah Garon MD, Lincoln Shade BS, Michael Derrick MD, Adrian Bejan PhD, Elizabeth Phillips MD

OBJECTIVES:
SJS/TEN and DRESS are life-threatening T-cell mediated severe cutaneous adverse drug reactions. Strong HLA associations offer a preventive screening strategy, but have not been defined for most drugs and populations.

METHODS:
Vanderbilt's de-identified synthetic derivative (SD) houses 2.63 million health records of which 261,460 are paired with DNA in the BioVu repository. ICD9/10/CPT codes, lab values, and text fields coupled with drug causality assessment were used to develop a best fit electronic-phenotype for phenytoin (PHT) SJS/TEN/DRESS that was validated for other anticonvulsants.

RESULTS:
Intersecting PHT use (+/-84 days) and 86 ICD9/10 rash codes produced 2577 records that were reviewed to identify true PHT SJS/TEN/DRESS (n=47). Only 4/20(20%) records coded for ICD9/10 SJS/TEN were identified as being true SJS/TEN, and 22/26(85%) of true cases lacked SJS/TEN specific ICD9/10 coding. '695.1- erythema multiforme'and/or '782.1- rash NOS,' and/or 'E936.1- Hydantoin derivatives causing ADR identified 100% of true PHT SJS/TEN and 95% of PHT DRESS. African Americans (AA) represented 3454 (13%) of 27,153 PHT exposed in SD, however 21/47(45%) of PHT SJS/TEN/DRESS cases were AA. A PHT SJS/TEN/DRESS algorithm was applied and validated against other aromatic amine anticonvulsant SJS/TEN/DRESS. SJS/TEN/DRESS cases with available BioVu DNA were matched 1:2 with race and gender matched controls tolerating the same anticonvulsant for >12 weeks. High resolution HLA typing identified significant HLA-B risk alleles.

CONCLUSIONS:
This is the first description of an electronic-phenotype for SJS/TEN/DRESS that has facilitated discovery of novel HLA associations. These electronic-phenotypes can now be validated against a larger EMR network to facilitate genetic discovery across diverse populations.

Plasma Methylated Reprimo as a Non-invasive Biomarker for Precancerous Gastric Lesions: A Cross Sectional Study in an Amerindian/Hispanic Population from an Endemic Region of Chile

James Leathers, Robinson Gonzalez, Maria Maturana, Juan Araya, Andres Rodriguez, Enrique Bellolio, Pablo Cortes, Maria Bufadel, Miguel Villaseca, Antonio Rollan, Alejandro Corvalan

OBJECTIVES:
Gastric cancer (GC) is one of the leading causes of cancer-related death in the world, due partially to advanced tumor burden at time of diagnosis. Thus, new diagnostic tools that allow for the early detection of precancerous gastric lesions are direly needed. DNA methylation of the tumor suppressor gene Reprimo (RPRM), has been identified as a potential biomarker for the detection of gastric cancer (GC) but its use as a biomarker for premalignant GC lesions such as atrophic gastritis and intestinal metaplasia, has been poorly studied. These premalignant lesions assessed using the Operative Link of Gastritis Assessment (OLGA) and the Operative Link of Gastric Intestinal Metaplasia (OLGIM) staging systems, respectively. We conducted a cross-sectional study in a region of Chile with one of the highest rates of GC in the world, to assess the association between plasma methylated RPRM, and OLGA/OLGIM.

METHODS:
We included 251 symptomatic patients who had undergone esophagogastroduodenoscopy with biopsies (Sydney protocol), and who also had a blood sample drawn for assessment of plasma methylated RPRM. We extracted DNA from blood plasma, performed bisulfite DNA modification and then measured plasma methylated RPRM using Real-time PCR. All statistics were conducted with STATA v14.2 using $p \leq 0.05$ as the criterion for statistical significance.

REULTS:
The median age of study participants was 56 (95%CI: 54-58), 69.7% (175/251) of patients were women, 15.5% (39/251) smoked tobacco and 20.3% (51/253) had a positive family history of GC. Plasma methylated RPRM was positive in 24.3% (61/251) of patients. Summary statistics were similar with regards to RPRM, with the exception of gender (Table 1). OLGA staging was available for 87.6% (220/251) of patients. Plasma methylated RPRM was positive in 21.4% (25/117) of patients with low risk OLGA (stages 1-2) and positive in 30.6% (19/62) of high risk OLGA (stages 3-4)[p=0.202]. However, this trend was more pronounced in men, where RPRM was positive in 13.2% (5/38) of low risk OLGA and 28.6% (6/21) of high risk OLGA [p=0.175] stages. OLGIM staging was available for 93.6% (235/251) of patients. RPRM was positive in 20.1% (19/91) of low risk OLGA stages and positive in 46.7% (7/15) of high risk OLGA stages [p=0.049]. This same trend was seen in both men and women (Table 2).

CONCLUSIONS:
Plasma methylated RPRM may be a useful non-invasive biomarker in the detection of precancerous gastric lesions. RPRM methylated in plasma was associated with female gender and high-risk OLGIM stages. These findings warrant further validation in larger longitudinal studies.

Underestimation of vision loss with idiopathic intracranial hypertension

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OBJECTIVES:
We sought to correlate clinical findings of vision loss with anatomical changes via optical coherence tomography (OCT) in a cohort of patients with idiopathic intracranial hypertension (IIH) who met entry criteria for the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT),(1) with the exception of perimetric mean deviation (MD) score. Our hypothesis is that the IIHTT may not capture the full extent of vision loss associated with IIH on initial presentation to academic medical centers.

METHODS:
A series of 299 patients diagnosed with IIH at an academic institution were retrospectively examined. Of these, 56 patients met stringent IIIHTT criteria except mild vision loss itself. Visual field data were compared by MD based on age. OCT measurements of retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) were correlated with visual function tests, including MD, visual field score (VFS), visual acuity score (VAS), and best corrected visual acuity (BCVA).

RESULTS:
Younger patients fulfilling IIHTT criteria were more likely to have visual field loss than older patients, both according to MD (Kendall rank correlation 0.27, p-value< 0.01) and VFS (Kendall rank correlation 0.28, p-value $= 0.02$). Both the overall average RNFL (n=18) and GCL (n=14) thicknesses each positively correlated with three different vision metrics (VFS, VAS, and BCVA; $p<0.05$).

CONCLUSIONS:
Younger IIH patients fulfilling strict IIHTT criteria may have higher visual loss risk compared to older patients. The finding of thinner RNFL and GCL in IIHTT eligible patients suggests that the IIHTT does not capture the extent of irreversible vision loss, given its inherent exclusion of patients outside the mild vision loss range.(2) Many patients meeting strict IIHTT criteria (over one third
based on MD and one quarter based on VFS) were found to have worse vision than those enrolled in IIHTT, underscoring the severity of vision loss possibly found with IIH.

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Respiratory Events Requiring Escalated Admission Status After Adenotonsillectomy in Children with Obstructive Sleep Apnea

Alexandra Arambula, Debbie Xie, Amy Whigham

INTRODUCTION:
Obstructive sleep apnea (OSA) is an increasingly common, sleep-related breathing disorder that affects 1-5% of children. Adenotonsillectomy (T&A) is the first-line treatment for children with OSA and adenotonsillar hypertrophy. The risk of postoperative respiratory compromise secondary to upper airway obstruction, a serious complication of T&A, is greater in children with OSA (rate of 16-27% compared to 0-1.3% among children without OSA). High-risk patients (weight <5th percentile for age, age <3 years, craniofacial anomalies, severe OSA on polysomnography findings, obesity) have an even greater likelihood of respiratory compromise, which has led to routine post-T&A PICU admission for this population. More recently, a handful of retrospective reviews found postoperative ICU care unnecessary for many of these patients. This study characterizes post-T&A respiratory complications in pediatric OSA patients to identify variables that may correlate with necessity of PICU care.

METHODS:
This study retrospectively analyzed pediatric OSA patients seen between 2014-2015 with prior T&A. Respiratory events were defined as laryngospasm, bronchospasm, apnea, stridor, and desaturations requiring supplemental oxygen, positive pressure, intubation, or rapid response during the postoperative hospital course. Comorbid risk factors for respiratory compromise were also assessed.

RESULTS:
Of 312 patients with OSA, 133 patients met criteria for analysis. Thirty-six (27.1%) required PICU care, 7 of which (19.4%) were unscheduled admissions. Seven (7.2%) of the non-PICU patients had unscheduled postoperative escalations of care. Eighty-one respiratory events, most commonly re-initiation of supplemental oxygen (65.4%), occurred in 59 patients (44.4%). Of these patients, 32 (54.2%) were cared for in the PICU and experienced 53 respiratory events (65.4%). Patients in the PICU group were younger (3.4±2.5 vs 6.1±4.2 years, $p=0.0004$) and had higher preoperative AHI (17.3±16.8 vs 6.0±4.6 events/hr, $p<0.0001$), lower BMI (18.8±5.9 vs 20.2±8.2, $p=0.34$), greater percentage of PACU time requiring supplemental oxygen (70.0%±37.9% vs 30.1%±29.3%, $p<0.0001$), and more comorbid risk factors for respiratory compromise (1.7±1.2 vs 0.9±1.1, $p=0.0002$).

CONCLUSIONS:
Pediatric patients requiring increased levels of care after T&A have more risk factors for airway compromise and greater PACU oxygen requirements. Given higher costs and limited resources for PICU care, future work will include development of an algorithm to determine appropriate post-T&A PICU care as a prospective cohort study.

Predicting long-term opioid use based on opioid exposure in patients undergoing spine surgery

Johnny Wei, David Edwards MD, PhD, Jesse Ehrenfeld, MD MPH, Edward Woo PharmD, Bob Lob PharmD, Byron Stephens MD

OBJECTIVES:
Prescription opioids are amongst the most-prescribed medications in the United States, and are associated with numerous negative health consequences. In recent years, surgery has been identified as an important risk factor for chronic opioid use post-operatively. There is significant clinical utility in identifying patients at risk for worsening opioid demand or long-term opioid use after surgery. Our study aimed to identify such factors in a cohort of patients undergoing spinal surgery, and to predict an expected duration of narcotic use after certain types of operations.

METHODS:
This was a retrospective cohort study of patients who underwent either a lumbar spinal fusion or a non-fusion spinal operation not requiring hardware implantation at Vanderbilt University between May 1, 2014 and December 31, 2015. Patients were selected based on CPT codes using our institution's perioperative database. Patients were excluded if underwent another surgical operation within 12 months prior to or after their surgery, if they were younger than 18 years old, or if the procedure was a revision of prior instrumentation, involved a malignancy, or were for an infection. Post-operative opioid and benzodiazepine medication data were obtained from our cohort from the RxStar database. Demographic data not available from data extraction were found through chart review.

RESULTS:
Our final cohort included 357 patients, 135 of which underwent a lumbar spinal arthrodesis and 222 of which underwent a procedure that did not require hardware (i.e. discectomy, laminectomy, foraminectomy). We found that a fewer proportion of patients continued receiving opioid prescriptions, and the average narcotic dosage per individual decreased each month in the year following surgery. However, patients who were exposed to opioids pre-operatively were more likely to continue receiving opioid prescriptions post-operatively. Furthermore, we found that the degree of preoperative exposure to opioids and benzodiazepines as well as the type of surgery involved were predictors of continued opioid use at various postoperative timepoints.

CONCLUSIONS:
The degree of preoperative opioid and benzodiazepine exposure as well as the type of operation performed may be important indicators of how long a patient may continue to require narcotics following spine surgery. Further research on the degree of preoperative exposure could prove to be an effective indicator of postoperative opioid use.

DOES BROW LIFT ADD RISK TO BLEPHAROPLASTY? ANSWERS FROM A PROSPECTIVE, MULTICENTER ANALYSIS OF 6,126 PATIENTS UNDERGOING AESTHETIC EYE SURGERY

Blair A. Wormer, Tim M. Rankin, Christodoulos Kaoutzanis, Salam Al Kissis, Varun Gupta, Kent K. Higdon

OBJECTIVES:
The aim of this study was to evaluate the incidence of major complications following blepharolasty and brow lift surgery and to determine if complication rates increase when blepharoplasty and brow lift surgery were performed simultaneously.

METHODS:
A prospective cohort of patients who underwent cosmetic blepharoplasty, brow lift, or a combination of the two procedures between 2008 and 2013 was identified from the CosmetAssure database (an insurance program that covers unexpected major complications from cosmetic surgical procedures not covered by a patients primary health insurer). The primary outcome was a perioperative major complication requiring emergency room evaluation, hospital admission, or reoperation within 30 days. Groups were compared with univariate analysis (significant $p<0.05$).

RESULTS:
A total of 6,126 patients underwent aesthetic eye surgery, of which 4,879(79.6%) underwent blepharoplasty, 441(7.2%) brow lift, and 806(13.2%) a combination of both. Patients who underwent a combined procedure were older than patients who underwent isolated blepharoplasty or brow lift(55.5±9.4 vs. 54.6±11.1 vs. 53.3±12.0years;$p<0.01$). Combined procedures were performed less often in males compared to blepharoplasty and more often in males when compared to brow lift(12.9% vs. 17.6% vs. 10.7%;$p<0.01$); but there were similar rates of smokers(5.7% vs. 8.0% vs. 6.6%;$p=0.06$) and diabetes (3.0% vs. 3.6% vs. 2.3%;$p=0.24$) among the three groups. Between combined procedures, blepharoplasty, and brow lift there were similar rates of major complications(0.4% vs. 0.4% vs. 0.7%;$p=0.65$) and hematoma (0.2% vs. 0.2% vs. 0.5%;$p=0.49$), which was the most common complication.

CONCLUSIONS:
Aesthetic eye surgery has a very low overall major complication rate (0.4%). When brow lift is combined with blepharoplasty it poses no additional risk of major complications compared to blepharoplasty or brow lift alone.

Behavioral Effects of Amphetamine on Obese Subjects with T2DM

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OBJECTIVES:

Obesity and insulin resistance (IR) have been associated with increased impulsivity and decreased inhibitory control. IR has been posited to modulate monoamine signaling both in the striatum and cortex by decreasing clearance of dopamine (DA) in the striatum while increasing the clearance of norepinephrine (NE) and DA in the cortex. However, the effects of amphetamine, a CNS stimulant, that increases both striatal and cortical monoamine tone, have not been studied in the setting of IR. We therefore compared, in obese T2DM and age matched lean healthy controls, the effects of amphetamine on critical stop signal delay (cSSD), a measure of overall impulsivity; stop signal response time (SSRT), a measure of inhibitory function; median go response time (mGRT), a measure of impulsion; and post error slowing (PES), a measure of adaptability.

METHODS:

Impulsivity, inhibitory control, and ability to inhibit a prepotent response were measured in obese T2DM and matched healthy lean control subjects using a Stop Signal Task. From this task, an individual's PES, SSRT, cSSD, and mGRT were calculated. Right-handed obese (BMI 30-50 kg/m2) men and women with T2DM were recruited for the obese/diabetic cohort. Healthy, right-handed men and women with a normal BMI (18-25 kg/m2) and no IR were recruited for the control group. Subjects participated in the Stop Signal Task on Day 1 without amphetamine and on Day 2 with amphetamine. The study was approved by the Vanderbilt University IRB.

RESULTS:

Data from 41 obese, T2DM subjects and 16 matched healthy lean control individuals were included in the analyses. At baseline, obese T2DM and lean groups differed only in SSRT ($p< 0.04$): for obese T2DM vs lean controls, cSSD = 305 +/- 19.4 vs 334 +/- 30.7 (mean +/- SE); SSRT = 291 +/- 5.53 vs 266 +/- 9.88; mGRT = 596 +/- 17.9 vs 603 +/- 19.38; PES = 58.1 ms +/- 10.1 vs 38.4 ms +/- 17.9. Amphetamine had no significant effect on the lean subjects, but increased cSSD ($p=.008$), and decreased SSRT ($p<.001$) and PES ($p=.03$) in obese T2DM with no change in mGRT ($p=.509$).

CONCLUSIONS:

AMPH improved inhibitory (SSRT) and overall (cSSD) impulse control, and reduced PES in obese T2DM, but had little effect in older healthy lean control subjects. These results are consistent with a model suggesting that central IR promotes subcortical hyper- and cortical hypo-NE/DAergia in IR. The former leads to faster psychomotor speeds that are only minimally increased by AMPH, while the latter blunt inhibition (longer SSRT) that is improved by the

Enhanced recovery after surgery in microvascular autologous tissue-based breast reconstruction: Should it become the standard of care?

Christodoulos Kaoutzanis, Nishant Ganesh Kumar, Dillon O'Neill, Blair Wormer, Kent Higdon

OBJECTIVES:
Enhanced Recovery After Surgery (ERAS) protocol has demonstrated improved perioperative care and shorter length of hospital stay (LOS) in several surgical disciplines. The purpose of this study was to compare the outcomes of patients undergoing autologous tissue-based breast reconstruction (ABR) before and after implementation of the ERAS protocol.

METHODS:
We retrospectively reviewed consecutive patients who underwent ABR by two surgeons before and after the implementation of the ERAS protocol at a university center over a two-year period. Patient demographics, perioperative data, and 45-day postoperative outcomes were compared between the traditional care after surgery (TRAS) and ERAS patients using two-tailed Student's t-test, Fisher exact test, or Pearson chi-square test.

RESULTS:
Between August 2014 and September 2016, a total of 84 women were identified; 42 in the TRAS cohort and 42 in the ERAS cohort. Both groups had similar demographics, co-morbidities, and reconstruction types. Postoperatively, the ERAS cohort used significantly less morphine equivalents (mean ± SD: 22.48 ± 19.78 mg vs. 63.76 ± 45.59 mg, $p<0.01$) and more acetaminophen (mean ± SD: 8726.79 ± 2474.74 mg vs. 5772.02 ± 2990.88 mg, $p<0.01$) when compared to the TRAS cohort. The use of patient-controlled analgesia pump was also significantly less for the ERAS group when compared to the TRAS group (7.1% vs. 100.0%, $p<0.01$). Mean LOS was shorter with ERAS than TRAS (mean ± SD: 3.2 ± 0.5 days vs. 4.8 ± 2.4 days, $p<0.01$), which resulted in an extrapolated $234,577 savings from freeing up inpatient beds and $159,048 savings from increased contribution margins. Overall 45-day major complication rates (9.5% vs. 19.0%, $p=0.35$), partial flap loss rates (0% vs. 7.1%, $p=0.24$), emergency room visits (11.9% vs. 7.1%, $p=0.71$), hospital readmissions (4.8% vs. 9.5%, $p=0.68$), and unplanned reoperations (4.8% vs. 11.9%, $p=0.43$) were similar between the ERAS and TRAS groups.

CONCLUSIONS:
ERAS protocol implementation should be considered as the standard approach for perioperative care in ABR since it does not affect morbidity and is associated with accelerated recovery with reduced postoperative narcotic use and decreased LOS leading to downstream healthcare cost savings.

Comparison of Leadless Pacemaker Systems to Externalized Active Fixation Leads After Implantable Device System Extraction

Holly Gonzales, Travis Richardson MD, Jay Montgomery MD, George Crossley MD, FHRS, FACC, Christopher Ellis MD, FHRS, FACC

OBJECTIVES:
Pacemaker-dependent patients with cardiac implantable electronic device (CIED) extraction in the setting of infection or lead failure present a challenge. We sought to determine the utility and safety of a leadless pacing system (MICRA, Medtronic, Inc.) in patients undergoing CIED and lead extraction, compared to temporary active-fixation right ventricular lead (temp-perm) placement.

METHODS:
Single-center retrospective cohort analysis of all MICRA and temp-perm with externalized pulse generators placed after system extraction from October 2013 to October 2016 at Vanderbilt University Medical Center. Retrospective chart review was performed to aquire procedure and outcome variables.

RESULTS:
The MICRA and temp-perm cohorts had 6 and 27 patients meeting inclusion criteria, respectively. There was no difference in baseline median age (72 vs 70 years, p=0.76), gender (83% vs 74% men, p=0.32), extraction indication (p=0.27), system type extracted (p=0.39), ejection fraction < 35% (17% vs 15%, p=0.92), anticoagulation use (66% vs 59%, p=0.75), or total lead age extracted (223 vs 225.5 months, p=0.71) between cohorts. The MICRA cohort had a shorter median procedure time (110 vs 177 minutes, p=0.017) and hospital length of stay after extraction (1 day vs 7 days, p=0.0017) with no difference in major complications (16.6% vs 18.5%, p=0.92) or 30-day mortality (16.6% vs 7.4%, p=0.61). There were no reinfections in the MICRA cohort, despite 3 of the 6 having active CIED infection at the time of implant.

CONCLUSIONS:
MICRA implantation in pacemaker-dependent patients after CIED extraction is associated with reduced total procedure time and hospital length of stay, with no difference in major complications or 30-day mortality. The use of leadless pacing systems may become a safe and cost-effective alternative to traditionally used temp-perm devices.

Age >65 Does Not Increase the Risk of 30-Day Readmission or Post-Embolization Syndrome in Patients Undergoing Transarterial Chemoembolization (TACE) for Hepatocellular Carcinoma (HCC)

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OBJECTIVES:
TACE is an efficacious treatment of HCC with acceptable toxicity. However, many of these patients are elderly and there is little data on the specific risks associated with advanced age. We assessed the rate of 30-day readmission (30D) and post-embolization symptoms in patients undergoing TACE, to test the hypothesis that elderly patients (>65 years; 65+) would experience different rates of complications than younger (<65 years; 64-) patients.

METHODS:
With IRB approval, we reviewed TACE for HCC patients from 7/2013-6/2016. The primary outcome measure was 30D for 65+ vs 64- using Chi-Squared (X2) analysis. The secondary outcomes were the incidence of post-embolization fever, pain, and nausea. A secondary aim was to identify baseline or treatment variables (Child Pugh score, creatinine, portal vein thrombosis, selective embolization) for independent association with 30D via X2. A $p<0.05$ was significant.

RESULTS:
191 patients underwent 261 TACE; 30D was not significant between 65+ (n=7, 7.5%) and 64- (n=17, 12.4%, p=0.286). Similarly, incidence of post-embolization fever, pain, and nausea did not differ significantly between the groups. Variables associated with 30D were Child-Pugh B/C ($X2=7.9$, $p<0.01$), history of encephalopathy ($X2=15.4$, $p<0.01$) and ascites ($X2=4.4$, $p<0.05$). Baseline laboratory values did not differ significantly between 65+ and 64-, nor did portal vein patency or extent of embolization.

CONCLUSIONS:
Patients> 65 years old are not at greater risk of 30-day readmission or post-embolization syndrome following TACE than younger patients.

Characteristics Associated with Problematic Pediatric Transport

Shelley Murphy, Lee Blair RN, CEN, EMT-P, IC, Rhonda Phillippi RN, BA, Donald Arnold MD, MPH

OBJECTIVE:

To examine patient and transport characteristics associated with problematic transports to a tertiary children's hospital ED.

METHODS:

We analyzed data from a prospectively recorded registry of patient transports to our children's hospital ED during the years 2011 – 2016. A problematic transport was defined as a transport during which a preventable, potentially adverse event occurred during the transportation of a pediatric patient by ground EMS, helicopter, or fixed-wing aircraft. These events could be identified by any health care professional (RN, RT, Charge Nurse, ARNP, or MD) at which time patient and transport characteristics were entered into the registry database, including age, gender, method of transportation, type of problem, and severity of problem.

RESULTS:

During the study period, there were 668 problematic transports, 646 of which had complete data. Patient characteristics and details of the transport were recorded for each event. Amongst these 646 problematic transports, median [IQR] age was 4 [1, 11] years and age range was 2 d – 23 years, 59 % male gender, 48% trauma patients, and 2 EMTALA violations. The 5 most prevalent problems included "Patient should have come via EMS, POV (personal vehicle) was inappropriate" (9.29 %), "Improper immobilization" (8.2 %), "Failure to Completely Assess the Patient" (7.59 %), "Maintenance of IV/IO" (5.73 %), and " Patient should have come via Specialty Care Team" (4.49 %). These top 5 problems totaled 35.5 % of all the problematic transports for a 6-year period. Age was associated with circulatory problems during transport after adjustment for gender and location of referring facility, such that each increase in age of 1 year was associated with a 10% increased odds of hemodynamic instability (aOR 1.1, 95% CI 1.0, 1.2).

CONCLUSIONS:

Problematic transports are not uncommon, occur approximately every 3 days, and involve predominantly young, male patients and the choice of mode of transport. The top five causes comprise 35.5 % of all the problems encountered. This knowledge may inform education to improve transport safety.

Apneic Oxygenation During Pediatric Intubations

Shelley Murphy, Craig Sneedy MD, Donald Arnold MD, MPH

OBJECTIVES:
To determine whether AO during pediatric ETI decreases progression to hypoxemia during the procedure.

METHODS:
We retrospectively reviewed standardized ETI documentation records during an era (2011) in which AO was not used for ETI attempts in our tertiary, urban children's hospital emergency department. We included all pediatric patients intubated within a 1-year period prior to initiation of AO. We then prospectively recorded variables for each patient requiring ETI after implementation of an AO protocol. Patient characteristics, pulse oximetry (SpO2) before, and the lowest SpO2 during ETI were recorded by a dedicated scribe on a standardized study form and entered into a REDCap database. Our primary outcome was the 25th percentile for the distribution of lowest SpO2 values during ETI, an outcome chosen because we desired to identify meaningful hypoxemia. Frequencies were used to describe patient demographic characteristics and Kruskal-Wallis was used to examine whether there were differences of 25th percentile for lowest SpO2 between patients receiving and those not receiving the intervention.

RESULTS:
The median [IQR] age of patients in the pre-AO was 1 [0.8, 4] in the pre-AO cohort and 4 [0.5, 13] years in the AO cohort. The 25th percentile for SpO2 in the pre-AO cohort was 71% and in the AO cohort was 93%. One quarter of patients in the pre-AO group experienced SpO2 during ETI attempt £ 71%, with 57% requiring one ETI attempt, 9% requiring two attempts, and 23% requiring > two attempts. In the AO group, one quarter of patients experienced SpO2 £ 93%, with 79% requiring one ETI attempt, 11% requiring two attempts, and 9% requiring > two attempts. There was a significant difference in the median lowest SpO2 between pre-AO patients (93%) and AO patients (99%, $P<0.001$).

CONCLUSIONS:
ETI with apneic oxygenation by nasal cannula is less likely to be associated with clinically meaningful hypoxemia in pediatric patients than ETI without apneic oxygenation.

Lung and Breast Screening Practices in Women: Use of a Selection Algorithm to Increase Enrollment in the Vanderbilt Lung Screening Program

Carolyn Scott, Alexis Paulson, Travis Osterman, Kim Sandler

OBJECTIVES:

Lung cancer is the leading cancer killer of women and is estimated to have caused more than 72,000 deaths in women in 2016. A former absence of screening guidelines resulted in traditionally late-stage diagnoses with limited treatment options and high mortality rates. In 2013, official lung screening criteria were endorsed by the US Preventive Services Task Force based on results from the National Lung Screening Trial which established the efficacy of lung screening with annual low-dose CT in patients who meet screening criteria (age 55-80 years and smoking history of 30 pack-years with current smoking status or cessation within the past 15 years). However, adoption of these screening guidelines has been slow in many practices. This study focuses on women enrolled in the Vanderbilt Lung Screening Program, 75% of whom have also had a mammogram at Vanderbilt. This fact makes it likely that women currently undergoing screening mammography at Vanderbilt are a target-rich population for further lung screening enrollment. This study estimates the number of women undergoing screening mammography at Vanderbilt who also qualify for lung screening through the use of a selection algorithm.

METHODS:

Data from 18,040 women who underwent screening mammography in 2015 at Cool Springs (CS) and One Hundred Oaks (OHO) imaging centers was collected. A selection algorithm capable of accessing data in the electronic medical record was run on these women to determine their smoking histories in pack-years and eligibility for lung screening. Manual chart review of women identified as eligible was completed to quantify smoking history and determine final eligibility status for lung screening.

RESULTS:

The selection algorithm identified 686 (3.8%) of the 18,040 women who had screening mammograms in 2015 at CS and OHO as qualifying for lung screening. Manual chart review revealed that 252 of these 686 (1.4% of total) women actually qualify for lung screening based on age and smoking history. Of these 252 women, 31 are currently enrolled in the lung screening program, leaving 221 newly identified eligible women.

CONCLUSIONS:

The Vanderbilt Lung Screening Program could more than double the number of women currently enrolled by including these newly identified women. It is also likely that even more women qualify from this mammography population than were identified because of underestimation of some smoking histories by the selection algorithm. Future directions will include providing outreach to theses women and their providers to ensure they have access to lung screening.

Surfactant Exposure Is Associated With Failure of Indomethacin Treatment for Patent Ductus Arteriosus

Sydney Rooney, Ronald Clyman, John Dagle, Kelli K. Ryckman, Tamorah Lewis, Elaine L. Shelton, Sara Van Driest, Jeff Reese, Prince Kannankeril

OBJECTIVES
Pre-term infants with a birthweight <1000g have a 70% likelihood of developing a patent ductus arteriosus (PDA) that necessitates medical or surgical treatment. PDA treatment with indomethacin has a 30% failure rate and significant risk for adverse effects. Some studies suggest that indomethacin dose should be increased for infants who receive surfactant. Thus, the objective of this study is to assess clinical factors, including surfactant exposure and respiratory distress syndrome (RDS), associated with indomethacin response in PDA treatment, enabling targeted use.

METHODS:
This nested cohort study of 171 infants used clinical data collected over five years for a larger "Genes Contributing to Preterm PDA" study of infants from neonatal intensive care units at three sites: Vanderbilt University Medical Center, University of California, San Francisco, and University of Iowa. Infants in the primary cohort 23-32 weeks estimated gestational age (EGA) who received at least one treatment course of indomethacin for PDA (0.1-0.25 mg/kg at 12 hour intervals) were included. Infants were excluded if they had multiple congenital anomalies, significant congenital heart disease, or died prior to an echocardiogram. Infants were classified as responders if no further intervention (i.e. surgical ligation) was required after indomethacin. Univariate and multivariate analyses for association of candidate clinical predictors of indomethacin response were performed using Fisher's exact test, Wilcoxon-Mann-Whitney test, and logistic regression.

RESULTS:
In univariate analyses of 171 patients (48% male), only female sex (OR 1.97; 95% CI 1.03-3.79; p-value 0.04), lower EGA (OR 0.71 per week older; 95% CI 0.58-0.87; p-value 0.001) and surfactant exposure (OR 11.9; 95% CI 1.56-91.2; p-value 0.02) were significantly associated with failure of indomethacin. In multivariate analysis correcting for EGA and sex, surfactant exposure remained a significant predictor for indomethacin failure (OR 11.55; 95% CI 1.46-91.33; p-value 0.020). When RDS was included in the model, surfactant exposure remained significant (OR 11.5; 95% CI 1.45-91.20; p-value 0.021).

CONCLUSIONS:
Higher gestational age, male sex, and lack of surfactant treatment are associated with successful indomethacin treatment for PDA. In this multicenter cohort, surfactant use serves as a more significant predictor of indomethacin response than RDS.

Urinary apolipoprotein A-I (apoAI): Potential new marker of tubulointerstitial kidney disease (TID)

Amanda J. Clark MD,Kathy Jabs MD, Tracy E. Hunley MD, Deborah P. Jones MD, Rene G VanDeVoorde III MD, Carl Anderson DNP, Jianyong Zhong MD, PhD, Valentina Kon MD

OBJECTIVES:

Rationale. Most pediatric kidney disease is due to congenital or hereditary nephropathies that involve TID. Albuminuria (ACR) is a commonly used urinary marker of kidney dysfunction. However, increased ACR primarily reflects glomerular disease. Other urinary markers of acute tubular injury have been proposed, but their utility to diagnose and monitor TID is inconsistent, especially in chronic TID. Circulating lipoproteins (LP) can predict cardiovascular disease and progressive kidney damage, but urinary LP have rarely been examined as kidney dysfunction biomarkers because most are too large to cross the glomerular filtration barrier. ApoAI, the primary component of high-density lipoprotein, is smaller than albumin and can cross the glomerulus to be taken up by the proximal tubule. *Hypothesis:* We hypothesized that renal damage affecting glomerular and/or tubulointerstitial handling of apoAI will alter excretion patterns of apoAI. Therefore, our objective is to determine whether urinary excretion of apoAI, compared with ACR, distinguishes children with glomerular and tubulointerstitial disease from those with isolated hypertension or no kidney disease.

METHODS:

Urine was collected from all patients seen in Pediatric Nephrology clinic during the study period and from healthy volunteers ages 3-18. Clinical data were obtained from medical records, and patients were sorted by primary diagnosis. Urinary apoAI and ACR were measured by ELISA and expressed as a ratio with urine creatinine. Mean values were compared to controls using a two-tailed t-test.

RESULTS:

164 patients and 10 controls (C) were enrolled. Mean urinary apoAI in C, isolated hypertension, and renal disease were 0.17, 0.18 (p=NS vs C), and 2.13 ug/mg ($p \leq 0.001$ vs C). Notably, patients with relapsed nephrotic syndrome (extreme disruption of filtration barrier) had urinary apoAI similar to C, 0.58 (p=NS) despite high ACR of 258 ug/mg (p=0.01) suggesting complete tubular uptake of filtered apoAI. By contrast, children with TID with/without glomerular damage had markedly elevated urinary apoAI at 3.86 (p=0.01) with ACR of 174 ($p \leq 0.001$).

CONCLUSIONS:

Post-glomerular damage characterizing TID hampers efficient uptake of apoAI that is not dependent on GFR. Injury involving the glomerular filtration barrier alone does not increase urinary apoAI indicating efficient salvage of filtered apoAI. Urinary apoAI may be a novel marker of congenital or acquired tubulointersitital injury that may present a new opportunity to specifically diagnose and monitor TID in children.

Predicting Trauma Volume and Acuity: how weather and timing effect trauma flow

David P. Stonko, Bradley M. Dennis, Richard D. Betzold, Oscar D. Guillamondegui

OBJECTIVES:
To describe the temporal and weather patterns associated with trauma admission frequency and severity, and to develop an Artificial Neural Network (ANN) to predict trauma volume, severity, and the resources required to treat these traumas.

METHODS:
We performed a cross-sectional analysis of trauma patients who presented to Vanderbilt between July 2013 and June 2016. These data were amalgamated with weather condition data taken from NOAA.
Initially we created a mathematical description of trauma prevalence at this large level 1 trauma center using descriptive statistics and with bivariate frequency analysis. Then we developed a two-layer, feed-forward ANN using 10 sigmoid hidden neurons and trained this with the Levenberg-Marquardt backpropagation algorithm. Mathematical analysis and ANN creation was performed in Matlab R2016b.

RESULTS:
We developed a novel machine-learning algorithm that can predict trauma prevalence for any given day with good accuracy. The study population was 1,096 days over July 2013 to June 2016, during which 10,740 trauma patients were admitted. Of these, 10,612 trauma patients had sufficient injury and admission to be considered.
This new model takes four input variables: the date, the day of the week (e.g. Monday, Tuesday, etc.), the daily high temperature (°F), and whether there is precipitation or not (binary variable). It then, based on training it has received from prior exposure to our database, makes four predictions: the number of total traumas, the number of penetrating traumas, the number of cases that need immediate operative management, and the mean daily ISS. It makes these predictions with good accuracy ($r = 0.9018 \pm 0.002$; validation $r = 0.8899 \pm 0.005$). With knowledge of typical daily admission rates and average daily ISS, the model can then predict whether the day of interest will have "low", "normal", or "high" admission rates or acuities.

CONCLUSIONS:
We have taken a large cohort of trauma admission data and coupled this with local weather readings at the time of injury to examine the role that weather conditions and temporal patterns play in driving differential trauma flow. We use these patterns to create a novel new machine-learning algorithm to predict trauma prevalence at this institution for a given day of interest. This will be useful for predicting resource usage throughout the trauma system: from helicopter availability to surgeon staffing. It will also be useful for predicting ideal times for handovers and trainee didactics, so as to avoid interruptions by trauma activations.

Why Share Data in Health Care Ethics Consultation?

Kelly Wolenberg Harris, MD, Joseph Fanning, PhD, Kelly Armstrong, PhD, Thomas Cunningham, PhD

OBJECTIVES:
Studies across the health care spectrum show that sharing data improves the quality of care. Yet questions continue regarding whether data sharing in Health Care Ethics Consultation (HCEC) would similarly improve quality. To foster a culture of data sharing, several challenges must be overcome: the plausibility that data sharing could improve practices of HCEC needs to be demonstrated; concerns that data sharing would undermine local practices of HCEC must be addressed; and the infrastructure for data sharing needs further development. This study begins to address the first challenge by reporting statistically significant findings from one institution and postulating the benefits of comparing this data with other institutions.

METHODS:
HCEC data was collected for twenty months at VUMC using the Armstrong Clinical Ethics Coding System. With IRB approval, this data was analyzed in a two-step process. First, hypotheses were generated for multiple key domains to see whether statistically meaningful relationships could be established. SPSS was used to run chi-square tests, one-sided ANOVA tests, and logistic regressions; odds ratios were calculated with 95% confidence intervals (alpha = 0.05). Next, descriptive and statistically significant findings were interpreted with one question: which findings could be generalized to enable comparison with other institutions in order to improve HCEC practice?

RESULTS:
Physicians requested over 50% of consults; patients or family members requested 1.2%. Over 90% of consults were patient related; 10% involved theoretical or policy questions. Case content most frequently involved goals of care, decision-making, and withholding/withdrawing life-sustaining treatment. Twenty unique content code associations were identified, including decisional capacity and refusal of recommended treatment/testing (OR 2.40, CI 1.13–5.11). Adult consults were more likely to focus on substitute decision-making (OR 2.07, CI 1.05–4.10); pediatric consults were more likely to focus on end of life decision-making (OR 2.21, CI 1.12–4.36). Residents were more likely to request adult consults while attendings were more likely to request pediatric consults (OR 6.45, CI 2.06–20.18).

CONCLUSIONS:
At VUMC, increasing pediatric resident exposure to HCEC may increase the likelihood of those individuals requesting consults. Inter-institutional comparisons can be facilitated by standardizing data collection through a shared coding system or possibly through a collective agreement to track common domains important for the practice of HCEC.

Evaluating the Sino-Nasal Outcome Test (SNOT-22) for the Pediatric Cystic Fibrosis (CF) Patient Population

Deborah Xie, Chevis N. Shannon, MBA, MPH, Frank W. Virgin, Jr., MD

OBJECTIVES:

The prevalence of chronic rhinosinusitis (CRS) in patients with cystic fibrosis (CF) approaches 100%. CRS rarely worsens mortality of CF, but can significantly impact a patient's quality of life (QOL). There are currently no validated surveys to evaluate health-related QOL (HRQOL) of CRS in children with CF. The Sino-Nasal Outcome Test (SNOT-22) has previously been used to evaluate adults with CRS. The Cystic Fibrosis Questionnaire-Revised (CFQ-R) is used to evaluate disease-specific HRQOL across multiple domains in patients over 6 years of age with CF. Our study aims to evaluate SNOT-22 as an instrument in the pediatric CF population, as well as assessing the ability of SNOT-22 to predict the need for surgical intervention and/or hospitalization in the same patient population as compared to CFQ-R.

METHODS:

This is a prospective cohort study evaluating English speaking pediatric patients ages 2-17 seen in the Cystic Fibrosis Clinic. Patients and their parents completed the age-appropriate SNOT-22 and CFQ-R surveys. Surveys were administered at every point of contact over the course of 1 year. Test-retest reliability and internal consistency were assessed with analysis of the kappa coefficient to determine reliability. Logistic and multivariate regression models were used to assess the impact of symptomatology, medical management, and surgical intervention on quality of life.

RESULTS:

Twenty-nine patients were seen over 31 encounters. Median age was 10 years (IQR 6-14). Of our patients, 93.1% are white and 6.9% are African American. SNOT-22 survey scores classified 14 patients (42.3%) as having mild symptoms, 18 (62.1%) with moderate symptoms, and 1 (3.4%) with severe symptoms. The CFQ-R domain with the highest median score was physical (91.67/100). Treatment burden had the lowest median score (55.56/100). Six of the 13 domains evaluated by the CFQ-R had scores ranging from 0-100.

CONCLUSIONS:

The patients seen in CF clinic have a wide range of HRQOL as captured by these two instruments. There is possibly a correlation between the CFQ-R and SNOT-22 scores, but this relationship represents a significant variation in the baseline data of our patients. Further work will analyze this relationship stratified by patients' versus parents' surveys, age, and correlation with reported symptoms. We will also confirm the reliability and validity of SNOT-22, and investigate the ability for both instruments to predict need for surgical intervention or hospitalization.

Systolic Blood Pressure within 24 Hours After Thrombectomy for Acute Ischemic Stroke Correlates with Outcome

Akshitkumar Mistry, Eva Mistry, Michael Froehler, Rohan Chitale, Robert James, Matthew Fusco, John Volpi

OBJECTIVES:

Stroke is a leading cause of death and disability worldwide. Current guidelines suggest only treating blood pressure (BP) above 180/105 mmHg during the first 24 hours in patients treated with any form of recanalization therapy for acute ischemic stroke (AIS). However, no studies exist to guide BP management in AIS patients treated specifically with mechanical thrombectomy (MT), which was proven by five randomized trials in 2015 to be superior to medical treatment. We aimed to determine the association between BP parameters within the first 24 hours after MT and patient outcomes.

METHODS:

We conducted a retrospective study of patients treated between 3/2015 and 10/2016 at three academic comprehensive stroke centers in three different states in the U.S. A consecutive sample of adult patients treated with MT for AIS were identified from prospectively collected stroke databases. The primary variables of interest included patients' maximum, minimum, range, and mean values of systolic (SBP), diastolic (DBP), and mean arterial pressures (MAP) in the first 24 hours after MT. The primary study outcome was patients' functional status at 90 days measured on the modified Rankin scale (mRS). Secondary outcome was the incidence intracranial hemorrhage within 48 hours after MT. Associations between these BP parameters and outcomes were explored using ordered multivariate logistic regression analyses, adjusting for patients' age, co-morbidities, antiplatelet/anticoagulant drug use, stroke location and severity and treatment with IV tPA, time from stroke onset to MT, extent of recanalization achieved by MT, and anti-hypertensive or vasopressor medication use post-MT.

RESULTS:

A total of 228 patients were included. Maximum and range of SBP independently correlated with a worse 90-day mRS (adjusted odds ratio (OR)=1.02 [1.01-1.03], p=0.004; 1.02 [1.00-1.03], p=0.01; respectively) and hemorrhagic complications within 48 hours after MT (OR=1.02 [1.01-1.04], p=0.002; and 1.03 [1.01-1.04], p<0.001; respectively). As a group, patients with SBP < 160 mmHg had better 90-day mRS (p<0.0001) and lesser incidences of hemorrhage (p<0.0001) than those with a peak value of SBP ≥ 160 mmHg.

CONCLUSIONS:

Higher peak values of and greater variability in SBP independently correlated with worse functional outcomes in patients at 90 days and a higher rate of inpatient hemorrhagic complications. Further prospective studies are warranted to identify whether BP is a therapeutic target to improve outcomes by preventing reperfusion injury, or is it merely a marker of poor outcome in stroke patients treated with MT.

Pregnancy Intention and Maternal Alcohol Consumption

Jason Pryor, MD, Stephen W. Patrick, MD, MS, MPH, Alexandra C. Sundermann, BS, Pingsheng Wu, PhD, Katherine E. Hartmann, MD, PhD

OBJECTIVES:
The Centers for Disease Control and Prevention has experienced a rough ride in the wake of new public health outreach defining "any alcohol use by women who are pregnant or might be" as drinking too much. Since half of US pregnancies are unplanned and effects of fetal alcohol exposure can be devastating, the guidance recommends that all women planning a pregnancy or not using reliable contraception abstain from alcohol. The CDC guidance presumes women who desire a pregnancy in the near term will abstain. We aimed to test this hypothesis and document patterns of alcohol use around conception and early pregnancy. We also investigated association of various maternal characteristics with risk of continued drinking.

METHODS:
Right From the Start (2000-2012) is a prospective, community-based pregnancy cohort. Maternal demographic, reproductive, and behavioral data were collected in telephone interviews at enrollment (mean ± SD: 48 days ± 13 days gestation) and in the first trimester (mean ± SD: 85 days ± 21 days). The interviews included detailed information about alcohol consumption including: current/past use, amount, frequency, type of alcohol, binge drinking, and changes in pattern of use. We used logistic regression to investigate the independent association of intendedness with alcohol use in pregnancy.

RESULTS::
Among 5,036 women, 55% reported using alcohol in the first trimester with 6% continuing use at the first trimester interview. Pregnancy was planned by 70% of participants. Alcohol use occurred in 55% of intended pregnancies and 56% of unintended pregnancies, respectively (p=0.32). Adjusting for confounders including maternal age, parity, education, ethnicity, income, and BMI, women with intended pregnancies were 31% less likely to consume alcohol in pregnancy (adjusted OR (AOR) 0.69, 95% CI 0.60-0.81). Women who were older, white, college educated, had higher incomes, and having their first pregnancy were most likely to use alcohol in pregnancy, adjusting for intention. Binge drinking episodes were also less likely among the intended pregnancies (AOR 0.68, 95% CI 0.54-0.86). Most women, regardless of intention, stopped or decreased alcohol consumption in early pregnancy.

CONCLUSIONS:
The majority of women, irrespective of intention, stopped or decreased decreasing after pregnancy recognition. This suggests promoting early pregnancy awareness could prove more effective than promoting abstinence from alcohol among all who could conceive.

Developing an Integrative Medicine Educational Program to Support Oncology Patients through Radiation Treatment: a Feasibility Study

Kareem Fakhoury, Mark Stavas

OBJECTIVES:
Radiation therapy is associated with situational anxiety in many patients due to a perceived lack of control. In contrast, integrative medicine uses complementary health approaches (CHAs) to improve self-efficacy in pursuing wellness. Patients acknowledge a need for improved education on CHAs and have shown interest in attending a hospital-based educational program. We collaborated between an academic institution's integrative medicine center and radiation oncology department to develop a novel, interactive lecture series. Our objective was to assess the feasibility of this program in improving self-efficacy (empowerment).

METHODS:
A structured curriculum of four one-hour lectures covered topics of meditation, yoga, massage therapy, and nutrition, each led by a topic expert. Lectures included didactic and interactive components. The primary outcome was self-efficacy measured by 5 items on 9-point Likert scales via pre- and post-lecture surveys.

RESULTS:
Overall, 43 surveys were completed. Between pre- and post-lecture surveys, median scores of agreement with the statements "I have tools to manage my disease on my own", "I have control over my cancer", and "I believe achieving wellness is due to my efforts" increased from 6/9 to 7/9, 5/9 to 6/9, and 7/9 to 8/9, respectively.

CONCLUSIONS:
Survey results demonstrate significant benefit to participants. However, the study posed major costs and barriers. Substantial time was needed to plan lectures and coordinate logistics. Additionally, patient attendance was limited by timing and transportation issues. To increase reach and minimize cost, we suggest further study on an educational program that is integrated into the oncology clinic visit or available in an online format.

Lower Serum Albumin Levels are Associated with Longer Lengths of Stay (LOS) Following Cystectomy: The National Surgical Quality Improvement Program

Rohan Bhalla, Li Wang, Sam S. Chang, Mark D. Tyson

INTRODUCTION & OBJECTIVES:
Serum albumin levels have been reported to be a valid measure of nutritional status for epidemiologic studies. However, contemporary population-based epidemiologic data evaluating the effect of preoperative albumin levels on LOS after cystectomy and urinary diversion is limited. In this study, we measure the relationship between preoperative serum albumin level and hospital LOS and hypothesized that decreasing preoperative albumin levels would be associated with increasing LOS. Such an association would strengthen the importance of preoperative nutritional optimization prior to cystectomy.

METHODS:
Data was acquired from the 2014-2015 National Surgical Quality Improvement Program database. We identified 2,469 adult patients who underwent a cystectomy between January 1st 2014 and December 31st 2015. The primary outcome was hospital LOS and the primary exposure was preoperative albumin. We fit proportional odds logistic model with patient-level variables that were either known to be associated with increased LOS or that we had hypothesized would be prior to model fitting. We allowed all continuous variables to have a nonlinear relationship with the primary outcome using restricted cubic spline with 5 knots.

RESULTS:
Multivariable proportional odds logistic regression determined that preoperative serum albumin was independently associated with LOS (OR: 0.81; 95% CI: 0.64-1.02; $p<0.001$). It was demonstrated that LOS increased significantly for patients with a serum albumin level of less than 4 g/dl. Other significant predictors include older age (OR 1.56; 95% CI 1.21-2.01; $p<0.001$), elevated BMI (OR 1.48; 95% CI 1.17-1.86; $p<0.001$), and non-Caucasian patients (OR 1.7; 95% CI 1.34-2.18; $p<0.001$).

CONCLUSIONS:
This study provides evidence that lower preoperative serum albumin levels are associated with increasing LOS. Efforts to optimize a patient's nutritional status prior to cystectomy undoubtedly have many benefits, including a shorter LOS.

Trial of labor versus cesarean delivery in women with superobesity

Jennifer L. Grasch, J.M. Newton, Jennifer L. Thompson, Sarah S. Osmundson

BACKGROUND:
Approximately 2% of the US obstetric population is superobese, defined as BMI >=50. Delivery in superobese women is associated with increased maternal and neonatal morbidity, both with labor and planned cesarean delivery (CD). To date, no studies have evaluated planned CD as opposed to an attempted vaginal delivery (trial of labor) in women with superobesity. This study aims to aid clinicians in delivery management and prenatal counseling for this population.

OBJECTIVE:
To assess maternal and neonatal outcomes among women with superobesity who undergo a primary cesarean delivery versus a trial of labor.

METHODS:
This is a retrospective cohort study of all women with BMI >= 50 admitted to Vanderbilt University Medical Center for delivery of a viable fetus between 1/1/2008 and 12/31/2015. Women with multiple gestations, carrying fetuses with major anomalies, or delivering at less than 34 weeks' were excluded. The primary outcome was perinatal morbidity, a composite of maternal and neonatal morbidities, including infections, severe maternal morbidity, wound complications, and various markers of adverse neonatal outcomes. Outcomes in women undergoing trial of labor versus primary CD were compared using a simple t-test, with statistical significance defined as $p<0.05$. Multivariate analysis was used to control for potential confounding variables.

RESULTS:
During the study period, 344 women met inclusion criteria. 58% of women (n=201) labored, while 42% (n=143) underwent a planned CD. Among women who labored, 45% ultimately required a CD, most commonly for labor arrest (61%) and non-reassuring fetal status (28%). Overall composite morbidity was reduced among women who labored due to lower risks of infectious, wound, and neonatal morbidities ($p<0.001$). After adjusting for maternal age, nulliparity, preexisting diabetes, gestational age at delivery and prior cesarean delivery, this relationship remained significant (adjusted OR 0.42, 95% CI 0.24-0.75). Severe maternal morbidity (SMM) was doubled in women who labored prior to CD, compared to those who underwent pre-labor CD (8.8% vs 2.1%, RR 4.2, 95%CI 1.14-15.4), but SMM could not be examined in logistic regression due to the small number of women with the outcome (n=12).

CONCLUSIONS:
Despite high rates of cesarean delivery in women with superobesity, labor is associated with lower perinatal morbidity than planned CD. Severe maternal morbidity may be higher in women who require a CD after laboring, a finding which warrants further investigation with a larger sample size.

Seronegative progressive encephalomyelitis with rigidity and myoclonus (PERM)

Ehtesham Khalid, Patrick Lavin, Dago

INTRODUCTION:

Tactile startle is an uncommon manifestation that localizes to the brainstem. It occurs in pediatric epileptic patients predominantly, but can occur in adults with brainstem disease such as infection, inflammation, and neurodegeneration. Our patient presented with multiple cranial neuropathies and an exaggerated tactile startle response.

CASE REPORT;

A 75-year-old man with a remote history of carcinoid lung cancer, and renal cell carcinoma, presented with progressive dysphagia, dysarthria and alternating facial weakness for about 2 weeks. He noticed abnormal tongue sensation, and dysarthria. A video swallowing study demonstrated oropharyngeal dysphagia. He had progressive fatigue, left facial dysesthesia, and frequent brisk startle responses to facial stimulation. He had no fever or weight loss. He developed episodes of tachypnea with oxygen desaturation, episodes of tachycardia-bradycardia, then a cardiac arrest responding to CPR. Subsequently, he developed ophthalmoplegia, pyramidal extremity weakness, transient hyponatremia responding to fluid restriction, and then stiffness in his lower limbs. Contrasted brain MRI, LP with cytology and flow cytometry, paraneoplastic panel, and HIV testing were negative. Sedimentation rate 78, C-reactive protein 23.3, and serum protein electrophoresis detected monoclonal bands (IgG lambda type). PET scan demonstrated focal mediastinal lymph gland up take. Bronchoscopy with biopsy confirmed SCLC. He received IVIG and high-dose steroids with no response. He began chemotherapy with a plan for radiation of the abnormal mediastinal glands.

DISCUSSION:

The spectrum of paraneoplastic disorders, particularly affecting the nervous system, is expanding rapidly with the discovery of new antibodies. Because the sensitivity of paraneoplastic antibody testing is low (sensitivity 34%, specificity 86%) neurologists must be aware of, and be vigilant for, such syndromes that often require total body imaging to uncover the offending neoplasm.

Initiative to Reduce Chest X-ray Use for Pediatric Patients with Acute Asthma Exacerbations

Caroline Watnick, MD, Donald H. Arnold, MD, MPH, Richard Latuska, MD, Michael O'Connor, MD, David P. Johnson, MD

BACKGROUND:
Chest radiography is not routinely recommended for pediatric patients with a history of asthma who present with acute asthma exacerbations. However, chest x-rays (CXR) are frequently obtained on these patients, contributing to unnecessary radiation exposure and cost. Initial implementation of an asthma clinical practice guideline (CPG) reduced CXR ordering, but not to our goal.

OBJECTIVES:
To use quality improvement methodology to further decrease the percentage of CXR obtained for pediatric patients with acute asthma exacerbations from a historical baseline of 29.5% to < 20% by December 2016. Additionally, to evaluate whether changes in CXR ordering practices are associated with decreased antibiotic use in asthmatic patients.

METHODS:
We included children ≥2 years presenting to our tertiary care children's hospital emergency department or inpatient units with ICD-9/ICD-10 primary billing codes for asthma. One year of baseline data was obtained prior to the initial CPG implementation in May 2014. To focus on CXR ordering, in December 2015 we formed a multi-disciplinary team to develop key drivers to identify potential areas to intervene including electronic ordering system updates, CPG revisions, and education. Due to the seasonality of exacerbations, patients were cohorted into groups of 40, and the percent of children receiving a CXR or systemic antibiotics was followed using an annotated p-chart with 8 points below the mean line indicating special cause variation.

RESULTS:
Data were collected for 40 months, including 5,640 patients receiving 1,368 CXR. CPG implementation reduced CXR use from 29.5% to 23.6%. Targeted QI methodology further reduced usage from 23.6% to 15.2%. The percentage of children receiving antibiotics decreased from 5.97% to 4.46% after initial CPG implementation. There was no difference in all cause 72-hour return ED visits after any intervention.

CONCLUSIONS:
Implementation of an asthma CPG is associated with slight reduction in CXR ordering, but targeted QI methodology is associated with further and sustained reductions that met our goal. Antibiotic administration remained low before and after interventions. Decreasing CXR use was not associated with increased return ED visits, likely representing very low numbers of missed diagnoses related to lack of imaging.

Chest Radiography in Pediatric Patients with Acute Asthma Exacerbation Rarely Influences Management

Evan Hawkins Allie, William Neil Johnson, Henry Evan Dingle, Jeffery Birnbaughm, Sudha Singh, Melissa Hilmes, Donald Hayes Arnold

OBJECTIVES:
To determine, in a population of pediatric patients with acute asthma exacerbations who have CXR performed, whether (1) Patient characteristics are associated with abnormal CXR findings; and (2) CXR findings change patient management that resulted in administration of antibiotic in the PED for pneumonia on CXR.

METHODS:
We performed a retrospective review of PED patients with acute asthma exacerbations who had CXR performed in our children's hospital PED during the period of January 1, 2014 to December 31, 2014. Inclusion criteria were age > 36 months, primary diagnosis of asthma, and no other chronic disease beside asthma. Each CXR was interpreted by a pediatric radiologist as definite or indeterminate pneumonia, with the latter studies adjudicated by two radiologists and excluded from analysis if there was non-agreement. We examined univariate associations between patient characteristics and pneumonia on CXR and between pneumonia on CXR and administration of antibiotic. We used multiple logistic regression models to examine adjusted associations between patient characteristics and pneumonia on CXR and between pneumonia on CXR and administration of antibiotic.

RESULTS:
Amongst 288 patients median [IQR] age was 7 [4, 10.5] years, 146 (60%) were African-American race, 157 (64%) male, and 61 (21%) were febrile. There were no associations between pneumonia on CXR and age, race, gender, insurance status, presence of hypoxia, mode of PED arrival, presence of fever (all p values > 0.5) or crackles on pulmonary exam (p=0.07), but an association with antibiotic within 7 days (p=0.002). In multiple logistic regression models adjusted for these covariates only use of antibiotic within 7 days of PED presentation was associated with pneumonia on CXR (aOR 3.6, 95% CI 1.5, 9.0)and with change in patient management by administration of antibiotic (aOR 3.3, 95% CI 1.4, 7.7).

CONCLUSIONS:
CXR rarely adds valuable information in the evaluation of pediatric patients with acute asthma exacerbation. Patients treated with antibiotic within the preceding 7 days for presumed pneumonia are more likely to have pneumonia on CXR and continued antibiotic administration by a PED clinician.

Respiratory rate predicts lung function and disease severity during acute asthma exacerbations

Cody H. Penrod, Donald H. Arnold

Background:
Respiratory rate (RR) is a key vital sign and a strong indicator of severity in respiratory illness. There is limited knowledge whether RR is associated with measures of lung function and disease severity during acute asthma exacerbations.

OBJECTIVES:
To examine whether there are associations between RR and %-predicted forced expiratory volume in 1-sec (%FEV1), %-predicted airway resistance by impulse oscillometry (%IOS) and the Acute Asthma Intensity Research Score (AAIRS), a validated, 0-16 point bedside severity score (16 most severe).

DESIGN/METHODS:
We prospectively studied patients, ages 5-17 with asthma exacerbations in an urban, tertiary pediatric emergency department. Complete pulmonary exams were performed, including measurement of RR on room air for a 60 second interval with participants at rest, supine with the head of the bed elevated to approximately 30 degrees. Participants attempted %FEV1, and %IOS measurement and had AAIRS calculated by a trained clinician before treatment. Associations of respiratory rate with %FEV1, %IOS, and AAIRS was assessed using multivariable linear regression models.

RESULTS:
Amongst 933 participants, median [IQR] age was 8.8 [6.9, 11.2], 551 (59%) were African-American, 569 (61%) were male, RR was 26 [22-31], %FEV1 was 50% [36-71%], and AAIRS was 5 [2-7]. In multivariable regression models adjusted for age, gender and race, there were associations of RR with %FEV1 (β-coeff -1.7, 95%CI -2.0, -1.4), %IOS (β-coeff 2.9, 95%CI 1.3, 4.5) and the AAIRS (β-coeff 0.25, 95%CI 0.23, 0.28).

CONCLUSIONS:
An accurately measured respiratory rate is strongly associated with measures of lung function and acute asthma exacerbation severity. An increase of respiratory rate by 1 bpm is associated with a %FEV1 decrease of 1.7%, a %IOS increase of 2.9%, and an AAIRS increase of 0.25 points. This readily available physical sign informs assessment and management of children with acute asthma exacerbations if accurately measured.

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Comparison of Etomidate and Ketamine for Induction during Rapid Sequence Intubation of Adult Trauma Patients

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OBJECTIVE:
Induction doses of etomidate during rapid sequence intubation (RSI) cause transient adrenal dysfunction, but its clinical significance on trauma patients is uncertain. Ketamine has emerged as an alternative for RSI induction. Among adult trauma patients emergently intubated, we compared clinical outcomes among those induced with etomidate and ketamine.

METHODS:
The study entailed a retrospective evaluation of a four-year (January 2011-December 2014) period spanning an institutional protocol switch from etomidate to ketamine as the standard induction agent for adult trauma patients undergoing RSI in the ED of an academic Level I trauma center. The primary outcome was hospital mortality evaluated with multivariable logistic regression adjusted for age, vital signs, and injury severity and mechanism. Secondary outcomes included intensive care unit (ICU)-free days and ventilator-free days (VFD) evaluated with multivariable ordered logistic regression using the same covariates.

RESULTS:
The analysis included 968 patients, including 526 with etomidate and 442 with ketamine. Hospital mortality was 20.4% among patients induced with ketamine compared to 17.3% among those induced with etomidate (aOR: 1.41; 95% CI: 0.92, 2.16). Patients induced with ketamine had similar ICU-free-days (aOR: 0.80; 95% CI: 0.63, 1.00) and VFDs (aOR: 0.96; 95% CI: 0.76, 1.20) as compared to patients induced with etomidate.

CONCLUSIONS::
In this analysis spanning an institutional protocol switch from etomidate to ketamine as the standard RSI induction agent for adult trauma patients, patient-centered outcomes were similar for patients who received etomidate and ketamine.

The Safety and Efficacy of Trimethoprim-Sulfamethoxazole Oral Challenge to De-Label HIV Negative Adults of Sulfa Antimicrobial Allergy

Andrew Abreo, Cosby Stone, Elizabeth Phillips

OBJECTIVES:
Patients who are labeled as sulfa antimicrobial allergic (SAA) with histories of unknown, remote or non-serious isolated cutaneous reactions are common, and this may lead to unnecessary lifelong avoidance. Multiple dose graded challenge or desensitization are guideline-favored approaches that have been studied primarily in HIV-infected patients with SAA associated with trimethoprim-sulfamethoxazole (TMP-SMX).

METHODS:
A retrospective chart review identified 57 SAA non-HIV infected patients who underwent a single (400/80 mg) or two-dose (40/8;400/80 mg) TMP-SMX oral challenge over a 3-year period. Patient demographics, reaction history, and the type of challenge were compared between individuals that were successfully and unsuccessfully de-labeled. A follow-up questionnaire was administered to determine the longer-term effectiveness of sulfa antimicrobial allergy de-labeling.

RESULTS:
Oral challenge was negative without immediate or delayed reactions in 54/57 (95%) patients. Successful label removal was associated with younger age at reaction (32.6±16 vs 54.0±14 years, P=0.03) and longer latency periods since the original reaction (24.8±17 vs 8±7 years, P=0.02). Of those who did not tolerate the challenge, all were female, had an original history of a delayed non-specific mild cutaneous reaction, and experienced mild delayed rash, fever, or myalgia following the challenge. There were no differences between baseline demographics, indication for de-labeling, co-morbidities or immunocompetency between these patients and those successfully de-labeled.

CONCLUSIONS:
his is the first study in non-HIV infected individuals that suggests single or two-dose TMP-SMX oral challenge is a safe and efficacious alternative to desensitization or graded oral challenge, with the additional benefit of successfully de-labeling SAA patients.

The Association of BMI and DM with Survival Among Patients with Metastatic or Castration-Resistant Prostate Cancer

Zachary A. Glazer, Svetlana Avulova, David F. Pinson, Kelvin A. Moses

INTRODUCTION AND OBJECTIVES:
The majority of deaths from prostate cancer are among men with metastatic (mPCa) and/or castration-resistant prostate cancer (CRPC). Long-term outcomes of these patients are generally not well characterized as data from most randomized trials were censored at interim analysis. The objective of our study is to investigate factors associated with survival in a dedicated outpatient clinic. Variables of interest included body mass index (BMI) and comorbidities such as diabetes (DM) at diagnosis.

METHODS:
All patients with mPCa and/or CRPC seen in the Vanderbilt Comprehensive Prostate Cancer Clinic were eligible. Demographic and pathologic information were extracted from the electronic record under IRB-protocol. Overall survival (OS) was estimated using the Kaplan-Meier method. Multivariate analyses using Cox proportional hazard models were also performed.

RESULTS:
Complete clinicopathological data was available for 79 patients. Median follow-up was 7.1 years, 18/79 (22.7%) patients had pre-existing DM and median BMI was 28.5 kg/m2. Disease characteristics included 39 (49.3%) with Gleason 8 or greater on biopsy, median PSA of 14.91, and 20 (25.3%) presenting with M1 disease. Preexisting DM was associated with worse 5-year mortality (22.9% vs. 9.3%, p=0.042). There was a trend towards significant association of BMI >30 kg/m2 with lower 5-year mortality (6.1% vs. 13.9% BMI <30 kg/m2, p=0.052). Multivariate analysis showed BMI is independently associated with OS (HR 0.84 (95% CI 0.71-0.98), p=0.027) correcting for age, DM, stage, PSA, Gleason score and performance status at diagnosis.

CONCLUSIONS:
We show BMI and DM are associated with survival for patients who develop advanced prostate cancer. Furthermore, BMI is significantly associated with survival in this cohort. Our findings should prompt further analysis of the impact of clincopathlogic factors and treatment response in a larger cohort.

Is there a preoperative morphine equianalgesic dose that predicts ability to achieve a clinically meaningful improvement following spine surgery?

Joseph Wick, Ahilan Sivaganesan, Silky Chotai, Kristin Archer, Samuel Posey, Parker Evans,Clinton Devin

OBJECTIVES:
Preoperative opioid use is widespread and associated with worse patient reported outcomes following spine surgery. The purpose of this study was to calculate a threshold preoperative morphine equianalgesic (MEA) dose above which patients have difficulty achieving minimum clinically important difference (MCID) following elective cervical and lumbar spine surgery as measured by Neck Disability Index (NDI) and Oswestry Disability Index (ODI), respectively.

METHODS:
The study included 543 cervical and 1293 lumbar elective surgery patients. NDI and ODI were prospectively collected at the preoperative and 12-month postoperative time points. Opioid use data were collected retrospectively and converted to MEA doses. Combined analysis of cervical and lumbar patients was performed using multivariable logistic regression models, and model parameters were assessed using Markov Chain Monte Carlo methods.

RESULTS: OVERALL
1020 (55.5%) patients used preoperative opioids. A total 61.9% of lumbar and 50.3% of cervical patients achieved MCID. With all patients included in the analysis, achievement of MCID decreased significantly between MEA doses of 25.7-85.8 mg/day. Repeating the analysis after excluding patients with MEA doses ≥ 90 mg/day demonstrated significantly decreased achievement of MCID for doses ≥ 47.8 mg/day, with a 95% confidence interval of 29.0-60.0 mg/day.

CONCLUSION:
Minimum and maximum MEA doses exist, between which increasing opioid dose predicts decreased ability to achieve clinically meaningful improvement following spine surgery. Patients with preoperative MEA dose exceeding 29 mg/day, the lower limit of the 95% confidence interval above which patients exhibit significantly decreased achievement of MCID, are less likely to benefit from surgery and should be considered for preoperative opioid weaning.

Building a Palliative Radiation Oncology Program: From Bedside to B.E.D

Benjamin Li, Mark Stavas, Jonathan Pagan, Sumeeta Varma, Lisa Kachnic

OBJECTIVES:

A growing body of evidence supports the integration of palliative care with standard cancer treatments. The advance of palliative care invites innovative collaborative care delivery models. We outline the impetus for change at VUMC and the inception of the inpatient Palliative Radiation Oncology Service at Vanderbilt (inPROV). We describe the structure and benefits of this service and seek to bring to light clinical value we can provide beyond dose and fractionation.

METHODS:

A radiation oncologist began the service after dedicating 6 months of inpatient training with the palliative care team. The palliative radiation oncologist provides three main services: prognosis, goals of care, and treatment planning. A dedicated attending-resident-nurse team oversees care of 400 inpatient consultations annually. In conjunction with morning rounds and daily consultations, care plans are developed with the primary oncology and palliative care services.

RESULTS:

During the first six months of inception, inpatient referral numbers increased by 15%. Goals of care and prognosis were documented in 65% of Radiation Oncology consult notes and short course radiotherapy ($\leq$ 5 fractions) increased from 30% to 70%. Palliative care was involved alongside radiation oncology in 60% of inpatient palliative radiation cases. Bedside rounds allowed close monitoring and adjustments in radiation if warranted. When patients declined treatment, they were discussed in a multidisciplinary fashion and often transitioned to the palliative care unit where a timely referral to hospice was arranged. Participation in family meetings allowed us to incorporate specific details about patient goals and prognosis into the radiation plan. A strong inpatient presence created new referral lines.

CONCLUSIONS:

The inPROV service improves goals of care conversations and informed decision making. Short-course radiotherapy to hospitalized patients aids treatment before hospice, timely discharge and appropriate transitions of care. Looking forward, potential benefits of this program to hospitals and clinicians are cost savings, improved patient and staff satisfaction, improved efficiency in handling complex interactions between patients and families, and enhanced reputation amongst referring providers. We hope to see Radiation Oncologists redefine their role as providers across the continuum of cancer care as we move away from fee-for-service payment and place further emphasis on supportive and palliative care services at the end of life.

Can Epiphyseal Unstable SCFE Be Reduced By Closed Reduction With Minimal AVN?

Emilie Amaro, Jeffrey E. Martus, MD, Megan E. Mignemi, MD, Gregory Mencio, MD, Jonathan G. Schoenecker, MD, PhD

OBJECTIVES:

Slipped capital femoral epiphysis (SCFE) evokes pathoanatomical changes to the proximal femur which can lead to osteoarthritis (OA). SCFE osteoarthritis is predominantly caused by i) external rotation deformity of the distal femur or ii) avascular necrosis of the epiphysis. To prevent OA, various treatment algorithms have been proposed with the intent of reducing the residual deformity while avoiding avascular necrosis. The vascular supply of the proximal femur creates a challenging scenario in which procedures designed to address SCFE place the lateral epiphyseal structures at risk. Injury to these vessels is significantly greater in an unstable SCFE where the epiphysis is acutely fractured from the metaphysis. In closed treatment protocols, it is suggested to obtain an incidental reduction. However, the angular correction which decreases the risk of an OA evoking deformity but does not cause AVN is unknown. Meta-analysis indicates that patients are at low-risk for OA with a preoperative Southwick slip angle of less than 35°. The purpose of this abstract is to determine if reduction of epiphyseal unstable SCFE to a goal Southwick angle of 35 is associated with AVN.

METHODS:

277 consecutive cases of slipped capital femoral epiphysis were identified from January 2007 to April 2016. The Southwick angle was determined for pre-operative and post-operative radiographs. A change in Southwick angle greater than 15° and patients with Loder unstable slips and a reduction noted in the operative report were classified as epiphyseal unstable. Osteonecrosis was evaluated on postoperative radiographs by femoral head collapse.

RESULTS:

There were 38 cases of unstable SCFEs and 239 cases of stable SCFE. Avascular necrosis occurred in 3 hips overall (1.1%). All cases of AVN occurred in the epiphyseal unstable group (7.9%). 34 total unstable slips were reduced to less than 35° (89.4%). The rate of AVN in unstable slips reduced to 35° or less was 8.8%. All cases of AVN were reduced to a Southwick angle of less than 30°. The average change in Southwick angle following reduction was 25.2° in the patients who developed AVN versus 25.5° in all patients with epiphyseal unstable slips. The average post residual deformity of all unstable slips was 25.3°, and the average post residual deformity of all stable slips was 23.2°.

CONCLUSIONS:

An epiphyseal unstable slipped capital femoral epiphysis may be treated with closed reduc-

IMPACT OF COMPLICATIONS ON HOSPITAL-FREE DAYS AFTER HEPATIC SURGERY

Jesse Wright, MD, Amelia Maiga, MD, Gretchen Edwards, MD, Kamran Idrees, MD

OBJECTIVE:
Traditional post-operative metrics, i.e., length of stay (LOS) and readmission rates, individually do not fully quantify the totality of deviation from normalcy for patients. In this study, we utilize a novel measure, termed Hospital-Free Days (HFD), which incorporates post-operative outcomes into number of days patients spend outside of any healthcare facility after hepatic resection (HR).

METHODS:
463 HR patients over a 7-year period were retrospectively reviewed. Patient demographics, ASA class, Elixhauser Comorbidity Index (ECI), Surgical Apgar Score (SAS), and post-operative major complications (PMC) during index hospitalization were evaluated. HFD in the 90 days from surgery were calculated by subtracting hospital LOS, readmission days, and days spent in rehabilitation/ nursing facilities. Multivariable analysis (MVA) was utilized to examine association with HFD.

RESULTS:
The median HFD after HR was 85 days (see table). Patients without PMC had a median HFD of 85 days compared to 78 days with a single PMC and 72 days for those with multiple PMC ($p<0.01$). Age ($p=0.04$), lower SAS ($p<0.01$), and PMC ($p<0.01$) were predictive of the lower HFD on MVA. In patients without PMC during the index hospitalization, SAS ($p=0.0007$) and ECI ($p=0.02$) were predictive of lower HFD.

CONCLUSIONS:
HFD is an intuitive, singular, and clinically meaningful endpoint to quantify the true amount of time a patient spends away from home in healthcare facilities. Complications have a significant impact on lowering HFD following HR. HFD is a novel, patient-centric metric which allows providers to better establish expectations for prospective patients and serves as a surrogate measure of healthcare resource utilization.

Thank You
for your participation
and attendance at the
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